

# Directions in Psychiatry

VOLUME 40 \* LESSONS 1 – 20 IN THIS VOLUME

CATEGORY 1

CME

VOLUME  
40

A HATHERLEIGH  
CME JOURNAL

## CME LESSON 1

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Syed Z. Iqbal, MD; Benjamin T. Li, MD;  
Lubna Khawaja MD; Asim A. Shah, MD

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### Human Trafficking

Donald Kushon, MD; Brandi J. Stewart, PsyD

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Daniel C. Marston, PhD, ABPP

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William A. Ramsey, PhD

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Aviv Weinstein, PhD

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Stephanie Hernandez, DO; Sonia Popatia, MD; Burhan Khan, MD; Hai Le, MD; Asim Shah, MD; Edore Onigu-Otite, MD

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Mujeeb U. Shad, MD, MSCS

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Mujeeb U. Shad, MD, MSCS

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Smita Saraykar, MD, MPH; Asim A. Shah, MD; Anis Rashid, MD

# Directions in Psychiatry

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The Hatherleigh Company, Ltd. designates this activity for a maximum of **40 AMA PRA Category 1 Credits**. Physicians should only claim credit commensurate with the extent of their participation in the activity.

The Hatherleigh Company, Ltd., is accredited by the *Accreditation Council for Continuing Medical Education* (ACCME) to provide continuing medical education for physicians.

The activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) by The Hatherleigh Company, Ltd.

## CME Information Page

**Overall Objective:** The objective of this continuing medical education program is to present participants with an expanded clinical skill set and raised awareness of clinically relevant issues in their profession. They will review key diagnostic criteria, cutting-edge treatment strategies, and practice points they can implement in the challenges of daily practice while providing evidence-based care to patients and clients suffering psychiatric and comorbid medical disorders. The expected outcomes include an increase in knowledge, competence, professionalism, and performance.

**Target Audience:** The primary target audience for this program includes, but is not limited to: psychiatrists, primary care physicians, psychiatric nurses, pharmacists, clinical psychologists, and social workers. Clinicians who have caseloads composed significantly of individuals with psychiatric disorders, and comorbid medical illnesses will find this course particularly useful.

**Duration of CME Status:** *Directions in Psychiatry* begins April 10 2020, and the preliminary expiration date is December 31, 2024. At that point, the Hatherleigh Medical Director and the editorial staff will review the CME material to determine whether the program continues to be consistent with current accreditation guidelines and standards of care. A determination will be made as to whether the program can be used to earn full CME credit after that date.

### Conflict of Interest Disclosure Policy

Faculty members were selected for their expertise and, most often, on the strength of their presentations from previously published papers or symposia. Hatherleigh Medical Education staff, contributing program faculty, and advisory board members, must disclose their relationships (also on behalf of their immediate family members), if they exist, with commercial and/or pharmaceutical companies prior to Hatherleigh Medical Education's distribution and publication of their contributions to Hatherleigh Medical Education CME programs. Any aforementioned relationship that poses a potential conflict of interest will be resolved prior to publication/distribution of the CME activity, and proper notification disclosed to program participants prior to the start of the activity.

Disclosure of any off-label medication usage for indications that are not currently approved by the Federal Drug Administration discussed within the CME content will be disclosed within the lesson.

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### How the Program Works \* Needs Assessment \* Evaluation

*Directions in Psychiatry* includes 78 CME questions focused on key learning points within the lessons. The answers to each question must be recorded on the supplied quiz response form or via the response form at Hatherleigh's website. All 78 questions should be answered on that form or online and submitted to Hatherleigh via the website, fax, e-mail, or regular mail for scoring. On average, participants will take up to 40 hours or more to complete this Hatherleigh CME program (i.e., reading and studying the lessons and answering the CME questions). Participants must complete and return the program assessment form which is included with each program. Participants can submit these forms with the quiz response form. Upon successful completion of the program (at least 75% correct), Hatherleigh will send participants a certificate of achievement worth 40 credit hours and a score report.

This CME program was created from a learning needs assessment of participants in previous CME programs, who are virtually all physicians and other mental health clinicians. Their expressed needs were assessed by the Medical Director, the Program Advisory Board members, and editorial staff in the development of this curriculum.

### About The Hatherleigh Company, Ltd. \* Contact Information

The Hatherleigh Company, Ltd. has published continuing medical education programs in psychiatry for more than 35 years. Dr. Frederic Flach, the company's founder, created *Directions in Psychiatry*, Hatherleigh's flagship CME program to ensure the presence of a truly independent and highly professional perspective on issues of immediate clinical import—ranging from pharmacotherapy to psychotherapy, from technical information to ethical priorities. We look forward to hearing from all subscribers via e-mail at: [support@hatherleigh.com](mailto:support@hatherleigh.com). For more information about Hatherleigh CME programs, visit our website at [www.hatherleigh.com](http://www.hatherleigh.com), or call: 1-800-367-2550.

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# Learning Objectives Evaluation Form

Directions in Psychiatry, Vol. 40

Full Name: \_\_\_\_\_ Date: \_\_\_\_\_ Customer No: \_\_\_\_\_

Please complete this evaluation form to help us assess how the continuing medication education lessons achieve the intended learning objectives. To what extent were the learning objectives achieved?

3 = good/high 2 = satisfactory/average 1 = poor/low

As a result of completing this course, participants will be able to:

## CME Lesson 1: Vaping and Its Effect on Physical Health

- \_\_\_\_\_ describe vaping, and the products used for vaping.
- \_\_\_\_\_ describe how vaping serves as a gateway toward addiction to nicotine and other drugs.

## CME Lesson 2: Human Trafficking

- \_\_\_\_\_ identify evidence of labor and sex trafficking in patients who come for treatment.
- \_\_\_\_\_ delineate the healthcare, socioeconomic, and legal needs of each victim.

## CME Lesson 3: Behavior Therapy for the Treatment of Dementia in Elderly Psychiatric Patients

- \_\_\_\_\_ list major behavioral issues associated with dementia and major neurocognitive disorders.
- \_\_\_\_\_ incorporate behavior therapy concepts into helping caregivers assisting individuals with dementia.

## CME Lesson 4: You Too Can Do Marital Therapy: Expanding Psychiatric Practice to Include Marital Therapy

- \_\_\_\_\_ discuss the relationship between many of the symptom complexes presented by their patients and an unhappy marital relationship.
- \_\_\_\_\_ explain the dynamics of successful and unsuccessful marital relationships.

## CME Lesson 5: Prevention of Mental Health Disorders Using Internet- and Mobile-Based Interventions: A Narrative Review and Recommendations for Future Research, Part 1: An Overview

- \_\_\_\_\_ review available evidence for the effectiveness of *internet- and mobile-based interventions* (IMIs).
- \_\_\_\_\_ recognize the challenges and need for future research using this modality in the field.

## CME Lesson 6: Telepsychiatry in the Time of COVID-19

- \_\_\_\_\_ delineate the advantages of using telehealth/telepsychiatry as means of healthcare delivery in COVID-19 infection settings.

- \_\_\_\_\_ describe recent changes in policies regarding reimbursement, technology use, and licensure at the state and federal level to facilitate the use of telehealth in the United States.

## CME Lesson 7: You Too Can Do Marital Therapy: Expanding Psychiatric Practice to Include Marital Therapy, Part 2

- \_\_\_\_\_ delineate the basic principles of marital therapy.
- \_\_\_\_\_ explain the difficulty in determining whether a marriage is sufficiently troubled to require intervention.

## CME Lesson 8: Clinically Relevant Psychotropic Drug Interactions in the Geriatric Population

- \_\_\_\_\_ identify adverse interactions among psychotropic drugs and other substances that are most likely to be seen in U.S. geriatric populations.
- \_\_\_\_\_ describe methods of diagnosis, treatment, and prevention for these disorders in older individuals.

## CME Lesson 9: Prevention of Mental Health Disorders Using Internet- and Mobile-Based Interventions: A Narrative Review and Recommendations for Future Research, Part 2

- \_\_\_\_\_ review available evidence for the effectiveness of *internet- and mobile-based interventions* (IMIs).
- \_\_\_\_\_ review how they may aid in the prevention of mental health disorders, and recognize the challenges and need for future research using this modality in the field.

## CME Lesson 10: Psychological Impact of Hurricane Harvey on Patients with Cancer

- \_\_\_\_\_ describe the impact of direct versus indirect exposure to a natural disaster (Hurricane Harvey) on the mental health of patients with cancer.
- \_\_\_\_\_ identify factors that may influence the severity of psychological symptoms that arise in such persons as a result of a natural disaster.

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3 = good/high 2 = satisfactory/average 1 = poor/low

As a result of completing this course, participants will be able to:

**CME Lesson 11: Review of Suicide Risk in the United States During the COVID-19 Pandemic**

- \_\_\_\_\_ identify risk factors for suicide.
- \_\_\_\_\_ explain the origin of COVID-19 and how the current pandemic unfolded

**CME Lesson 12: Counseling Individuals Who Engage in Nonsuicidal Self-Injury**

- \_\_\_\_\_ describe the etiology of NSSI.
- \_\_\_\_\_ identify the contingencies necessary to maintain NSSI behaviors.

**CME Lesson 13: The Association Between Excessive Use of Smartphones Cognition, Emotion, and the Brain**

- \_\_\_\_\_ define excessive use of digital media for children and adolescents, as reported in recent literature.
- \_\_\_\_\_ explain the effect of excessive smartphone use on human behavior and mental health.

**CME Lesson 14: Pediatric Anger Management**

- \_\_\_\_\_ describe pediatric anger and irritability.
- \_\_\_\_\_ discuss relevant abnormalities in brain structure and function.

**CME Lesson 15: Sports-Related Concussions in High School Athletes**

- \_\_\_\_\_ define a sports-related concussion (SRC).
- \_\_\_\_\_ describe the symptoms of concussion, discuss the mechanisms involved in concussion in adolescents.

**CME Lesson 16: A Review of the Impact of Wearing Masks on COVID-19 Transmission and the Psychology behind Resistance to Wearing Masks**

- \_\_\_\_\_ recognize the benefits of wearing masks in slowing down and preventing the spread of *coronavirus disease 2019* (COVID-19).
- \_\_\_\_\_ recognize the psychological factors associated with resistance to wearing masks.

**CME Lesson 17: Neuropsychiatric Complications of COVID-19**

- \_\_\_\_\_ describe the effects of COVID-19 on the central nervous system.
- \_\_\_\_\_ delineate the neuropsychiatric manifestations during previous viral epidemics and pandemics.

**CME Lesson 18: A Review of Psychopharmacotherapy for Geriatric Depression, Part 1**

- \_\_\_\_\_ identify available antidepressants to manage geriatric depression.
- \_\_\_\_\_ identify various options for selecting antidepressants in a high-risk population known for suboptimal response, treatment resistance, increased vulnerability from adverse effects, age-related changes in drug disposition, and high prevalence of polypharmacy.

**CME Lesson 19: A Review of Psychopharmacotherapy for Geriatric Depression, Part 2**

- \_\_\_\_\_ review evidence-based advantages and disadvantages regarding the efficacy and tolerability of antidepressants in older adults.
- \_\_\_\_\_ identify augmentation strategies in managing treatment-resistant depression in older adults.

**CME Lesson 20: Psychiatric Consultations from an Oncology Perspective: Medical Students' Clerkship Experience at a Comprehensive Cancer Center**

- \_\_\_\_\_ view the unique experience of medical students going through psychiatric oncology clerkship.
- \_\_\_\_\_ delineate medical students' learning curve on the six competency domains outlined by the Accreditation Council of Graduate Medical Education.



# Accreditation Standards: IOM; ACGME / ABMS Competencies

## Directions in Psychiatry, Vol. 40

In accordance with accreditation guidelines set forth by the ACCME, we encourage you to review the following areas of core competency and desirable physician attributes endorsed by the *Institute of Medicine* (IOM); *The Accreditation Council for Graduate Medical Education* (ACGME) / *American Board of Medical Specialties* (ABMS). Each CME lesson in this activity addresses at least one or more of the following attributes in each of the three areas of competency as listed below.

### Institute of Medicine Core Competencies:

**Provide Patient-Centered Care:** Identify, respect, and care about patients' differences, values, preferences, and expressed needs; relieve pain and suffering; coordinate continuous care; listen to, clearly inform, communicate with, and educate patients; share decision-making and management; and continuously advocate disease prevention, wellness, and promotion of healthy lifestyles, including a focus on population health.

**Work in Interdisciplinary Teams:** Cooperate, collaborate, communicate, and integrate care in teams to ensure that care is continuous and reliable.

**Employ Evidence-Based Practice:** Integrate best research with clinical expertise and patient values for optimum care, and participate in learning and research activities to the extent feasible.

**Apply Quality Improvement:** Identify errors and hazards in care; understand and implement basic safety design principles, such as standardization and simplification; continually understand and measure quality of care in terms of structure, process, and outcomes in relation to patient and community needs; and design and test interventions to change processes and systems of care, with the objective of improving quality.

**Utilize Informatics:** Communicate, manage, knowledge, mitigate error, and support decision-making using Information technology.

### ACGME / ABMS Competencies:

**Patient Care and Procedural Skills** demonstrate compassionate, appropriate, and effective care for the treatment of health problems and promote health.

**Medical Knowledge** about established and evolving biomedical, clinical, and cognate (e.g. epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

**Practice-Based Learning and Improvement** that involves investigation and evaluation of their own patient care, appraisal and assimilation of scientific evidence, and improvements in patient care.

**Interpersonal and Communication Skills** that result in effective information exchange and teaming with patients, their families, and other health professionals.

**Professionalism** as manifested through a commitment to carrying out professional responsibilities, adherence to ethical principles, and sensitivity to a diverse patient population.

**Systems-based Practice** demonstrates awareness of and responsibility to the larger context and system of health care as well as the ability to call on system resources to provide care that is of optimal value.

**Part I-Professional Standing:** Medical specialists must hold a valid, unrestricted medical license in at least one state or jurisdiction in the USA, its territories or Canada.

**Part II-Lifelong Learning and Self-Assessment:** Physicians participate in educational and self-assessment programs that meet specialty-specific standards that are set by their member board.

**Part III-Cognitive Expertise:** They demonstrate, through formalized examination, that they have the fundamental, practice-related and practice environment-related knowledge to provide quality care in their specialty.

**Part IV-Practice Performance Assessment:** They are evaluated in their clinical practice according to specialty-specific standards for patient care. They are asked to demonstrate that they can assess the quality of care they provide compared to peers and national benchmarks and then apply the best evidence or consensus recommendations to improve that care using follow-up assessments.

| Directions in Psychiatry, Vol. 40 * Part 1 |          |          |          |          |          |
|--|----------|----------|----------|----------|----------|
| IOM Core Competencies                      | Lesson 1 | Lesson 2 | Lesson 3 | Lesson 4 | Lesson 5 |
| Provide patient-centered care              | X        | X        | X        | X        |          |
| Work in interdisciplinary teams            |          | X        |          |          |          |
| Employ evidence-base practice              |          |          | X        | X        | X        |
| Apply quality improvement                  |          | X        |          |          | X        |
| Utilize informatics                        | X        |          | X        |          | X        |
| ACGME Competencies                         |          |          |          |          |          |
| Patient care                               | X        | X        | X        | X        |          |
| Medical knowledge                          | X        | X        |          | X        | X        |
| Practice-based learning and improvement    | X        |          | X        | X        |          |
| Interpersonal and communication skills     |          |          | X        | X        |          |
| Professionalism                            |          |          |          | X        |          |
| System-based practice                      |          | X        | X        |          | X        |
| ABMS MOC Competencies                      |          |          |          |          |          |
| Professional standing                      |          |          |          |          |          |
| Commitment to lifelong learning            | X        | X        | X        |          |          |
| Cognitive expertise                        |          | X        |          | X        | X        |
| Performance in practice                    |          |          | X        | X        |          |

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| Directions in Psychiatry, Vol. 40 * Part 2 |          |          |          |          |           |
|--|----------|----------|----------|----------|-----------|
| IOM Core Competencies                      | Lesson 6 | Lesson 7 | Lesson 8 | Lesson 9 | Lesson 10 |
| Provide patient-centered care              |          | X        |          |          |           |
| Work in interdisciplinary teams            |          |          |          |          | X         |
| Employ evidence-base practice              | X        | X        | X        | X        |           |
| Apply quality improvement                  | X        |          | X        | X        |           |
| Utilize informatics                        | X        |          | X        | X        |           |
| ACGME Competencies                         |          |          |          |          |           |
| Patient care                               |          | X        | X        |          | X         |
| Medical knowledge                          | X        | X        | X        | X        |           |
| Practice-based learning and improvement    |          | X        |          |          |           |
| Interpersonal and communication skills     |          | X        |          |          | X         |
| Professionalism                            | X        | X        | X        |          |           |
| System-based practice                      | X        |          |          | X        | X         |
| ABMS MOC Competencies                      |          |          |          |          |           |
| Professional standing                      | X        |          |          |          |           |
| Commitment to lifelong learning            | X        |          | X        |          | X         |
| Cognitive expertise                        | X        | X        |          | X        |           |
| Performance in practice                    | X        | X        | X        |          |           |

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**Part III-Cognitive Expertise:** They demonstrate, through formalized examination, that they have the fundamental, practice-related and practice environment-related knowledge to provide quality care in their specialty.

**Part IV-Practice Performance Assessment:** They are evaluated in their clinical practice according to specialty-specific standards for patient care. They are asked to demonstrate that they can assess the quality of care they provide compared to peers and national benchmarks and then apply the best evidence or consensus recommendations to improve that care using follow-up assessments.

| Directions in Psychiatry, Vol. 40 * Part 3 |           |           |           |           |           |
|--|-----------|-----------|-----------|-----------|-----------|
| IOM Core Competencies                      | Lesson 11 | Lesson 12 | Lesson 13 | Lesson 14 | Lesson 15 |
| Provide patient-centered care              | X         | X         |           | X         | X         |
| Work in interdisciplinary teams            |           |           |           |           |           |
| Employ evidence-base practice              |           | X         | X         | X         | X         |
| Apply quality improvement                  |           |           | X         | X         |           |
| Utilize informatics                        |           |           | X         |           |           |
| ACGME Competencies                         |           |           |           |           |           |
| Patient care                               |           |           |           | X         | X         |
| Medical knowledge                          | X         |           | X         | X         | X         |
| Practice-based learning and improvement    | X         |           |           | X         |           |
| Interpersonal and communication skills     |           | X         |           |           |           |
| Professionalism                            |           |           | X         |           |           |
| System-based practice                      | X         |           |           | X         |           |
| ABMS MOC Competencies                      |           |           |           |           |           |
| Professional standing                      |           |           |           |           |           |
| Commitment to lifelong learning            | X         |           |           | X         | X         |
| Cognitive expertise                        |           |           | X         |           |           |
| Performance in practice                    |           | X         |           |           |           |



# Accreditation Standards: IOM; ACGME / ABMS Competencies

## Directions in Psychiatry, Vol. 40

In accordance with accreditation guidelines set forth by the ACCME, we encourage you to review the following areas of core competency and desirable physician attributes endorsed by the *Institute of Medicine (IOM)*; *The Accreditation Council for Graduate Medical Education (ACGME)* / *American Board of Medical Specialties (ABMS)*. Each CME lesson in this activity addresses at least one or more of the following attributes in each of the three areas of competency as listed below.

### Institute of Medicine Core Competencies:

**Provide Patient-Centered Care:** Identify, respect, and care about patients' differences, values, preferences, and expressed needs; relieve pain and suffering; coordinate continuous care; listen to, clearly inform, communicate with, and educate patients; share decision-making and management; and continuously advocate disease prevention, wellness, and promotion of healthy lifestyles, including a focus on population health.

**Work in Interdisciplinary Teams:** Cooperate, collaborate, communicate, and integrate care in teams to ensure that care is continuous and reliable.

**Employ Evidence-Based Practice:** Integrate best research with clinical expertise and patient values for optimum care, and participate in learning and research activities to the extent feasible.

**Apply Quality Improvement:** Identify errors and hazards in care; understand and implement basic safety design principles, such as standardization and simplification; continually understand and measure quality of care in terms of structure, process, and outcomes in relation to patient and community needs; and design and test interventions to change processes and systems of care, with the objective of improving quality.

**Utilize Informatics:** Communicate, manage, knowledge, mitigate error, and support decision-making using Information technology.

### ACGME / ABMS Competencies:

**Patient Care and Procedural Skills** demonstrate compassionate, appropriate, and effective care for the treatment of health problems and promote health.

**Medical Knowledge** about established and evolving biomedical, clinical, and cognate (e.g. epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.

**Practice-Based Learning and Improvement** that involves investigation and evaluation of their own patient care, appraisal and assimilation of scientific evidence, and improvements in patient care.

**Interpersonal and Communication Skills** that result in effective information exchange and teaming with patients, their families, and other health professionals.

**Professionalism** as manifested through a commitment to carrying out professional responsibilities, adherence to ethical principles, and sensitivity to a diverse patient population.

**Systems-based Practice** demonstrates awareness of and responsibility to the larger context and system of health care as well as the ability to call on system resources to provide care that is of optimal value.

**Part I-Professional Standing:** Medical specialists must hold a valid, unrestricted medical license in at least one state or jurisdiction in the USA, its territories or Canada.

**Part II-Lifelong Learning and Self-Assessment:** Physicians participate in educational and self-assessment programs that meet specialty-specific standards that are set by their member board.

**Part III-Cognitive Expertise:** They demonstrate, through formalized examination, that they have the fundamental, practice-related and practice environment-related knowledge to provide quality care in their specialty.

**Part IV-Practice Performance Assessment:** They are evaluated in their clinical practice according to specialty-specific standards for patient care. They are asked to demonstrate that they can assess the quality of care they provide compared to peers and national benchmarks and then apply the best evidence or consensus recommendations to improve that care using follow-up assessments.

| Directions in Psychiatry, Vol. 40 * Part 4 |           |           |           |           |           |
|--|-----------|-----------|-----------|-----------|-----------|
| IOM Core Competencies                      | Lesson 16 | Lesson 17 | Lesson 18 | Lesson 19 | Lesson 20 |
| Provide patient-centered care              | X         | X         | X         | X         |           |
| Work in interdisciplinary teams            |           |           |           |           |           |
| Employ evidence-base practice              | X         | X         | X         | X         |           |
| Apply quality improvement                  | X         | X         | X         | X         | X         |
| Utilize informatics                        |           |           | X         | X         |           |
| ACGME Competencies                         |           |           |           |           |           |
| Patient care                               | X         | X         | X         | X         | X         |
| Medical knowledge                          | X         | X         | X         | X         | X         |
| Practice-based learning and improvement    | X         |           | X         | X         | X         |
| Interpersonal and communication skills     |           |           |           |           | X         |
| Professionalism                            | X         | X         | X         | X         | X         |
| System-based practice                      | X         | X         | X         | X         |           |
| ABMS MOC Competencies                      |           |           |           |           |           |
| Professional standing                      |           |           |           |           |           |
| Commitment to lifelong learning            | X         | X         |           |           | X         |
| Cognitive expertise                        |           |           | X         | X         |           |
| Performance in practice                    |           | X         |           |           |           |

# Directions in Psychiatry

## Breakdown of Tested Areas for Volume 40

In an effort to help program participants determine their personal learning plans and address any gaps in their knowledge, every volume of *Directions in Psychiatry* presents lesson categorized into tested areas, listed below. To determine your score in any tested area, review the answer sheet included with your certificate. Add your correct answers for the questions listed in each tested area and compare it to the total possible number of correct answers, listed next to each tested area. Below is an example.

|           | Question | Your response | Correct response | You received                                |
|-----------|----------|---------------|------------------|---|
|           | 1        | D             | ⇔ A              |   |
| Lesson 1  | 2        | B             | B                | 3/4   |
| Questions | 3        | C             | C                | 3 out of 4 correct questions for the lesson |
|           | 4        | A             | A                |   |

| Topic Areas<br>Lesson numbers and possible correct questions                          | Topic Areas<br>Lesson numbers and possible correct question                         |
|---|---|
| <b>Addictions:</b><br>Lesson: 1, 13      x/8  | <b>Mood Disorders:</b><br>Lesson: 5, 18, 19      x/12                               |
| <b>Anxiety Disorders:</b><br>Lesson: 9, 10      x/8                                   | <b>Neurobiology:</b><br>Lesson: 15, 17      x/8                                     |
| <b>Child/Pediatric, Adolescent Psychiatry:</b><br>Lesson: 9, 12, 13, 14, 15      x/20 | <b>Pain/Palliative Care:</b><br>Lesson: NA      x/0                                 |
| <b>Cognitive Disorders:</b><br>Lesson: 3, 13, 15, 17, 19      x/20                    | <b>Personality Disorders:</b><br>Lesson: NA      x/4                                |
| <b>Cultural Competence:</b><br>Lesson: NA      x/0                                    | <b>Professional Standards:</b><br>Lesson: 4, 7, 20      x/12                        |
| <b>Developmental Disorders:</b><br>Lesson: 14      x/4                                | <b>Psychopharmacology:</b><br>Lesson: 8, 14, 18, 19      x/16                       |
| <b>Dissociative Disorders:</b><br>Lesson: NA      x/0                                 | <b>Psychotic Disorders:</b><br>Lesson: 17      x/4                                  |
| <b>Domestic Violence:</b><br>Lesson: 2      x/4                                       | <b>Psychosocial Treatment / Psychotherapy</b><br>Lesson: 3, 12, 14      x/12        |
| <b>Eating Disorders:</b><br>Lesson: NA      x/0                                       | <b>PTSD/Trauma/Disaster Psychiatry:</b><br>Lesson: 10, 17      x/8                  |
| <b>Ethical Issues:</b><br>Lesson: NA      x/0   | <b>Sexuality: Dysfunction, Gender, Paraphilia, Disorders:</b><br>Lesson: 2      x/4 |
| <b>Family Psychiatry:</b><br>Lesson: 4, 7, 14, 15      x/16                           | <b>Sleep Disorders:</b><br>Lesson: 13      x/4                                      |
| <b>Geriatrics:</b><br>Lesson: 3, 8, 18, 19      x/16                                  | <b>Somatoform Disorders:</b><br>Lesson: NA      x/0                                 |
| <b>HIV/AIDS/Infectious Disease:</b><br>Lesson: NA      x/0                            | <b>Suicide &amp; Suicide Prevention:</b><br>Lesson: 11, 12      x/8                 |
| <b>Impulse Control Disorders:</b><br>Lesson: NA      x/0                              | <b>Technology in Psychiatry:</b><br>Lesson: 5, 6, 9, 13      x/16                   |
| <b>Malpractice Risk/Forensics:</b><br>Lesson: 11      x/4                             | <b>Women's Issues:</b><br>Lesson: 2      x/4  |
| <b>Medical Errors:</b><br>Lesson: 18, 19      x/8                                     | <b>Other Clinical Issues:</b><br>Lesson: 16      x/4                                |

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*In Memory of*  
**Leah J. Dickstein, MD**

**August 17, 1934 – December 16, 2019**

*With gratitude, we remember Dr. Leah Joan Dickstein who has served on the editorial advisory board of **Directions in Psychiatry** for more than two decades and most recently as Senior Content Advisor. Her dedication to Hatherleigh Medical Education has been integral to the continuity and development of Hatherleigh's continuing medical education programs.*

Dr. Dickstein, 85, former president of the *American Medical Women's Association* (AMWA), Vice President of the American Psychiatric Association, and Founder and President of the *Association of Women Psychiatrists* (AWP) passed away after a short illness on December 16, 2019 in Cambridge, MA.

Born on August 17, 1934, in Brooklyn, NY, to William David Chernoble, an immigrant from Russia and printing press operator, and Sadie Rebecca Engelman, a teacher, she developed an early interest in mental health as she helped care for her own mother who struggled with depression, and her younger sister Renee, during her father's service in the Navy during World War II, which included almost three years without any communication. Leah graduated at 16 from Erasmus Hall High School. At Brooklyn College, she was told she had no scientific ability and should not consider attending medical school. Instead, Leah earned MA in teaching. She married Herbert Dickstein, another Brooklyn native, in 1955, and helped him complete medical school in Ghent, Belgium, which he attended due to restrictive quotas on Jews in U.S. medical schools. When they returned to the U.S., Leah spent seven years as a sixth-grade teacher at PS 110 in Greenpoint, Brooklyn, NY and had her first son, Stuart.

It was then Herbert's turn to help realize Leah's dream of becoming a physician, as Leah completed premedical courses at Queens College, NY. The family moved to Louisville because Leah was accepted at the University of Louisville School of Medicine. Leah graduated in 1970 as one of only six women in a class of over 120.

"Dr. D" as she became known to her patients and students then spent the next 37 years in Louisville as a Psychiatrist, Professor, and Administrator at the medical school, where she treated, mentored, and befriended thousands of medical students, medical residents, faculty, staff, and others. She served as Associate Dean of Faculty and Student Advocacy, Associate Dean for Student Affairs, and Director of the Division of Attitudinal and Behavioral Medicine and Arts in Medicine Program. Decades of medical school graduates will remember

---

her as the Co-founder and Director of the Health Awareness Workshop, an innovative weeklong orientation event that sought to develop physician physical and mental health before it was en vogue. She had two more sons, Daniel and Steven, and the entire family helped in Dr. D's nationally recognized program that taught generations of future physicians how to maintain their humanity during their careers. As a clinician, Dr. D was available day or night, giving out the family's home number to all patients in an era when there were no cell phones.

Leah was a regional and national leader, including the above roles. She loved attending professional meetings nationally and worldwide, developing a large cadre of physician women leaders whom she helped break the "Lexan ceiling"—a term coined by her husband, Herbert, to describe the barriers that women faced which were even harder than glass. She also helped mentor men, too, as she felt that "men of good conscience"—were essential to stand up for what was right, regardless of if it was to advocate for women or for men.

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# Vaping and Its Effect on Physical Health

Syed Z. Iqbal, MD; Benjamin T. Li, MD;  
Lubna Khawaja MD; Asim A. Shah, MD

*No commercial support was used in the development of this continuing medical education lesson.*

**KEY WORDS:** Vaping • E-cigarettes • Dabbing • Addiction • Nicotine • ENDS • EVALI • Lung injury • Vitamin E acetate

**LEARNING OBJECTIVES:** Upon completion of this lesson, the clinician will be able to: (1) describe vaping, and the products used for vaping; (2) describe how vaping serves as a gateway toward addiction to nicotine and other drugs; (3) discuss the mechanisms involved in vaping that can lead to lung injury and exacerbate cardiovascular disease; (4) identify cost factors associated with vaping; and (5) delineate FDA regulations designed to control vaping, particularly among minors and young adults.

**LESSON ABSTRACT:** This review highlights the increasing popularity of vaping among minors and young adults in the United States and the physiological and psychosocial risks associated with it. It provides detailed information about vaping devices, including the nicknames under which they are sold and how they function. The authors explain the relationship between vaping and nicotine/drug addiction and elaborate on the mechanisms by which vaping contributes to injuries to the lungs and cardiovascular system. It also details the limitations of legislation that have been proposed or passed in an attempt to curtail the use of the products, especially by minors and young adults.

**COMPETENCY STATEMENT:** This lesson addresses the gaps in learning in the areas of knowledge, patient care, and practice-based learning related to the impact of vaping on physical health. Many clinicians lack understanding of how vaping can be harmful to physical health and that it can lead to addiction. Upon the conclusion of this lesson, readers will have a better understanding of the process of vaping, including the devices used, their function, and knowledge about the e-liquids. They will gain an understanding of how vaping can be related to fatal lung injuries. This lesson also gives readers a perspective about FDA recommended smoking cessation therapies, the role of vaping in addiction, and its cost implication.

## Introduction

**Vaping is the inhalation of vapors generated by heating liquid in a vaping device.<sup>11</sup> The liquid in these devices—known as e-liquid—usually contains nicotine and/or flavoring agents, but may also contain chemicals that are added by the user or released through the heating process.<sup>2</sup>** Most of the e-cigarettes contain nicotine, whereas THC, the psychoactive ingredient in marijuana or CBD oil, which is a cannabis-derived liquid, are also used by this method.<sup>1</sup> Devices such as e-cigarettes, e-vaporizers, and *electronic nicotine delivery systems* (ENDS), are sold under common nicknames: e-cigs, E-hookahs, hookah pens, vapes, vape pens, and mods.<sup>2</sup> Vaping is becoming increasingly popular and the most common manner of nicotine use among US teens and young adults today.<sup>2</sup> The chemicals that are released when the e-liquid is heated can induce physiological injury, especially to the cardiovascular and respiratory systems.<sup>3</sup> Once touted as a potential strategy for overcoming nicotine addiction, vaping is now seen as a gateway to addiction to nicotine and other drugs.<sup>3</sup> The potential threats of vaping to health and social stability and its rise to epidemic proportions in younger populations spurred the *US Food and Drug Administration* (FDA) to implement regulations restricting the sales and marketing of these products, especially to the younger population.<sup>4</sup>

This lesson presents information that healthcare providers can use to help stem the tide of this epidemic. By identifying “vapers” and monitoring them for signs of disorders that can arise from vaping, the clinician can start treatments early enough to be effective, while counseling patients regarding the dangers of vaping and steering them toward professionals who can encourage them to stop.

## Vaping Devices

**The first electronic cigarette was developed in 1965.<sup>5</sup>** Thirty-five years later, Chinese pharmacist Lik Hon patented the “electronic cigarette atomizer,” which contained nicotine without tar.<sup>6</sup> **Vaping devices were first introduced in the United States in 2007.<sup>5</sup>** Nicotine-free or low-nicotine devices were thought to serve as an aid for smoking cessation.<sup>5</sup> Soon, a variety of vaping devices appears on the scene, some delivering nicotine to

the user (ENDS devices) and some serving as *electronic non-nicotine delivery systems* (ENNDS devices).<sup>7</sup> Today, more than 460 brands of e-cigarettes are available in the market,<sup>2</sup> with 30% to 50% of sales being made over the internet.<sup>5</sup>

### Vaping Device Components:

All vaping devices contain two main components: an atomizer or coil containing an e-liquid and a battery that sends an electrical current to the atomizer or coil to heat the liquid and produce the vapor.<sup>8</sup> In e-cigarettes, the e-liquid is contained in a cartridge, rather than an atomizer or coil.<sup>8</sup>

### E-Liquid

The liquid in vaping devices comes in various flavors, including mint, mango, apple pie, and watermelon.<sup>1</sup> Out of an estimated 7700 available flavors, the most popular are tobacco and mint.<sup>3</sup> In most e-cigarettes, the e-liquid also contains nicotine with or without *tetrahydrocannabinol* (THC), the psychoactive ingredient in marijuana.<sup>1</sup> In the vape pen, which includes the same equipment as e-cigarettes,<sup>1</sup> the e-liquid (also called vape juice) is 90% propylene glycol or vegetable-derived glycerin.<sup>1</sup>

Studies have shown that e-cigarette liquid and vapor also contain propylene glycol, glycerin, acetone, formaldehyde, nitrosomonocotine, tobacco-specific nitrosamine, and various metals, including chromium, cadmium, nickel, lead, and silver.<sup>3</sup> These elements may have been released during the heating process or might represent contamination. In either case, any of them may put the user at risk for serious adverse effects.

### Vaping Devices

Vaping devices can be customized in appearance (e.g., to mimic “real” cigarettes) and effect (i.e., by adjusting the strength of various components). The ability to customize their effects has resulted in various levels of user-friendliness with each generation of the device.

Thus, familiarity with the history of the development of these devices may shed some light on the rationale for a particular patient’s choice of device or decision to change from one device to another and help guide a clinician in providing personalized advice regarding the risks of continued vaping.

### *First-generation E-cigs:*

Referred to as “cigalikes,” the first generation of vaping devices were made to look and feel as much like a real cigarette as possible. Some even mimic the filter pattern of a regular cigarette, i.e., they are fitted with an LED tip that looks like ash and turns red when activated.<sup>10</sup> The earliest models of ENDS were mostly cigalikes and designed to appeal to the casual vaper, who wanted ease of use, as well as traditional smokers, to make it relatively easy for them to switch to e-cigarettes.<sup>10</sup> This is considered to be the simplest form of vaping: the user only has to attach a cartridge (prefilled, disposable, or refillable) to the battery before use.<sup>11</sup> The shortcomings of first-generation devices include a lower-capacity battery, which requires more frequent charging, and a smaller e-liquid capacity, which requires more frequent refilling than later counterparts.<sup>10</sup>

### *Second-generation E-cigs:*

The second generation of ENDS—known as “vape pens,” “egos,” “advanced personal vaporizers,” or simply “second-generation e-cigs,”<sup>12</sup> has a larger battery and vape tank than first-generation devices. As a result, they can produce more vapors than a cigalike<sup>11</sup> and still be portable, rechargeable, and small (approximately the size of a fountain pen). Several features of the second-generation device make it more appealing than its first-generation counterpart: (1) Instead of being activated by inhalation, the second-generation device is activated by pressing a power button to heat the coil,<sup>13</sup> (2) additional e-liquid can be added manually to the tank whenever needed; (3) a greater variety of flavors and nicotine strengths are available; (4) they allow greater customization, allowing the user to open the device and change its components (e.g., style of coil or preferred e-liquid);<sup>13</sup> and (5) it may contain a chip that can regulate the duration of device firing to prevent overheating.<sup>8</sup>

### *Third-generation E-cigs:*

Third-generation devices allow the user to modify the atomizer voltage and temperature, thereby modulating the amount of vapor it produces.<sup>14</sup> This is considered the most powerful and flexible version of the device. Its battery is more powerful, and its tank is larger than previous generations. The battery power settings also can

be controlled by the user to customize the flow, thickness, and volume of vapor produced.<sup>13</sup> Being boxlike in appearance with a tube-like projection, third-generation devices lack any resemblance to a cigarette.<sup>13</sup> Still, these devices (known as “mods” or “advanced personal vaping devices”) are popular among those who vape. They may be classified as “regulated mods”—having variable voltage to control the power level, and a safety mechanism that utilizes a chip to regulate the electrical current. Or, they may be “unregulated mods,” which lack a chip to prevent overheating.<sup>8</sup> Users must be careful when adjusting the power, because it can be dangerous if the battery is pushed to its limits. Also, they should exercise caution to prevent an explosion.<sup>8</sup>

### *The “Pod Mod”: JUUL:*

A newer vaping device surfaced in 2015 called the “pod mod,” of which JUUL is the most well-known brand.<sup>15</sup> Pod mods have become popular among adolescents and young adults because of its design, user-friendliness, desirable flavors, and size.<sup>15</sup> Unlike previous generations of vaping devices, the desired flavor can be obtained by simply sliding a flavor pod into the device before use. Having a compact form, pod mods may require less electrical power to deliver high doses of nicotine compared with e-cigarettes.<sup>16</sup> They resemble USB drives and, thus, are easy to conceal in places where vaping is forbidden, e.g., school.<sup>3</sup> The JUUL device has held the largest US market share of vaping devices since 2017, with an estimated 72.1% of shares as of August 2018.<sup>3</sup>

## Vaping vs Health

**Research on the effects of vaping on human health indicates that it is far from harmless.**<sup>3</sup> Studies have shown that it may facilitate addiction to nicotine and other drugs.<sup>3</sup> It also increases the risk for various physiological disorders, particularly cardiovascular and respiratory disorders.<sup>17</sup> Its association with lung disease is so strong that the terms *Vaping related acute lung injury (VpALI) or e-cigarette- or vaping-product use-associated lung injury (EVALI)* are used synonymously by local health departments to report vaping-related injuries to the *Centers for Disease Control and Prevention (CDC)*.<sup>18</sup> Many of the products associated with lung injuries contain THC, a mixture of nicotine and THC, or nicotine

only.<sup>2,18</sup> The CDC and FDA are still investigating the effects of other e-cigarette ingredients on human health. Of particular concern is vitamin E acetate, which was recently found to contribute to lung injuries.<sup>2</sup>

## Role of Vaping in Addiction

Vaping appears to be a gateway toward addiction to nicotine, marijuana, and other substances.<sup>3</sup> Research has shown that any heat-stable psychoactive substance can be vaped.<sup>3</sup> That includes synthetic cannabinoid receptor agonists and nicotine, as well as crack cocaine, *lysergic acid diethylamide* (LSD), and methamphetamines.<sup>3</sup> Hard-core vapers have been known to use the process of “dripping” to intensify the effect of the substance, i.e., they take apart the vaping device and pour the liquid directly onto the heated coils to increase the concentration of the substance(s) in the liquid for a greater effect.<sup>3</sup>

### Addiction to Nicotine:

Studies of e-cigarette users have shown that serum levels of nicotine vary with the duration of use and the user’s puffing practices.<sup>19</sup> They can be as high with e-cigarette use as they are in people who smoke traditional cigarettes.<sup>19</sup> In one study, urine levels of cotinine (a biomarker for nicotine exposure) in adolescents using JUUL was even higher than in those who smoked traditional cigarettes.<sup>20</sup> Another recent study suggests that e-cigarettes may have a higher addictive potential than smoked cigarettes among young adults.<sup>20</sup>

The exposure to and consequent effects of nicotine in e-cigarette users can be intensified in various ways. “Dripping” has been an effective way to increase nicotine exposure. Unfortunately, nicotine may be accompanied by formaldehyde, acetaldehyde, and acetone in e-liquids,<sup>3</sup> and any of these can cause serious adverse effects. Increased exposure to nicotine can also occur because of the vaping flavor selected, given that preferred flavors promote more frequent vaping by younger people. The increased frequency of vaping, in turn, increases the total exposure to nicotine, thereby increasing the risk for nicotine addiction.<sup>3</sup> Vaping itself could be a precursor to the use of combustible cigarettes. Studies have shown that a past history of e-cigarette use correlated strongly with the current use of combustible cigarettes.<sup>21</sup> Thus, even without increasing the concentration of nicotine

or frequency of exposure, long-term exposure to low levels of nicotine through vaping can increase the user’s tolerance and result in a craving that leads to a desire for combustible cigarettes.<sup>21</sup> This finding supports that within 6 to 12 months after the initial use of e-cigarettes during adolescence or early adulthood, users begin the use of combustible cigarettes, cigars, or hookahs.<sup>21</sup>

### Addiction to Marijuana:

The use of marijuana is generally common: One in seven US adults reported using it in 2017.<sup>22</sup> Marijuana is usually smoked but may also be vaped or consumed in edibles and as concentrates or topicals added to edibles.<sup>22</sup> The non-smoking routes are most likely used in states where marijuana is legal.<sup>22</sup> A 2018 survey of 16,280 US adults aged 18 years and older revealed that 14.6% of respondents had used marijuana in the last year and 8.7% in the last 30 days.<sup>22</sup> In terms of the route of consumption, 12.9% reported smoking marijuana, 6% reported consuming it in edibles, and 4.7% reported vaping it,<sup>22</sup> including 10.9% of college students who reported vaping marijuana in the past 30 days.<sup>3</sup> Although the “vapers” made up the smallest portion of marijuana users, vaping is not always benign, even when toxic contaminants are not taken into account. **The act of inhaling vapors given off by a concentrated form of marijuana, known as “dabbing,” results in a faster and more potent “high,” because “dabs” have a much higher concentration of the psychoactive chemical in marijuana, THC, than other forms of the drug, reaching concentrations as high as 80%.<sup>23</sup> Exposure to such high levels of THC places users at increased risk of marijuana addiction.**

### Addiction to Other Substances:

Given the strong correlation between combustible cigarette use and alcohol and drug use disorders,<sup>21</sup> the catalytic effects of e-cigarettes can lead to the use of other substances. E-cigarette use is comorbid with the use of alcohol and other substances.<sup>21</sup> Studies have shown that the prevalence of e-cigarette use was higher in adults seeking substance use treatment than in the general US population of smokers.<sup>21</sup> Study has shown that adolescent using e-cigarettes are more likely to use alcohol (heavy drinking), oral tobacco, sleeping pills, sniffed glue, marijuana, and amphetamine use than the non-users.<sup>21</sup> In a survey of substance use distributed among people who use



e-cigarettes, to which 758 participants with a mean age of 20.3 years (range: 18-23 years; SD = 0.79) responded, researchers found that 28.3% reported using e-cigarettes and 27.6% reported using combustible cigarettes.<sup>21</sup> Interestingly, the prevalence of substance use (including the use of alcohol, marijuana, cocaine, amphetamine, inhalants, hallucinogens, and ecstasy) and misuse of over-the-counter medication was more common among e-cigarette users than nonusers.<sup>21</sup>

## Impact of Vaping on Physical Health

E-cigarettes affect the cardiovascular system as well as the lungs.<sup>17</sup> The carbonyl compounds generated by high temperatures (e.g., acrolein, formaldehyde, acetaldehyde) contribute to oxidative stress by releasing inflammatory mediators.<sup>17</sup> This can result in cardiovascular damage, injury to airway epithelium, and alterations in platelet function that can affect gas exchange across the respiratory epithelium.<sup>17</sup> Similarly, repeated exposure of the heating element to high temperatures results in the emission of nanoparticles, which further potentiates harmful effects on the respiratory system.<sup>17</sup> Flavoring agents can impair mucociliary and mitochondrial function.<sup>17</sup> The aerosol components can alter cytokines, macrophages, and neutrophils, and, consequently, antimicrobial function, thereby facilitating bacterial colonization in the lungs.<sup>17</sup>

### Lung Disorders:

Certain clinical syndromes that result in lung injuries similar to those caused by vaping include hypersensitivity pneumonitis, eosinophilic pneumonia, diffuse alveolar hemorrhage, organizing pneumonia, lipoid pneumonia, and *acute respiratory distress syndrome* (ARDS).<sup>17</sup> The presenting symptoms usually include a nonproductive cough, shortness of breath, constitutional symptoms, and hypoxemia.<sup>17</sup> Patients most likely to develop lung disease are those who had modified their vaping devices or used modified e-liquids purchased on the black market.<sup>17</sup> The use of THC and the presence of vitamin E acetate in bronchoalveolar lavage samples taken from patients with VpALI raise the suspicion that these compounds are having a causative role in the development of lung injury.<sup>17</sup>

The FDA, CDC and other health authorities are making progress in identifying the exact triggers in vape causing lung injuries with special emphasis on vitamin E acetate. In the latest report from the CDC, dated January 14, 2020, out of 2668 patients who have been hospitalized with EVALI in all 50 states plus the District of Columbia and two US territories (Puerto Rico and the US Virgin Islands),<sup>24</sup> half of the patients provided the source of their vaping products. Of these, 16% obtained them from commercial sources such as recreational or medical dispensaries, vape or smoke shops, stores, and pop-up shops; 78% acquired them from family/friends, dealers, online, or other sources; and 6% acquired them from both commercial and informal sources.<sup>24</sup> In a study conducted in Illinois, 14% of 121 individuals with EVALI reported using e-cigarettes or vaping products containing nicotine only.<sup>24</sup> Thus, further research is needed to elucidate the exact process involved in lung injury in “vapers.” Until that is known, clinicians need to remain vigilant for early signs of VpALI in patients who use e-cigarettes.

UCSF (University of California, San Francisco) researchers asked tens of thousands of individuals over 12 years of age about their use of tobacco products, e-cigarettes, and their health, and conducted follow-up questions over three years.<sup>1</sup> They found the development of lung problems like emphysema, bronchitis, asthma, and chronic obstructive pulmonary disease in individuals who had used e-cigarettes in the past or currently use them. The combined use of e-cigarette and tobacco products dramatically increased lung disease risks by an incredible 330 percent.<sup>25</sup> The researchers concluded that “*Use of e-cigarettes is an independent risk factor for respiratory disease in addition to combustible tobacco smoking.*”<sup>25</sup> The study’s senior author, Stanton Glantz, told CNN “*I was a little surprised that we could find evidence on incident lung disease in the longitudinal study, because three years is a while, but most studies that look at the development of lung disease go over 10 to 20 years.*”<sup>26</sup>

### Cardiovascular Disease:

In a cross-sectional study, Alzahrani and colleagues used data from the National Health Interview Surveys of 2014 and 2016 to explore the relationship between e-cigarette use and the incidence of *myocardial infarction* (MI).<sup>27</sup> They found that daily e-cigarette use is independently associated with an increased risk for an MI (OR 1.79)

compared with daily conventional cigarette smoking (OR 2.72).<sup>27</sup> One of the limitations of this study is that its findings could not be used to establish a temporal relationship between e-cigarette use and incidence of MI because many of the e-cigarette users were former traditional cigarette smokers. Therefore, a patient who had an MI while smoking traditional cigarettes and then switched to e-cigarettes could easily be misclassified as an e-cigarette user with an MI. In another study, investigators uncovered inconclusive but disturbing findings regarding the long-term cardiovascular effects of e-cigarettes.<sup>28</sup> Several other studies have reported adverse effects of e-cigarettes on endothelial dysfunction, oxidative markers, platelet aggregation and arrhythmogenesis risk etc.<sup>28</sup> Further research, in the form of longitudinal and long-term studies, are needed to address these concerns.<sup>28</sup>

### Other Disorders:

Serious burns and projectile injuries caused by exploding e-cigarette batteries have also been reported, as well as the intentional or unintentional ingestion of the e-liquid, which has been reported to cause many adverse health effects, including seizures, anoxic brain injury, lactic acidosis, and even death.<sup>29</sup> Traditional cigarette smoking by pregnant women is well known to increase the risk of premature delivery, low birth weight, stillbirths, and congenital disabilities.<sup>30</sup> A review by Whittington and colleagues noted that pregnant women who use e-cigarettes share the belief that e-cigarette use is less harmful than cigarette smoking. The fact that the amount of nicotine consumed by e-cigarette users is comparable to that consumed by traditional cigarette smokers raises a valid concern over the use of e-cigarettes during pregnancy presenting as much of a risk to the fetus as conventional smoking.<sup>30</sup> Keeping in mind that it took decades, if not centuries, to prove that cigarette smoking causes cancer, these new e-cigarette studies suggest that the products are not just understudied and possibly dangerous, but increasingly just dangerous, associated more frequently with chronic disease, heart problems, and even cancer.<sup>31</sup>

## Cost Implications

**Retail sales of e-cigarettes and vaping devices in the United States have approached \$7 billion annually.**<sup>3</sup> Across the country, sales in vape shops have increased

considerably.<sup>32</sup> A cross-sectional survey of purchases of vape products in vape shops revealed that overall spending ranged from \$10/month to more than \$250/month, with an average expenditure of \$50 to \$75/month.<sup>32</sup> Consumers who spent more than \$50/month were generally using devices containing less nicotine and a greater quantity of e-liquid.<sup>32</sup> Sales of vaping products have increased since 2007 in line with widespread advertising featuring celebrities.<sup>3</sup> Spending on advertising increased from \$6.4 million in 2011 to \$115 million in 2015.<sup>3</sup>

The cost of e-cigarettes in Missouri ranges from \$10 to \$100;<sup>5</sup> disposable devices are less expensive. A pack of flavor cartridges or a refill of e-liquid costs \$10 to \$15 and is equivalent to 150 cigarettes.<sup>5</sup> A pack-a-day cigarette smoker may end up spending \$2000 annually, whereas someone using mid-range e-cigarettes that cost \$20 with refills costing \$15 a week will end up spending \$800 a year.<sup>5</sup> The annual cost will also vary with state tax rates.<sup>5</sup>

## Can Vaping/E-Cigarettes Be Used As Smoking Cessation Aids?

The fact that smoking is a difficult habit to quit is reflected in the fact that 80% of smokers who attempt to quit resume smoking within 30 days.<sup>3</sup> There is a 50% chance of success with the help of nicotine replacement therapy and counseling.<sup>3</sup> Currently, five FDA-approved nicotine replacement products are available: gum, patch, lozenges, inhaler, and nasal spray.<sup>3</sup> Additionally, two non-nicotine prescription drugs (varenicline and bupropion) are approved to help individuals overcome tobacco dependence.<sup>3</sup> The question that remains is whether vaping devices can be included on the list of nicotine replacement products. When e-cigarettes were introduced, it was assumed that they would be helpful for smoking cessation.

Although they are not approved by the FDA as smoking cessation aids, some manufacturers have tried to market their devices as such. Their ability to function in that capacity has been the subject of several studies. Bullen and colleagues, for example, conducted a *randomized control trial* (RCT) in which smokers who were interested in quitting were randomized to receive either e-cigarettes, nicotine patches, or placebo (nicotine free) e-cigarettes. After 6 months, the rate of smoking cessation was less than anticipated for the entire study population,



which resulted in insufficient power to determine the efficacy or superiority of any single method.<sup>3</sup> The investigators concluded that nicotine-containing e-cigarettes were “modestly effective,” resulting in an abstinence rate similar to that seen with the nicotine patch.<sup>3</sup> By contrast, one year after randomizing 886 smokers to e-cigarettes or a nicotine replacement product of their choice, Hajek and colleagues found that 18% of e-cigarette users had stopped smoking compared with 9.9% of smokers using other nicotine replacement products.<sup>33</sup> Interestingly, 80% of those who quit smoking with the help of e-cigarettes were still using e-cigarettes at the 1-year follow up point compared with 9% of those who continued using other methods during the same time.<sup>33</sup> Several other observational studies and RCTs had mixed results. Many have shown that daily e-cigarette use may be associated with “more quitting attempts” and “fewer traditional cigarettes smoked/day,” but not necessarily higher rates of quitting.<sup>34</sup> **We do not have conclusive data that long-term e-cigarettes are harmless, given their effects on the cardiovascular and respiratory systems. Therefore, patients should be encouraged to use FDA-approved nicotine replacement treatments and medicines for smoking cessation instead.**

## Regulation of Vaping Products

The FDA started regulating the sale and marketing of vaping products on August 8, 2016.<sup>4</sup> These regulations covered the packing, labeling, advertising, promotion, and sale of these products, making it illegal to sell them to anyone younger than 18 years of age.<sup>35</sup> The age was raised to 21 years in December 2019<sup>2</sup> to make federal regulations consistent with regulations in 18 states (Arkansas, California, Connecticut, Delaware, Hawaii, Illinois, Maine, Maryland, Massachusetts, New Jersey, New York, Ohio, Oregon, Texas, Utah, Vermont, Virginia, and Washington), where the minimum age for buying tobacco products is 21 years.<sup>3</sup> The regulations require retailers to verify the age of the purchaser by checking that individual’s ID.<sup>35</sup> ENDS manufacturing facilities and vape shops have to be inspected regularly to make sure they are not marketing tobacco products without premarketing approval or selling them to minors. **Since June 2019, manufacturers have been required to register existing products.**<sup>35</sup> Thus, they must

submit labeling and advertisement materials and a list of ingredients to the FDA for review.<sup>35</sup> **Additionally, the following warning label must appear on the product: “WARNING: This product contains nicotine. Nicotine is an addictive chemical.”**<sup>35</sup>

In 2018, the FDA issued 1300 warning letters to violators of anti-vaping laws.<sup>6</sup> In early 2019, the FDA commissioner announced that if vaping rates among minors and young adults continued to rise, the FDA would remove some or all ENDS products from the market.<sup>6</sup> On January 2, 2020, the FDA finalized its policy regarding the sale of flavored vaping cartridges<sup>2</sup> by prioritizing the enforcement of FDA regulations restricting the promotion of nicotine-containing vaping products that do not have premarketing authorization.<sup>36</sup> This policy applies to companies that are in the process of manufacturing, distributing, and selling flavored cartridge-based ENDS products other than those containing tobacco or menthol, which will risk FDA enforcement action within 30 days.<sup>36</sup>

Before these regulations were implemented, the consumer had no way of knowing how much nicotine they were inhaling or the contents of the e-cigarettes. Despite these regulations—new information about the product contents, and how they could affect the health of the user—e-cigarette use rose by 78% (from 11.7% to 20.8%) among high school students and by 48% (from 3.3% to 4.9%) among middle school students between 2017 and 2018<sup>6</sup> and by 900% among high school students between 2011 and 2015.<sup>5</sup> **In 2018, the US Surgeon General issued an advisory declaring e-cigarette use by minors an “epidemic” affecting more than 3.6 million children. By then, 20% of high school students and 5% of middle school students were using e-cigarettes.**<sup>37</sup> According to the 2019 *National Youth Tobacco Survey* (NYTS), this epidemic does not show signs of stopping. It reported that approximately 6.2 million US middle and high school students had used some type of tobacco product during the month preceding the survey, with e-cigarettes being the most common tobacco product listed.<sup>38</sup> Another possible reason for some to continue vaping is that some individuals continue to support the use of e-cigarettes as smoking cessation aids, even though evidence of that function is lacking<sup>5</sup> and it is still not listed among the seven smoking cessation aids that have been approved by the FDA.<sup>2</sup>

## Conclusions

Vaping is a mode of inhalation that makes smoking nicotine or THC more addicting. The epidemic of vaping is spreading rapidly among adolescents and younger populations. The lack of effort to curtail it until recently allowed its continued use by minors, who find vaping devices easy to use and easy to conceal resulting in an increase in vaping-associated deaths. The FDA has implemented strict controls to minimize its use by minors while controlling and monitoring the marketing

of vaping products and their accessories. These have not been very effective. Among the regulations that have been established to discourage the use of e-cigarettes or vaping products are: a ban on their use in public; increased cost; labeling requirements that show the ingredients clearly to increase consumer awareness of the risks associated with these products; and the elimination of flavored e-cigarettes (which can make them particularly attractive and appealing to youth). Similarly, public awareness about its harmful effects is of paramount importance in discouraging their use by both minors and young adults. ■

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L003443

## Multiple-Choice Questions

1. **What is a common characteristic of second-generation *electronic nicotine delivery systems* (ENDS)?**
  - A. Physically similar to combustible cigarettes
  - B. Fixed voltage/power level
  - C. Larger tanks compared with first-generation ENDS
  - D. Resemblance to a USB drive
  
2. **Cigalikes have which of the following properties?**
  - A. Large tanks and variable voltage
  - B. A power button to heat the coil
  - C. Close resemblance to a USB
  - D. Belongs to first-generation ENDS
  
3. **All of the following statements are correct, *except*:**
  - A. Retail sales of e-cigarettes and vaping devices in the United States have approached \$7 billion annually.
  - B. Conclusive data shows that long-term e-cigarettes have minimal effects on the cardiovascular and respiratory systems.
  - C. The first electronic cigarette was developed in 1965.
  - D. Vaping devices were first introduced in the United States in 2007 as smoking cessation aids.
  
4. **Which health effect of e-cigarettes has recently emerged as an alarming epidemic?**
  - A. E-cigarette-related myocardial infarction
  - B. Preterm labor in pregnant e-cigarette users
  - C. Vaping-associated acute lung injury
  - D. Serious burns and projectile injuries

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# Best Practices in Continuing Medical Education

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## Vaping and Its Effect on Physical Health

Syed Z. Iqbal, MD; Benjamin T. Li, MD;

Lubna Khawaja MD; Asim A. Shah, MD

ID#: L003443

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

The information in this lesson is meant to educate mental health professionals, primary care providers, psychologists, social workers, mental health counselors, and anyone else who works with patients to address the impact of vaping on physical health. Vaping plays a role in the development of addiction to nicotine and other drugs, including marijuana, cocaine, LSD, and methamphetamines. Vaping also affects physical health by increasing the risk for such conditions as vaping associated lung injury EVALI and myocardial infarction. The practice of vaping has accelerated in many communities, especially among young teens and adults. Most vaping products deliver nicotine to the user. There has been a misconception that vaping can help in smoking cessation; however, it is now seen as a possible gateway toward nicotine and drug addiction. Vaping devices are marketed in the form of pens and flash drives, which can be easily concealed by children. The FDA is working hard to enforce regulations controlling the sale and marketing of these products. Its success appears to be limited, however, given that retail sales of e-cigarettes and vaping products continue to rise, having reached \$7 billion annually. Continued health education projects and vigilance of healthcare providers for signs of vaping in their patients will be essential to slow the vaping epidemic.

#### **Key Point 1: Vaping Is Popular In Younger Population**

The use of vaping and e-cigarettes is increasingly popular among the youth. Knowledge of the various nicknames for these devices and the ingredients used in them is of paramount importance to identify “vapers” and be prepared to treat them. These devices come in different shapes so that they can be easily disguised by children in school. They are now marketed in the shape of USB flash drives.

#### **Key Point 2: Manufacturers Should Display Ingredients and Warning Label**

The FDA is trying to regulate the sale, marketing and advertising of vaping products. Manufacturers must display the ingredients and warning label about nicotine addiction.

#### **Key Point 3: Vaping Is Not a Smoking Cessation Aid**

Vaping or e-cigarette use is not approved by the FDA as a smoking cessation aid.

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**Key Point 4: Vaping Can Lead to Addiction**

Vaping and e-cigarette use can be a gateway for nicotine and drug addiction.

**Key Point 5: Vaping Is Injurious to Lungs**

Vaping and the use of e-cigarettes are far away from being harmless. They have resulted in VpALI/EVALI in different states.

# Human Trafficking

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*No commercial support was used in the development of this continuing medical education lesson.*

**KEY WORDS:** Human trafficking • Sex trafficking • Labor trafficking

**LEARNING OBJECTIVES:** Upon completing this module, the clinician should be able to: (1) identify evidence of labor and sex trafficking in patients who come for treatment; (2) delineate the healthcare, socioeconomic, and legal needs of each victim; and (3) help the victim access resources that can help them meet their individual needs.

**LESSON ABSTRACT:** Human trafficking is a global criminal enterprise that is growing at an alarming rate. Victims of labor trafficking are at risk for serious health issues associated with physical abuse, exposure to toxins, or infectious diseases contracted while living/working under overcrowded, unsanitary conditions. Victims of sex trafficking are also at risk of physical abuse, as well as for addiction, sexually transmitted diseases, and coerced abortions. The United States (US) is both a destination for international trafficking and a source for its internal trafficking networks. As a result, the majority of US sex trafficking victims are women and children who are US citizens. Runaways and children in the US child welfare system are at particularly high risk for such victimization. US healthcare professionals are likely to encounter victims of human trafficking in a variety of clinical settings; as such, they are in a unique position to provide immediate assistance. Under the protection of US Safe Harbor Laws, they are required to identify victims. This lesson will help them learn how to help them secure essential services in addition to medical services, e.g., psychological treatment, as well as provide guidance for resolving legal issues, obtaining housing, and resuming educational pursuits.

**COMPETENCY AREAS:** This lesson provides knowledge of human trafficking—labor trafficking and sex trafficking—in terms of how each kind is perpetrated and its effects on the psychological and physical health of its victims. The healthcare provider is in a unique position to identify signs of human trafficking and assisting its victims in obtaining the resources they need for physical and mental healthcare, as well as social and legal services.

## Introduction

Human trafficking is defined as “the recruitment, harboring, transporting, providing or obtaining, by any means, a person for labor or services involving forced labor, slavery or servitude in any industry, such as forced or coerced participation in agriculture, prostitution, manufacturing, or other industries or in domestic service or marriage.”<sup>1</sup> Human trafficking involves the use of force, fraud, or coercion to obtain some type of labor or commercial sex act.<sup>2</sup> Human trafficking has become the third largest criminal enterprise in the world and continues to grow at an alarming rate.<sup>3</sup> The Global Slavery Index estimates that approximately 45.8 million people are enslaved worldwide, and that slavery is present, in one form or another, in 167 countries. The majority of trafficking victims are taken from less developed regions of the world (Africa, South and Southeast Asia, Central and South America) and transported to areas where they will be the most “profitable.”<sup>4</sup> Developed nations also face human trafficking concerns. The United States, for example, is both a destination for international trafficking and a source for its internal trafficking networks. Approximately \$150 billion a year is generated worldwide through human trafficking, with sex trafficking accounting for 66% of this amount.<sup>5</sup>

Psychiatrists and other healthcare professionals may encounter victims of human trafficking in a variety of clinical settings. By learning about the various forms of human trafficking and understanding how victims may present, healthcare professionals may be able to improve their ability to identify victims of this crime, report these cases appropriately, and utilize all of the resources that are available to help them.

## The Demographics of Human Trafficking Victims

The largest number of forced laborers are employed in Asia, particularly South and Southeast Asia; many others are employed in Africa, Latin America, and the Caribbean.<sup>6</sup> In 2013, the largest number of sex-trafficking victims were from Mexico, the Philippines, Thailand, Honduras, Guatemala, India, and El Salvador.<sup>7</sup> Although developing nations provide the majority of human trafficking victims globally, the *United States* (US) has one of the

highest amounts of trafficking among developed countries. An estimated 199,000 trafficking incidents occur in the United States every year. California, New York, and Texas are the top three states with the most human trafficking.<sup>8</sup> These victims are either trafficked within the United States or “exported” to other industrialized countries, including the Netherlands, Germany, and Japan.

Worldwide, approximately 71% of trafficking victims are female, and many are younger than 18 years of age.<sup>9</sup> The age and gender distribution are different between labor trafficking and sex trafficking, however. Labor trafficking victims comprise a more heterogeneous group that includes young children, teenagers, and both male and female adults, with males comprising 42% of victims of state-imposed labor exploitation, (e.g., prisons), or in work imposed by the state military, or by rebel armed forces including child soldiers. Sex trafficking victims also include male and female adults and children, but the majority are women and girls. Men and boys tend to be overlooked as victims of sex trafficking because they make up only 2% of this population (~400,000 men and boys).<sup>10</sup> The gender distribution is different overall for minors in the sex trade, however, particularly in the United States, where 35% are male, 60% are female, and 5% are transgender.<sup>11</sup>

## Labor Trafficking: A Closer Look

**Labor trafficking is defined as “the recruitment, harboring, transportation, provision, or obtaining of a person for labor or services, through the use of force, fraud or coercion for the subjection to involuntary servitude, peonage, debt bondage or slavery.”** Either bonded or forced labor may be involved. Oftentimes, bonded labor is based on debt bondage, which may be the least known but most common method of enslaving people. Victims become bonded laborers when their labor is demanded as a means of repaying a loan or service. This may occur when the terms and conditions of the loan are not defined, or the value of the victim’s services is not reasonably assessed or applied to the liquidation of the debt. Forced labor involves the spheres of domestic help, agriculture, construction, landscaping, sweatshops, and service industries (e.g., janitorial, food service, nail salons, spas, bars), as well as begging. Victims are forced to work against their will under the threat of punishment,

including violence. Their freedom is restricted, and their captors exert a degree of ownership over them.<sup>12</sup>

The practices used to recruit labor trafficking victims may involve a wide variety of criminal, civil, juvenile, and family legal processes. Trafficking victims can be coerced to recruit more victims; gang members can be coerced into criminal activity; a victim can be coerced into shoplifting or stealing to provide extra income for the trafficker; traffickers may seek guardianship over minor victims as a means of control, and; family members may traffic other family members.

Victims are often kept isolated to prevent them from getting help. Their activities are restricted, and they are typically watched, escorted, or guarded by associates of their traffickers. Traffickers may “coach” them to answer questions with a cover story, e.g., about being a student or tourist. Victims may be blackmailed by traffickers who threaten to use the victim’s status as an undocumented alien or participation in an “illegal” industry against them. By threatening to report them to law enforcement or immigration officials, traffickers keep their victims compliant. People who are trafficked often come from unstable and economically devastated places characterized by oppression, high rates of illiteracy, little social mobility, and few economic opportunities. As such, they are unlikely to have any support systems “back home” available to help them. Women and children are the overwhelming majority among victims of labor trafficking because of their relative lack of power, social marginalization, and overall lower social status compared to men.

Unlike sex trafficking victims, labor trafficking victims are typically engaged in work that is legal. Thus, they are less likely to come to the attention of the criminal justice system unless a victim comes forward to complain, and a government official is willing to take action based on that complaint.

### Vignette I:

*A 21-year-old Mexican woman raising two children responded to a newspaper ad for a job at a cardboard box factory in Seattle, Washington. The rate of pay—\$10 per hour—was three times the amount she could earn at home. She was poor and was trying to pay off her father’s medical bills. The agency that posted the ad informed her*

*that they would arrange for her to have this job if she paid them \$3000. She borrowed the money, including the cost of airfare to Seattle. When she arrived, a man picked her up at the airport and brought her to a building in the suburbs, where a woman took her passport for “safekeeping.” The woman then told her that the factory job did not come through, and instead, she would be working in the laboratory downstairs. She discovered they were producing crystal metham-phetamine in the lab. She refused to work at first, but then realized she had no other options to pay her bills or support her family. She was paid and fed, but worked long hours and slept in a room next to the lab with 10 other men and women. She grew concerned that she would be seen as a criminal for working in an illegal drug lab. She asked the woman to return her passport because she wanted to leave. The woman told her that she could not go because she knew too much and that if she tried to leave, they would kill her.<sup>13</sup>*

## Evidence of Labor Trafficking Victimization:

**Many labor trafficking victims suffer serious health issues, including physical abuse (e.g., bruises, broken bones, burns, scarring); skin or respiratory problems caused by exposure to toxins used in agriculture or other industries; infectious diseases (e.g., tuberculosis and hepatitis) that usually spread under overcrowded, unsanitary conditions or with limited ventilation; and untreated chronic illnesses (e.g., diabetes or cardiovascular disease). Other indicators of trafficking may reflect the restrictions placed on these workers, e.g., not being allowed to speak to anyone alone; being underpaid, either because the wages are small or their money is applied directly to their debt; not being able to leave the jobsite; not coming and going freely; living in the workplace or with many others in a confined area; or not having access to identification or travel documents.**

## Sex Trafficking: A Closer Look

Sex trafficking is a form of slavery in which a commercial sex act occurs as a result of force, fraud, or coercion or is performed by someone who is younger than 18 years of

age. Trafficked men, women, and children are typically taken to brothels, escort services, massage parlors, strip clubs, or hotels; prostituted on the streets; or forced to participate in pornography.<sup>14</sup>

In the United States, anyone younger than 18 years who engages in commercial sex acts is automatically considered a victim of sex trafficking. The *Trafficking Victims Protection Act* of 2000 (TVPA), which defines a “commercial sex act” as the performance of any sex act in exchange for anything of value that is given to or received by any person, made sex trafficking a violation of federal law. **The TVPA recognizes that traffickers use psychological as well as physical coercion and bondage, including threats of serious harm or physical restraint of the victim and schemes, plans, and patterns of activity intended to cause the intended victim to believe that his/her failure to perform a sex act will result in serious harm or physical restraint of any person.**

## Vignette 2:

*A 29-year-old homeless Caucasian woman with a history of intravenous drug use was brought to the emergency department (ED) by police officers after a reported sexual assault. The patient was reluctant to discuss specific details about the attack but did reveal that she had been held captive at gunpoint and was forced to have sexual intercourse with numerous individuals over several days. Her clinical exam was unremarkable, except for an abrasion on the forehead, which she reported was the result of being struck with a pistol 2 days before. She declined a genitourinary examination. A psychiatric consult was not performed during the visit, although in his report of the findings of a brief psychiatric examination, the clinician described an anxious patient who denied any suicidal intent. The patient politely persisted in her refusal of any further medical assessments or interventions. She was discharged at her request after she stated that she planned to spend the night with a friend with whom she felt safe. The following day, the patient presented again to the ED, this time with acute suicidal ideation and symptoms of opioid withdrawal. She stated she would rather die than return to*

*her drug dealer or let him find her. She also said that she had been encouraged to come to the ED by her therapist. A psychiatric consultation and an evaluation by a social worker revealed that the patient had a history of child abuse and had been in multiple substance abuse treatment programs. She had one prior suicide attempt and a history of posttraumatic stress disorder (PTSD). Three weeks before, she left a substance abuse rehabilitation center and relapsed on heroin. She was then kidnapped and forced to engage in commercial sex work while locked in a room at gunpoint to pay off debts to her drug dealer. The ED physician and social worker recognized that her condition was consistent with that of victims of sex trafficking, and the patient chose to have her abuse reported to the police. She was notified later that day that her traffickers were arrested. Then, she was transferred to an inpatient psychiatric unit.<sup>15</sup>*

## Demographics of Sex Trafficking Victims:

It has been estimated that there are 4.5 million victims of sex trafficking worldwide, including 1.2 million children.<sup>16</sup> This number includes the estimated 14,500 to 17,500 people who become victims of sex trafficking in the United States every year, of whom 80% are women and children.<sup>8</sup> Interestingly, 83% of sex trafficking victims in the United States are US citizens.<sup>17</sup> A review of 586 cases in Pennsylvania involving 1127 potential victims of trafficking revealed a representative breakdown of US victimization: 201 were US citizens or legal permanent residents vs 139 foreign nationals; 466 were female vs 89 males vs 3 of a gender minority; and 392 were adults vs 151 minors. These statistics are non-cumulative. Cases may involve multiple victims, and in some cases, callers do not provide demographic information.<sup>18</sup>

## Luring Victims to Sex Trafficking:

Common methods of luring victims into the sex trade in developing countries include the promise of a good job in another country or a false marriage proposal that results in bondage. Individuals are also sold into the sex trade by parents, husbands, or boyfriends or are kidnapped by traffickers. Sex traffickers frequently subject their victims to debt-bondage, telling their victims that they owe the



trafficker money (e.g., for the victims' living expenses and transport into the country) and that they must pledge their personal services to repay the debt. In the United States, homeless and runaway children are especially vulnerable to sex trafficking. According to a 2009 report by the National Runaway Switchboard, one-third of runaway youths in the United States are lured into prostitution within 48 hours on the streets.<sup>19</sup> A study of over 600 homeless youth conducted by Loyola University's Modern Slavery Research Project, challenges this claim.<sup>20</sup>

Sex traffickers use a variety of methods to "condition" their victims, including starvation, confinement, beatings, physical abuse, rape, threats of violence to the victim and the victim's family, forced drug use, and the threat of shaming them by revealing their activities to their family and friends.

## Sex Trafficking and the Internet

Supply and demand for sex trade workers have increased over the years in part because of increased use of the internet, which facilitates transactions between sex traffickers and customers. **Traffickers utilize encryption and dark web technologies to market their victims, particularly minors, on social media, including dating sites and online advertisements.** In 2018, information technology companies reported the posting of more than 45 million photos and videos of children being sexually abused—more than twice as many as the year before.<sup>21</sup> Traffickers lie about the victim's age and may even disguise themselves as the person in the ad when communicating via internet or phone. Some websites try to screen ads for trafficking, but the sheer volume of these advertisements makes this a daunting task. For instance, when the US Craigslist Adult Services Section was available, 10,000 to 16,000 adult services postings were made each day in the United States alone. Additionally, it is difficult to determine whether the advertiser is working independently or for a trafficker. There is a consensus that increased funding and cooperation among law enforcement agencies, the information technology industry, and the government is needed to protect potential victims of human trafficking.

### Signs of Sex Traffic Victimization:

**Victims of sex trafficking face numerous health risks, including drug and alcohol addiction; physical**

**injuries (e.g., broken bones, concussions, burns, vaginal/anal tears); traumatic brain injury resulting in memory loss, dizziness, headaches, or numbness; sexually transmitted diseases (e.g., HIV/AIDS, gonorrhea, syphilis, urinary tract infections, pubic lice); sterility, miscarriages, and menstrual problems; and other diseases (e.g., tuberculosis, hepatitis, malaria, pneumonia). They may also receive unwanted brandings or tattoos or become victims of forced or coerced abortions.**<sup>22</sup>

### Signs of Sex Traffic Victimization in Children:

*Commercial sexual exploitation of children* (CSEC) is defined by the Office of Juvenile Justice and Delinquency Prevention as "crimes of a sexual nature committed against juvenile victims for financial or other economic reasons."<sup>23</sup> CSEC involves street exploitation, pornography, stripping, erotic/nude massage, escort services, phone sex lines, private parties, gang- and organized crime-based exploitation, familial exploitation, sex tourism, and internet-based exploitation. Victims of CSEC may exhibit several unexpected behaviors, including unexplained absences from class; inappropriate dress; overly sexualized behavior; being overly tired in class; being withdrawn, depressed, or distracted; bragging about having lots of money; displaying expensive clothes, accessories, or shoes; having a new tattoo (especially a tattoo of someone's name, a symbol of money, or a barcode); having an older boyfriend or new friends with a different lifestyle; talking about wild parties; or showing signs of gang affiliation (e.g., a preference for specific colors or doodling gang symbols in a notebook). The Stockholm Declaration and Agenda for Action (1996) considers CSEC to be a form of violence against children.<sup>24</sup>

Under US federal law, anyone under the age of 18 years who is induced to commit a commercial sex act is considered a victim of sex trafficking, regardless of whether the trafficker used force, fraud, or coercion. In the United States, it has been estimated that 300,000 children are at risk for CSEC and that 1 out of 6 endangered runaways (> 233,000 children) become victims of CSEC. Between 50% and 98% of children identified as victims of CSEC had previously been involved with the child welfare system.<sup>25</sup>



## The Stockholm Syndrome

**Oftentimes, traffickers sporadically give gifts and make kind gestures to their victims—which causes their victims to become confused, mentally, and emotionally placing the trafficker in the position of “victim.”** As a result, the victim finds it difficult to leave the trafficker. This phenomenon is referred to as the Stockholm Syndrome (also known as the Hostage Identification Syndrome, the Survival Identification Syndrome, or traumatic bonding). Conditions that lead to this phenomenon include a perceived threat to survival, the perception of kindness on the part of the trafficker, or isolation and the perceived inability to escape. The Stockholm Syndrome is not recognized as a psychological diagnosis of a mental illness or disorder in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5). Instead, it is viewed as a clinical explanation of the symptoms of a unique relationship that may develop between a kidnapper and hostage.<sup>26</sup>

## Physician Encounters With Human Trafficking

Specialists in obstetrics/gynecology, emergency medicine, and pediatrics are among the physicians most likely to encounter victims of human trafficking.<sup>27</sup> In a survey of sex trafficking victims in the United States, 71.2% of the 66 respondents reported at least one unwanted pregnancy during the period of their exploitation, and 21.2% reported five or more pregnancies. The same survey revealed that 55.2% of the 67 female survivors reported having at least one abortion, and 29.9% reported multiple abortions, with half of those who had had an abortion indicating that they had been forced to have at least one of the abortions.<sup>28</sup> In another study, the investigators reported that approximately 25% of labor- and sex-trafficked persons stated that they saw an obstetrician during their period of exploitation.<sup>29</sup> In a third study, 87.8% of sex trafficking victims reported having had contact with a healthcare provider while they were being trafficked. They were seen most frequently by emergency medicine physicians in healthcare settings, with 63.3% of victims reporting contact there.<sup>13</sup> The American Academy of Pediatrics has issued a policy statement on human trafficking and child

victimization, in which it indicated that pediatricians are most likely to encounter these victims.<sup>30</sup>

## Mandatory Reporting

All 50 states have mandatory laws for reporting child abuse. Healthcare professionals are designated as mandatory reporters, i.e., they must report suspected abuse or neglect of minors. In the past few years, several states have amended their mandatory reporting laws to cover all forms of human trafficking. As of December 2015, 14 states had included sex trafficking as a reportable act, and 10 also included labor trafficking.<sup>31</sup> The physician's duty to report any suspicion that a minor is being trafficked is supported by these mandatory reporting laws. If the individual is 18 years or older and exhibits serious bodily injury that is believed to have been inflicted by another person using a knife, gunshots, or strangulation, it must be reported to local law enforcement. If an adult is believed to be a victim of trafficking, the consent of that individual is required before social services can get involved. The healthcare worker can then call a hotline to describe the situation, provided s/he keeps the victim's identity anonymous. Calling a hotline is the best way for healthcare providers to determine if law enforcement needs to be notified.

## Assistance for Victims of Human Trafficking

Healthcare professionals are in a unique position to reach out to victims of human trafficking. There should be a concerted effort to raise awareness of this issue among healthcare professionals so that they can recognize signs of victimization and safely refer victims to appropriate programs to receive the care they need.

### Mental Health Needs:

Human trafficking can have a devastating effect on the psychological health of the individual. Victims can present with signs of acute and PTSD, dissociative disorders, substance-related disorders, trauma bonding, anxiety and mood disorders, and sexual dysfunction. High-risk behaviors, impaired judgment, suicidal ideation, stress related to acute and chronic medical problems, and difficulty establishing and maintaining healthy personal

relationships are all quite common. A comprehensive assessment should include psychological, psychiatric, and medical components. Trauma-focused cognitive-behavioral therapies have the most empirical evidence of efficacy with PTSD spectrum disorders. Pharmacotherapy to manage symptoms of anxiety, mood disturbances, and trauma should be a component of the treatment plan. Clinicians should also address substance use and ongoing medical conditions.<sup>32</sup>

### **Immigration Issues:**

Immigration status is more likely to be an issue for victims of labor trafficking than sex trafficking, at least in the United States, where the majority of sex trafficking victims are US citizens. When immigration is an issue, every effort should be made to help victims stabilize their immigration status and obtain assistance in rebuilding their lives. Once noncitizens have been certified as victims of human trafficking, it may be possible to have them categorized as refugees and, thus, become eligible for federally funded benefits and services, including food, healthcare, and employment assistance, as well as English language instruction and job skills training. Because many human trafficking victims are reluctant to come forward out of fear of being deported, it is imperative to connect them with nonprofit organizations that can assist them and address specific needs. These organizations can provide counseling, case management, and benefit coordination services.<sup>33</sup>

### **Special Needs of Children: Safe Harbor Laws**

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Any minor under the age of 18 is under federal law considered a victim of sex trafficking—regardless of whether or not there was the use of force, fraud, or coercion. Children who become victims of human trafficking have specific needs. Many have been treated as criminals and prosecuted accordingly. Arrest and prosecution can further traumatize these victims, leaving them with a profound distrust of law enforcement that prevents them from seeking assistance. Furthermore, the criminal record resulting from prosecution can serve as a barrier to future employment and other opportunities.

Thirty-four states have enacted laws that both protect and assist children who have been exploited for labor or

sex. **These laws—known as Safe Harbor Laws—have two components: legal protection and the provision of services.** Legal protection provides immunity from prosecution or places the child in a diversion program through which charges will be dismissed if the child completes the program. The services component ensures that the child is provided with medical and psychological treatment; emergency and long-term housing; legal services; and assistance in obtaining an education, a job, or translator.<sup>34</sup>

### **The Role of the Healthcare Professional**

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All healthcare professionals who think they have come in contact with a victim of human trafficking should call the National Human Trafficking Resource Center hotline: 1-888-373-7888. The hotline can also be reached by email: [help@humantraffickinghotline.org](mailto:help@humantraffickinghotline.org), by text: text HELP to 233733 (BEFREE) or by online chat: [www.humantraffickinghotline.org](http://www.humantraffickinghotline.org). This Center serves victims of human trafficking and the anti-trafficking community across the United States and its territories 24 hours a day in more than 200 languages. The Center will help determine whether the person identified is a victim of human trafficking and identify resources that are available in the individual's community to help. It will also assist in the coordination of local social service organizations.<sup>35</sup> 📄

**Table 1:**  
**Red Flags of Human Trafficking<sup>36</sup>**

**The trafficked individual:**

- is with a person who speaks for them
- is unsure of current day, date, month, or year
- moves frequently
- is not in control of personal identification
- doesn't know where s/he lives
- gives a story that sounds scripted
- is not allowed to come and go at will
- wears the same clothes over and over
- seems to be afraid to answer questions
- works long hours; seems exhausted; hungry
- has someone else controlling his/her money
- sleeps/lives at the worksite
- can't move freely
- is in debt to his/her employer

**Table 2:**  
**Approach to Suspected Cases of Human Trafficking<sup>37</sup>**

- Establish a rapport with the victim, assuming a nonthreatening position (i.e., sitting rather than standing).
- Use eye contact, facial expressions, and body language that communicate an empathic stance; use active listening skills; be respectful and nonjudgmental.
- Recognize red flags.
- Treat immediate medical and basic needs first.
- Secure privacy (the process of separating a client/patient from accompanying persons requires tact).
- Examine the intake process to determine the steps at which this can be done naturally without the raising the suspicion of accompanying persons.
- Ask culturally sensitive, open-ended questions about safety, employment, living environment, documents.
- Use a multidisciplinary approach that involves social workers, interpreters, and law enforcement when appropriate.
- Recognize that your patients may not be ready to leave their situation for a wide variety of reasons, including fear of harm to themselves or loved ones.
- Create a trusting and safe environment to which the individual will feel comfortable returning.

## *About the Faculty*

**Donald Kushon, MD:** *Dr. Kushon is a Board-certified Psychiatrist and Associate Clinical Professor in Psychiatry at Drexel University College of Medicine. He is Medical Director of Adult Services at Joseph J. Peters Institute, which offers survivor services for victims of all types of trauma and treatment for those who have engaged in sexually abusive and domestic violence offenses. He has published mostly in the area of Consult-Liaison and Medical Psychiatry.*

**Brandi J. Stewart, PsyD:** *Dr. Stewart has been working in the field of sexual abuse and trauma for more than 20 years. She is licensed to practice psychology in the State of Pennsylvania. Currently, Dr. Stewart is Director of Clinical Services at Joseph J. Peters, one of very few agencies in the nation that provide a comprehensive approach to trauma, addressing the entire cycle of abuse. Dr. Stewart oversees outpatient programs for adult, adolescent, and child survivors of trauma, as well as five Safety and Responsibility Programs serving adolescents who have exhibited sexually inappropriate behaviors and adults who have engaged in sexually abusive behaviors and/or relational violence, as well as a Johns' school and a partial hospitalization program for adult males with serious mental illness and sexually inappropriate behaviors. Dr. Stewart has also operated her own private practice since 2006.*

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## Multiple-Choice Questions

**5. Signs of sex trafficking victimization include all of the following, *except*:**

- A. Tattoos or brandings.
- B. Coerced abortions.
- C. Gender identity confusion.
- D. Traumatic brain injury.

**6. Hostage identification syndrome:**

- A. Explains why most victims accept help.
- B. Is associated with traffickers giving gifts and making kind gestures to their victims.
- C. Is recognized as a mental health disorder by the DSM-5.
- D. Explains why victims risk their lives to escape their traffickers.

**7. Safe Harbor Laws:**

- A. Provide legal protection and ensure the provision of services.
- B. Do not apply to noncitizens of the United States.
- C. Support prosecution for child prostitution.
- D. Cover all victims of sex trafficking, regardless of age.

**8. The incidence of internet sex trafficking:**

- A. Has declined due to ad screening.
- B. Is limited by the requirement of authentic identification from would-be traffickers.
- C. Has been curtailed substantially through collaboration among the police, governmental agencies, and information technology companies.
- D. Is aided by encryption and the dark web.



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# Best Practices in Continuing Medical Education

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## Human Trafficking

Donald Kushon, MD; Brandi J. Stewart, PsyD

ID#: L003444

This valuable take-home reference translates research and theory that are presented in the accompanying *continuing medical-education* (CME) lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.

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### CME Lesson Overview

The incidence of human trafficking is increasing at an alarming rate. Healthcare professionals may encounter victims of human trafficking in a variety of clinical settings and are in a unique position to reach out to them and refer them to programs that can provide the care they need. Many victims of human trafficking experience serious emotional and physical health issues. In the United States, the majority of sex trafficking victims are women and children who are US citizens. US Safe Harbor Laws are designed to protect anyone under the age of 18 years who has been induced to commit a commercial sex act. Determining the mental health needs of victims of human trafficking begins with a comprehensive assessment that includes psychological, psychiatric, and medical components. Trauma-focused behavioral therapy, along with appropriate psychopharmacotherapy and medical care, are the main components of the initial treatment plan.

#### Key Point 1: Human Trafficking Has Become the Third Largest Criminal Enterprise in the World and Continues to Grow at an Alarming Rate

The Global Slavery Index estimates that approximately 45.8 million people are enslaved worldwide, and that slavery is present, in one form or another, in 167 countries. The majority of trafficking victims are taken from less developed regions of the world (Africa, South and Southeast Asia, and Central and South America) and transported to areas where they will be the most “profitable.”<sup>4</sup> Developed nations also face human trafficking concerns. Approximately \$150 billion a year is generated worldwide through human trafficking, with sex trafficking accounting for 66% of this amount.

#### Key Point 2: The United States Has One of the Highest Rates of Trafficking Among Developed Countries

The United States is both a destination for international trafficking and a source for its internal trafficking networks. It also has one of the highest rates of human trafficking among all the developed countries. An estimated 199,000 trafficking incidents occur in the United States every year. California, New York, and Texas are the top three states in terms of frequency of human trafficking events.

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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**Key Point 3: Most of the Sex Trafficking Victims in the United States Are Women and Girls Who Are US Citizens**

Approximately 14,500 to 17,500 people become victims of sex trafficking in the United States every year. Of these, 80% are women and children.<sup>8</sup> Interestingly, 83% of sex trafficking victims in the United States are US citizens.

**Key Point 4: Safe Harbor Laws Protect and Assist Children Who Have Been Exploited for Labor or Sex**

Under federal US law, any minor under the age of 18 years who has been exploited for labor or sex is considered a victim of sex trafficking, even in the absence of force, fraud, or coercion. Thirty-four states have enacted laws to protect and assist children who have been exploited for labor or sex. These laws—known as the Safe Harbor Laws—have two components: legal protection and the provision of services.

# Behavior Therapy for the Treatment of Dementia in Elderly Psychiatric Patients

Daniel C. Marston, PhD, ABPP

*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Dementia • Major neurocognitive disorder • Behavior therapy

**LEARNING OBJECTIVES:** On completion of this lesson, the reader should be able to list major behavioral issues associated with dementia and major neurocognitive disorders, review how behavior therapy can help individuals with dementia, and incorporate behavior therapy concepts into helping caregivers assisting individuals with dementia.

**LESSON ABSTRACT:** Dementia is a major medical disorder that causes difficulties with behaviors, cognitive functioning, mood, and general functioning. These difficulties with cognitive functioning are typically diagnosed as “major neurocognitive disorders” in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5). Behavior therapy for dementia helps individuals learn and use effective skills to manage the changes associated with cognitive decline. This is achieved by working with both the individual who has dementia and relevant caregivers. Individual approaches focus on helping individuals learn skills to compensate for losses and not become overwhelmed by negative changes. Behavioral planning provides approaches that caregivers can use to help people with dementia better deal with major changes. Effective behavioral programs start with a “functional behavioral analysis,” which is used to identify the purpose(s) of the problem behaviors. It is also essential to consider memory issues when implementing behavioral approaches for individuals with dementia.

**COMPETENCY AREAS:** Readers will obtain knowledge about how to utilize behavior therapy for the treatment of individuals with dementia. Clinicians will learn how to apply patient-centered care and employ evidence-based practices in the administration of behavior therapy. This lesson describes interpersonal skills in relating to patients with empathy and understanding.

## Introduction

Impairments in memory, attention, comprehension, and other areas of cognitive functioning often occur with aging. While everyone faces some degree of cognitive impairment when they get older, some neurological conditions involving impairments typically associated with aging are much worse and impact functioning much more severely than typical cognitive decline. These cognitive impairments are most often associated with a medical, specifically, neurological diagnosis known as “dementia.” Some neurological diagnoses associated with different types of dementia include Alzheimer’s disease, Parkinson’s disease, stroke, Huntington’s disease, and chronic alcoholism.

Whereas “dementia” is the diagnosis for medical conditions leading to severe cognitive impairment, “major neurocognitive disorder” is the psychiatric diagnosis category that encompasses cognitive impairment. **Different types of dementia are listed in the medical diagnostic codebook, the *International Classification of Disease (ICD)*, and different types of major neurocognitive disorders are listed in the psychiatric codebook, the *Diagnostic and Statistical Manual of Mental Disorders (DSM)*** At the time of writing this report, the most current version of the ICD is “ICD-10,” and the most current version of the DSM is “DSM-5.” These two categories are directly related, as all forms of major neurocognitive disorders are related to some forms of dementia.

DSM-5 lists the following as the cognitive areas that can be impacted by major neurocognitive disorders:<sup>1</sup>

- **Attention**
- **Executive functioning**
- **Learning and memory**
- **Perceptual motor skills**
- **Social cognition**

Diagnoses of dementia and major neurocognitive disorders target the medical and cognitive aspects of the diseases leading to significant cognitive changes. These are cognitive changes most often, though not always, associated with old age. However, the most common complaints associated with these conditions are behavioral and emotional, rather than medical or cognitive.

Even the cognitive complaints that make people seek help are often related to behavioral functioning (e.g., being unable to function in social environments because one forgets people’s names or becoming anxious because one can no longer follow directions).

Listed below are the most common types of behavioral and emotional problems associated with dementia and major neurocognitive disorders:<sup>2</sup>

- **Agitation**
- **Depression**
- **Apathy**
- **Repetitive questioning**
- **Psychotic symptoms**
- **Aggression**
- **Sleep problems**
- **Wandering**
- **Socially inappropriate behaviors**

## Behavior Therapy and Dementia

Behavior therapy is a type of psychotherapy that addresses the triggers and consequences of problematic behaviors and endeavors to find alternative approaches and outcomes that can help diminish the frequency of those behaviors. This approach to therapy is based on the theory of human psychology made famous by behavioral psychologists such as Ivan Pavlov and B. F. Skinner. This theory proposes that all behaviors exist because they are reinforced when desired outcomes follow the behaviors. When a person exhibits a behavior, it is because that behavior previously resulted in a positive outcome. Conversely, this means that undesired outcomes make it less likely that a behavior will be exhibited in future situations. When there are multiple responses to a behavior, the strongest response will have the greatest impact on the behavior.

People often associate behavior therapy, “behavioral approaches,” and “behavior modification” with a person obtaining concrete rewards (e.g., money, tokens, or food) in response to behaviors. However, other desired outcomes that can reinforce behaviors include attention

and praise. Furthermore, one powerful type of reinforcer can be the belief that one has control over their environment. Helping a person obtain the desired outcome can be reinforcing because it helps the person feel that they exert some control over their environment.

This latter point is important because experiencing a loss of control is a significant negative change for many people with dementia. Confusion and problems with memory often cause people to feel that they will no longer have the ability to make decisions or do necessary activities. Individuals with dementia often express concern that others might take advantage of them because of their confusion. These difficulties all exacerbate the depression and anxiety related to dementia.<sup>3</sup> **Behavior therapy approaches often help individuals learn skills that they can use to compensate for the increased cognitive challenges. Moreover, behavior therapy focuses on helping individuals find more effective means of dealing with emotional distress and reinforce behaviors that can mitigate the emotional impact of losing cognitive abilities.**

A positive perception of oneself can also be reinforcing. We all want to feel positive about ourselves, and we accomplish this through the statements we make to ourselves and to others. When we consider that statements we make about ourselves, both positive and negative, are basic behaviors (any type of speech), it becomes clear that this is also a component of behavior therapy.<sup>4</sup> Helping people to more strongly believe positive statements about themselves is a common goal in behavior therapy. This is particularly important when working with individuals with dementia because decreasing cognitive functioning can be emotionally devastating. Helping patients focus on ways to reinforce positive statements about themselves is highly important (e.g., *"I am still a good person, even though I cannot do as much as I did,"* and *"There are still positive parts of my life, even if I am more confused."*).

**Behavior therapists generally work on two primary levels in terms of providing dementia care. The first is an individual level, wherein the therapist helps the individual learn and use practical skills to manage the cognitive deficits associated with dementia.** These interventions also focus on specific steps that can help minimize problems with anxiety, depression, and anger, which often accompany dementia. **The second level**

**focuses on developing behavioral plans that can be used by caregivers who interact regularly with the individual.** These interventions primarily address skills caregivers can use to help diminish the individual's difficulties dealing with the impact of dementia.

## Individual Behavior Therapy Approaches

Maintaining memory functioning and compensating for memory loss is one of the major treatment goals for people in the early stages of dementia.<sup>5</sup> This may include helping the person learn compensatory skills for dealing with memory loss and confusion and also encouraging behaviors that can help the person deal more effectively with negative changes.<sup>6</sup> Some examples might include using calendars and written reminders. Behavior therapists typically work with patients to determine the approaches that are most likely to help the person remember or understand things and then work out a plan for how they will implement these strategies.

Keeping memory strategies as basic and concrete as possible is essential because it helps one remember and use them. Once the behavior therapists choose the specific types of approaches that are likely to be most helpful, they can then work with patients with dementia to develop a plan for implementing these strategies in their daily lives. Behavior therapy sessions are also used for role-playing and to practice employing the strategies. In addition, behavior therapists work with patients and help them overcome any negative statements they make about themselves about having to use memory aids (e.g., *"I must be stupid to have to use a calendar to remember everything."*) and replace them with positive and realistic self-statements (e.g., *"Being forgetful does not make me stupid."*).

These compensatory approaches often minimize depression and anxiety associated with dementia.<sup>7,8</sup> When people learn methods to compensate for memory loss, they feel that they have some control over their lives and how dementia impacts them. A greater sense of control reinforces the behaviors that lead to improvement and also diminish anxiety and depression.

**"Behavioral activation" is another essential behavioral therapy approach used to treat dementia-related depression. It emphasizes increasing the number of**



**positive activities in a person's day.**<sup>9</sup> Maximizing positive activities helps lessen the impact of losses and stress associated with dementia. This also helps because dementia tends to lessen one's ability to continue with positive activities. Continuing these activities at a high level sets the stage for maintaining a balance between positive and negative activities because dementia interferes with one's ability to improve how one deals with adverse changes.

Behavioral activation sessions involve reviewing the activities the dementia patients deem positive and how they participate in these activities. These activities need not be substantial (e.g., "go out with my friends"); they may include even minor activities persons with dementia find positive (e.g., "I look at the birds outside"). This review also includes activities the person remembers as positive but no longer engages in. All of this data is collected along with the person's ranking of the activity's positivity ("0" meaning "not positive at all" and "10" meaning "the most positive thing imaginable"). The behavior therapist then works with the patient to determine means to maximize the number of positive activities the person engages in each day. Discussions during sessions should focus on finding means to increase the frequency of positive activities and removing the obstacles hindering persons from participating in more of them. Keeping records of positive activities is important for these sessions, and written reminders should be used to prompt the patient to engage in positive activities throughout each week.

Phone apps can also help individuals keep track of their positive activities throughout each week.<sup>10</sup> Stress management techniques are helpful during the early stages of dementia. This helps not only to reduce anxiety related to cognitive decline but has also been shown to slow cognitive decline.<sup>11</sup> Traditional muscle relaxation techniques that teach individuals how to reduce tension in all muscle areas are helpful.<sup>12</sup> But the most effective stress management approaches for dementia are meditation and mindfulness. The specific type of meditation helpful in dementia is Kirtan Kriya meditation.<sup>13</sup> The following highly useful website outlines the steps involved in this meditation: <http://alzheimersprevention.org/research/kirtan-kriya-yoga-exercise/>.

Approaches to mindfulness<sup>14</sup> involve exercises that help the person not react to stress and anxiety and methods to effectively "let go." One form of behavior

therapy that stresses mindfulness is *acceptance and commitment therapy* (ACT). This therapy has not been studied specifically with dementia patients, but a form of ACT used to diminish emotional distress in individuals with psychotic symptoms does present an approach that could be similarly helpful for individuals with dementia.<sup>15</sup> This approach emphasizes teaching patients to accept unavoidable negative thoughts (considered to be a form of behaviors that are not observable to other people), focus on actions that are directed toward goals consistent with the person's value system, disconnect from "odd" types of thinking (so the individual treats this thinking as simply a behavior that does not warrant any specific response), and "just noticing" negative thoughts as behaviors rather than treating them as necessarily true or false (or as something to which she or he has to respond).

Dementia is often considered a disorder of social communication because it creates difficulties interacting with others.<sup>16</sup> Communication and social skills training in behavior therapy are similar.<sup>17,18</sup> Both use basic instructions, role-playing, problem-solving, and practice. Instructions should focus on teaching the important factors influencing effective communication and social interactions. For older individuals, this often involves reminders of what is involved. Role-playing involves identifying types of situations that are likely to cause problems and determining means to manage them. Role-playing exercises entail identifying the types of situations that cause problems and finding methods to deal with them effectively. The increasing strength of learning helps prevent individuals from forgetting skills, even as cognitive impairment increases. Problem-solving helps individuals learn specific steps for handling challenging situations effectively.<sup>19</sup> This approach often involves breaking problems down into smaller concrete steps and adopting a systematic approach to addressing each step.

Combining behavioral approaches and emotionally supportive interventions in sessions can be highly effective in mitigating the emotional distress associated with worsening dementia.<sup>20</sup> In fact, one specific type of psychotherapy, called "supportive psychotherapy," combines well with behavior therapy when it comes to helping dementia patients. Supportive therapy can be helpful in decreasing the emotional impact of dementia on individuals who recognize that their memory and thinking

are getting worse.<sup>20</sup> Specific behavioral approaches that are associated with supportive psychotherapy (and fit well when combined with behavior therapy) include the following:<sup>21</sup>

- **Formulating a clear conceptualization of the problems and issues the patient faces in terms of difficulties dealing with worsening dementia**
- **Providing clear guidance on steps the person can take to achieve therapy goals**
- **Showing concern and unconditional support for the patient**
- **Using the therapy session to help the person practice how to effectively communicate with others when dealing with emotional distress and cognitive difficulties**
- **Helping the person use effective coping mechanisms**

Dementia and its associated cognitive impairment is a condition that typically becomes worse over time. This decline might be progressive (continually getting worse on a straight path over time) or stepwise (getting worse, leveling off for a time, and then getting worse again). Progressive worsening is associated with medical conditions such as Alzheimer's disease, and stepwise worsening is associated with conditions such as strokes. Behavior therapists are often called upon to provide methods to continuously help individuals with dementia deal with cognitive impairment as their functioning declines.

Yokoi et al. developed a behavior therapy approach that helped individuals with dementia find means of maintaining positive perceptions of themselves and others' positive perceptions of them, even as the individuals' worsening functioning led to nursing home admissions.<sup>22</sup> They worked with the residents and had them start wearing jewelry that they liked, which evoked positive responses from other people. Finding the best jewelry was important, as was increasing the consistency with which the individuals kept the jewelry. This resulted in many positive comments from staff during the week. The researchers found that the increase in positive comments reduced the resident's irritability and lability, even as

their confusion and physical limitations increased. They hypothesized that this improvement occurred because the positive feedback from others helped to increase the residents' self-esteem and self-awareness.

## Behavioral Planning

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Behavior therapy also involves working with caregivers of individuals with dementia. This could be family members if the person is still living at home, or it could be nursing staff if the person is living in a nursing home or rehabilitation facility. Behavior therapists work with caregivers to help them understand the approaches they can use to diminish the behavioral and emotional difficulties experienced by individuals with dementia. Behavior therapists often help caregivers work out a plan for the effective implementation of these interventions. They also provide stress management and other interventions to lessen difficulties faced by caregivers when implementing these approaches.

The level of approach (i.e., individual-focused or caregiver-focused) emphasized in behavior therapy is typically dependent upon the remaining communication abilities of the individual with dementia. If the person's ability to communicate is adequate, even if it is below average, then the emphasis will be individual-focused, addressing skills the person can use to reach his or her goals and meet his or her needs. If the person's communication skills and independence are more impaired, then the focus will be on helping the caregiver to learn and use approaches that can help mitigate the person's difficulties managing cognitive impairments.

Behavioral planning should start with a thorough assessment that identifies factors contributing to behavior problems. This requires a highly specific definition of the behavior problems and methods to measure when the behaviors occur, as well as the frequency and the severity of the behaviors. Conducting such an assessment creates behavioral approaches that are ideal for helping the person experience the same outcomes with behaviors that cause fewer difficulties. Behavioral planning can also focus on reducing the emotional distress that might contribute to behavioral outcomes. Once these approaches are developed, behavioral therapists can then focus on maximizing the consistency and frequency of use of these approaches. This type of assessment is called "*functional*

*behavioral analysis* (FBA).” In a review of behavioral research on dementia, Moniz-Cook et al. demonstrated the importance of functional analysis for addressing behavior problems.<sup>23</sup>

**Functional behavioral analysis emphasizes the “ABC” approach to analyzing behaviors, wherein A stands for “antecedent” (i.e., what occurs before a target behavior), B stands for “behavior” (i.e., where the target behavior is defined in measurable and observable terms), and C stands for “consequences” (i.e., what occurs after a behavior).**

Conducting FBA requires the observation of these aspects of target behaviors multiple times every day. This data can be collected by family members, spouses, or health-care facility staff. Nursing home staff can be taught by behavior therapists how to conduct FBA.<sup>24</sup> Each episode of problem behavior is described in terms of what happened just prior, what specific behavior was observed, and what happened right after the problem behavior occurred. The data is collected over days or weeks (the longer the time involved, the better) and analyzed to identify the specific factors most commonly associated with the target behaviors.

FBA provides important and useful information for analyzing the factors that contribute to the occurrence of problem behaviors. Once this information is available, the behavior therapist can try to address these factors.

Every behavior has a goal (or “function”), and the task of an FBA is to identify the factors perpetuating the problem behaviors. Once these functions are identified, the behavior therapist can then develop approaches that can help the individual reach those goals in less problematic ways. Some of the common functions of problem behaviors in dementia include escaping difficult situations, challenging problematic environments, reducing emotional distress, and getting attention.

Mansfield et al. presented a model of behavior problems in dementia emphasizing that the function of behavior problems is often that they help to satisfy “unmet needs.”<sup>25</sup> Problem behaviors such as yelling, screaming, wandering, and hitting, in this model, occur specifically because they help a person meet needs that he or she has been unable to fulfill. The four most common unmet needs include sensory stimulation (to combat boredom),

social interactions (to combat loneliness), meaningful activity, and having physical pain addressed.

Behavior therapists conduct FBAs to collect data on what perpetuates behavior problems. If, for example, boredom is found to be a function of problem behaviors, then the behavior therapist would work with caregivers to identify methods to reduce boredom. Knowing when the behavior problems occur would also help the behavior therapist work with caregivers to ensure steps are taken to prevent boredom at the most difficult time of the day. If getting attention is a function contributing to yelling and screaming, then the behavior therapist can work with caregivers to ensure that the individual receives attention on a regular basis. Ensuring that caregivers check on the person throughout the day, even if nothing is happening, is an important way to give the person attention. Attending to the person is the optimal means to address this type of behavior, as opposed to giving the person negative attention for their behaviors (e.g., yelling at the person for their yelling behaviors). A general rule is applicable here: “People want attention, and if they can’t get good attention, they’ll usually settle for the bad attention.”

Giving persons with dementia more options can help them exert more control over their lives. Losing cognitive functioning entails a considerable amount of emotional distress because the affected person loses their ability to do things independently and even to remember what needs to be done. Disruptive behaviors such as yelling and screaming can often occur as the person attempts to maintain control over environments in which they feel their ability to exert any control is disappearing. Staff at nursing facilities often help patients with dementia by finding ways to help the patients gain control and make choices.<sup>26</sup> Very often, for nursing home residents, this will take the form of “forced choices,” wherein persons with dementia are given a limited number of options from which to choose (e.g., “*would you like to wear the blue shirt or the green shirt today?*”). This helps the individual feel a sense of control without overwhelming or confusing him or her by offering too many options.

Behavior therapists also play a role in helping individuals with dementia make use of memory aids and support available at nursing facilities. Nursing facilities generally have their own plans for helping residents remember where they are, what rooms they are in, and how to participate

in activities and therapies. However, merely having these aids and supports is often insufficient to ensure they are being used. When, for example, nursing homes use aids to help residents navigate hallways and different rooms to find important areas, the residents often need practice and support to ensure they are actually using those aids and paying attention to them.<sup>27</sup> Ensuring that persons with dementia remember that they have memory deficits is important, as it helps them make more consistent use of behavioral cues.<sup>28</sup> Behavior therapy sessions can focus on providing opportunities to practice these cues and increasing the attention individuals pay to those cues and reminders.

In terms of deciding what type of responses are likely to increase positive behaviors, it is important to note that determining effective reinforcement can be a detailed process. One factor that prevents professionals not trained in behavior therapy from using reinforcement effectively is that they often assume that identifying reinforcers is a simple and straightforward process. They presume that giving something positive to someone with dementia for doing what you want them to do will cause the behavior to increase. But human beings are much more complicated than that and deciding what a person with dementia will find reinforcing is also more complicated. Behavior therapy is most effective when the therapist interviews the patient to determine what they deem reinforcing. There are also instruments, called “preference assessments,” that are specifically designed to identify the reinforcers that are likely to help specific individuals.<sup>29</sup> In addition, nursing homes benefit from behavior therapists conducting interviews to identify the activities persons with dementia will find meaningful (and not just “fun” or “pleasant”). Research has demonstrated that individuals in nursing homes are much more likely to participate in and benefit from activities they find meaningful. It has also found that factors such as being connected with the immediate environment and not feeling alone are strongly associated with finding activities meaningful.<sup>30</sup>

## Memory Issues in Behavior Therapy for Dementia

Memory is an important issue for dementia care because remembering approaches discussed in the session is important for effectiveness. If someone cannot recall what

is discussed from session to session, then approaches will not be effective. This does not mean that the person must remember every detail of what is covered in each session, but it is important that the person recalls something about each session and about therapy in general.

When discussing behavior therapy for someone with memory problems, it is essential to recognize that there are different types of memory. Focusing only on one type of memory (e.g., memory exclusively dealing with facts) can minimize the importance of other types of memory. This presents a challenge in relation to helping someone with dementia: If an approach emphasizing one type of memory does not work, this does not mean that an approach emphasizing another type of memory will not work.

For example, if a woman with dementia cannot recall her daughter’s name, it does not mean that she does not remember her daughter. Memory concerning facts is different from what memory regarding those facts means.

**Emotional memories are recalled more effectively than neutral memories.**<sup>31</sup> Therapy sessions often focus on addressing emotional material, and this can be a means to make therapy sessions memorable. If the patient is given an opportunity to express their concerns emotionally in an open and supportive environment, this can help to ensure the person better remembers what was discussed in sessions. Expressing deep concern about how they are feeling also helps persons with dementia remember what is being addressed.

**Making the therapy sessions an emotionally pleasurable experience is also helpful.** This author tends to wear colorful shirts and ties and has noticed that individuals with dementia tend to remember him and what he says more than other professionals because of the way he dresses tends to stand out. This increases the likelihood that individuals with dementia will experience the sessions as pleasant and even joyful. It also helps individuals with dementia remember who the author is and what he has come to talk to them about.

**Social interactions are also more helpful for remembering material than non-social interactions.**<sup>32</sup> Behavior therapists help individuals with dementia remember therapy interactions when they focus on the social aspects of therapy. The therapy opens with positive social introductions that emphasize and ensure



that persons with dementia remember the therapist and what the therapist does (or reminding the individual of that information). Subsequently, keeping the therapy approaches in a focused, but also a friendly and congenial manner helps with recall. Therapists need to clarify that they are not “just visiting” when conducting therapy; the social pleasantries that accompany social visits can be incorporated into therapy work.

**Consistency is also vital to increase the probability that someone will remember what you talked to them about.** Presenting approaches, in the same manner, helps to increase the likelihood that persons with dementia will remember what the behavior therapist discussed with them.

If the therapist meets with individuals every week, the approach must be consistent each week. How the behaviors are addressed, and what approaches are presented must be the same each time which maximizes the effectiveness of behavioral approaches.

For example, imagine a therapist who is helping someone with dementia learn better anger management skills. The therapist might start each session by asking the individual how the week went. Each week, the same question should be asked at the beginning of each session for consistency. The therapist would then ask about specific problems the person faced. Each time, the therapist would focus on specifics regarding what caused the problems and how the person dealt with the problematic situation. This consistent approach (the therapist asks about problems the same way each time) would make it more likely that the person recalls what the therapist expects each time and better recalls what was discussed during these sessions.

## Case Study I

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### Presenting Clinical Issues:

Rebecca was recently diagnosed with dementia. She began taking a medication prescribed by her physician that was intended to slow down her cognitive deficits. However, she noticed that she was forgetting things and struggling to learn new information. When she was referred to a behavior therapist, it was to help with the depression that she was experiencing because she noticed she was getting worse. She also stated that she felt like she was “losing her mind,” as

she perceived her cognitive ability slipping away. She reported to her therapist that her problems were related not only to depression but also to her considerable frustration.

### Therapeutic Approaches:

Her therapist initially worked with her to identify where she was noticing the most difficulties. They developed a list that identified specific challenges Rebecca experienced during the week and then rated how much the difficulties impacted her functioning. If she forgot an appointment, it would be rated an 8, as it would reflect that she had the potential for missing that appointment. Conversely, forgetting her television show would be rated a 4, as this was not as important, and there was an opportunity that she could record it later. This list was used as a starting point to identify where she was experiencing the most frustration and the situations that were causing her the most difficulties. Rebecca’s therapist then worked with her to record her thoughts when she was feeling depressed or frustrated about what was going on. As Rebecca was told to record a feelings journal to identify emotional responses to these difficulties, they noted that she tended to react strongly to any problem she faced. She tended to think that any problem related to her memory difficulty meant that she was “losing her mind.” Her behavior therapist then developed a treatment plan based on the conceptualization that Rebecca was responding to any difficulties with “all or none thinking” (a therapy term referring to when a person makes negative statements about themselves whenever a situation does not turn out exactly how they think it should). This was a good starting place to help her be more realistic in terms of rating the degree of difficulty she was experiencing. This produced a more detailed hierarchical list of her memory-related difficulties. Once this list was developed, Rebecca and her therapist worked on identifying memory aids she could use to minimize her recall problems. This included writing things down and using alarms on her phone to remind her of things she needed to

do. Going through this list with Rebecca helped her therapist work on getting her to open up about her feelings regarding what always happened to her.

#### Case Resolution:

Rebecca was experiencing a considerable degree of depression because she felt the positive aspects of her life slipping away. Her therapist was then able to work with her to help her keep track of the remaining positive elements of her life and to find ways to incorporate more positive elements to minimize her depression. This had to be modified over time, given Rebecca's worsening memory difficulties. As her memory problems intensified, her therapist worked with her to identify other positive aspects of her life that Rebecca could recall. Rebecca's therapist also worked with her during her session to develop a more realistic focus on what she could still do and how losing her memory did not mean that she was "losing all of herself" or "losing her mind." Adopting this approach diminished her depression and frustration during the two years when she noticed she was having increased memory problems.

## Case Study Two

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#### Clinical Presentation:

Joseph was an elderly man diagnosed with dementia several years before starting behavior therapy. When the behavior therapist began working with him, he had been placed in a nursing home. He was depressed due to not being able to live independently and being uncertain about why he had to live away from home. His wife had passed away two years earlier. His family visited on a regular basis but lived out of state; therefore, they were not able to visit as much as they wanted. He was seen for behavioral therapy due to problems with refusing to participate in any activities. He also was refusing care and was devoting only limited effort to the physical therapy provided at the facility.

#### Therapeutic Approaches:

When his behavior therapist started working with him, the first step was to gather information about the occasions when Joseph was refusing to participate in care. Staff at the facility were asked to collect data about when he refused care and when he made statements suggesting that he was devoting limited effort to what he was told to do. It became clear from the collection of data that Joseph's refusals were often attempts to gain a feeling of control over what was happening. Data revealed that he would most often refuse when being told what to do (as opposed to being asked to do things, which he preferred) and when he was given the option to not exert effort. The data also revealed that he would make statements indicating that his desire for control over his environment was the reason that he was refusing. These would include statements such as "*I don't want to do that thing right now,*" and "*I am tired of people telling me what to do.*" His behavior therapist began with a plan which entailed giving him basic choices whenever possible. This involved staff involvement to identify ways that they could provide him with choices during the day. This was done while simultaneously working with staff to remove the choice aspect of when he needed to do things. Thus, when staff needed him for physical therapy, he was not asked "Do you want to go to therapy?" Instead, a supportive statement was made specifically about what he was expected to do. Staff would then offer him choices about matters such as what he wanted for dinner and what he wanted on the television so that he would be given as many choices as possible throughout the day. This last step was taken after data also revealed that Joseph focused on choices that were easiest. Statements suggested that one of the reasons he was refusing to do things was because he was finding it too difficult to understand what people were telling him to do. Therefore, he often would refuse as a means of minimizing his difficulties understanding what he needed to do. He would do this to avoid a situation that was causing him difficulties. The staff would



present highly direct and concrete statements of what he was expected to do, without creating complications by offering him multiple choices regarding what he needed to do. This caused him to express less emotional distress about not understanding what was expected of him.

#### Staff Recommendations:

Joseph's behavior therapist also worked with staff to increase the consistency of his environment and schedule each day. Making things more consistent and predictable for Joseph diminished the frequency of his problems with confusion. His behavior therapist also worked on means to ensure that Joseph remembered who he was and why he was working with him. This included wearing shirts and ties that Joseph tended to remember and reviewing with him what they had discussed previously. These approaches were all employed to minimize Joseph's problems with remembering what was going on around him. This helped Joseph experience fewer episodes in which he did not recall what was going on throughout the day. It also made the times when he did have difficulties seem less severe (because they were not happening, as he put it, "all of the time").

#### Case Resolution:

As Joseph was helped in compensating for his confusion and memory difficulties, his behavior therapist worked with him to increase his positive statements about himself and his life, even as he still recognized that he struggled with confusion. Helping him make statements about how he had been able to do his best handling

his problems and reminding him of ways that he handled problem situations effectively helped mitigate Joseph's concerns that he would not be able to find ways of dealing with whatever problems he faced. Some of these statements included "*I am doing the best that I can,*" and "*everything is going to be okay regardless of what problems come up.*" These statements were repeated in session, and Joseph could repeat them consistently on his own after several sessions. Repeating these positive statements helped him develop a more positive attitude about himself and his life. Keeping the therapy sessions consistent and memorable, focusing on highly specific behaviors and statements that could decrease his level of depression, increasing his use of positive statements, helping staff keep his schedule and environment consistent, as well as encouraging Joseph to participate in more activities were all behavior therapy interventions that helped to improve Joseph's mood over time.

## Conclusion

Patients with dementia and their families face many difficulties that severely disrupt their lives. Changes in mood, behavior, memory, and thinking substantially alter how people with dementia feel about themselves and how they act towards and around important people in their lives. Medical treatments play only a minimal role in helping to improve these difficulties. Behavior therapy serves an even more important role in helping individuals and families confront challenges associated with dementia by helping patients adapt to the changes in how they process information and respond to what is happening around them. ■

### *About the Faculty*

Daniel C. Marston, PhD, ABPP: Dr. Marston is the owner of Marston Psychological Services in western Pennsylvania. He is a licensed psychologist who is board-certified by the American Board of Professional Psychology (ABPP) in Behavioral & Cognitive Psychology. He is the author of two books and numerous professional articles on the application of behavioral science research to clinical work.

L003445

## Multiple-Choice Questions

**9. Behavior therapy is a type of therapy focused on:**

- A. Agitated and withdrawn behaviors.
- B. Unconscious and conscious feelings.
- C. Triggers and consequences of problem behaviors.
- D. Past and future difficulties.

**10. There are two levels of behavior therapy for dementia: individual approaches and \_\_\_\_\_:**

- A. Sleep studies
- B. Behavioral planning
- C. Feelings journal
- D. Research reviews

**11. Which one of the following is a behavior therapy approach focused on increasing positive activities throughout each day?**

- A. Systematic desensitization
- B. Mindfulness
- C. Behavioral activation
- D. Gestalt training

**12. In functional behavioral analysis, the focus is on the “ABCs” of behavior problems, where the “C” stands for:**

- A. Consequences
- B. Culpability
- C. Changes
- D. Cantankerousness

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# Best Practices in Continuing Medical Education

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## Behavior Therapy for Treatment of Dementia in Elderly Psychiatric Patients

By Daniel C. Marston, PhD, ABPP

ID#: L003445

**This valuable take-home reference translates evidence-based, continuing medical education research and theory, acquired from reading the associated CME lesson, into a stepwise approach that reviews key learning points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### Overview Head

Behavior problems occur in dementia due to the individual trying to find ways of dealing effectively with his or her cognitive decline. These cognitive problems are associated with the psychiatric diagnosis “major neurocognitive disorder.” Behavior therapy involves both individual approaches and behavioral planning to help address the behavioral and emotional difficulties associated with dementia and major neurocognitive disorders. Individual approaches focus on helping the individual learn skills to deal with functional and emotional challenges associated with decreased cognitive abilities. Behavioral planning focused on ways caregivers can help individuals with dementia obtain behavioral goals (i.e., goals that behaviors accomplish, otherwise known as the “functions” of behaviors) without relying on problem behaviors. Therapists need to keep in mind strategies to help maximize the likelihood that patients with dementia will remember what is addressed in each session.

### Key Point 1: Individual Behavior Therapy Approaches

**Focus individual behavior therapy on compensatory strategies for memory loss and cognitive deficits, skills for handling emotional distress and behaviors for improving mood and outlook.**

### Key Point 2: Assessment

**Conduct a formal functional behavioral analysis for behavioral planning that focuses on identifying factors that contribute to the behavior problems being targeted.**

### Key Point 3: Behavioral Plans

**Behavioral approaches used by caregivers make up behavioral plans and focus on helping individuals with dementia use more effective behaviors to reach the same goal as their problem behaviors.**

### Key Point 4: Memory Issues

**Individuals with dementia can remember what therapists and caregivers do for them without necessarily remembering facts about them. Therapists and caregivers can use consistency, social interactions, emotional support, and specific environmental and interpersonal strategies to help maximize the likelihood that individuals with dementia will remember at least some of what is addressed with them.**

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This image shows a single sheet of white paper with horizontal ruling lines. The lines are evenly spaced and run across the width of the page. There are no margins, text, or other markings on the paper.

**Professional Development Series**

# You Too Can Do Marital Therapy: Expanding Psychiatric Practice to Include Marital Therapy

Otto Kausch, MD

*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Marital therapy • Expanding psychiatric practice • Successful and unsuccessful relationships

**LEARNING OBJECTIVES:** Upon completion of this program, the psychiatrist and other clinicians will be able to (1) discuss the relationship between many of the symptom complexes presented by their patients and an unhappy marital relationship; (2) explain the dynamics of successful and unsuccessful marital relationships; and (3) express confidence in his/her ability to conduct basic marital therapy.

**LESSON ABSTRACT:** This lesson not only aims to help psychiatrists learn how to expand their practice to include marital therapy, but is beneficial to all clinicians who encounter patients with marital challenges. The author reviews several factors that lead to unhappy relationships and the factors that can strengthen relationships. This lesson will teach a structured communication approach for use with couples. It is essential to learn the four most destructive communication patterns that cause a relationship to fail. One of the major tasks of the psychiatrist in marital therapy is to provide education on what is scientifically known about successful vs unsuccessful marriages.

**COMPETENCY AREAS:** This lesson addresses the gap in understanding by psychiatrists and other clinicians of how unsuccessful relationships contribute to the suffering of our patients. Psychiatrists will come to appreciate some of the barriers which may prevent them from adding marital therapy into their practices. They will learn knowledge of the basics of how to intervene in problematic marriages to improve the quality of life for patients. After reading this lesson, psychiatrists will better understand the dynamics of marital relationships and will hopefully feel confident and more competent that they can expand their practice to include basic marital therapy.



## Introduction

My intended audience is psychiatrists, both novice and more seasoned clinicians, who have little or no experience conducting marital therapy in their practice. This lesson is not meant to update psychiatrists who are already proficient and knowledgeable in this area. Further, I am not adopting an objective third-person voice, as is common in journal articles. Instead, I am using the first person and a more informal tone, similar to a teacher talking privately to the reader in a supervisory session. (In this, I am guided by the approach of Levine et al.).<sup>1</sup> While I understand that many readers are already very sophisticated in their general and also specialized areas of psychiatry, I view my role as guiding readers through the beginning stages of learning a new skill to perhaps expand their practice. I am avoiding a scholarly review of the research literature. The reader will see that I have certain biases or strong opinions in my approach to the subject in terms of what I choose to emphasize and the authors whom I reference.

**I have developed my interest in doing marital therapy by reading certain authors who I find especially interesting and who I have found to be inspiring. While there is a vast literature on the study of marital couples, marital therapy, and treatment approaches, I have chosen to narrow my focus, to simplify, so that the concepts are easily understood, and to inspire the reader to delve deeper into the subject. My references are limited in scope.**

It is uncommon for psychiatrists to engage patients in marital therapy, but it is not unheard of. Of interest, even Sigmund Freud tried marital therapy one time, but hated the experience, and in 1919 wrote a paper condemning it and recommended no psychoanalyst ever try to help any couple!<sup>2</sup> There is really not much scientific literature on psychiatrists adding marital therapy on to their usual practice. In fact, I recently received a flyer in the mail from the American Psychiatric Association titled "*Psychotherapy Resources*." Numerous books are listed which encourage psychiatrists to add various forms of individual psychotherapy to their practice. But, nothing at all about adding marital therapy.

Interestingly, specific subgroups of family physicians have embraced adding marital therapy to their practices, encouraging the principle of a preventive, holistic approach to improve the emotional and physical

well-being of their patients, and there is a small literature on this (e.g., 3). Among factors listed for this approach for family physicians is the stigma many patients attach to seeing mental health professionals. Such patients often prefer seeing a primary care provider for their relationship concerns.

Another small group of psychiatrists and other physicians who routinely see couples for treatment are those, such as Stephen Levine, MD, who specializes in sexual medicine.<sup>1</sup> In this, they follow in the footsteps of Masters and Johnson.<sup>4</sup> Dr. William Masters is an intriguing individual who was a prominent obstetrician and gynecologist specializing in human reproduction at The University of Washington in St. Louis, who then veered into his seminal work on human sexual response and physiology. While in medical school at the University of Rochester, he came under the influence of Dr. George Washington Corner, who was researching reproductive problems in animals and humans. Dr. Corner acted as a Master's mentor and inspired him to expand on the work done previously by Alfred Kinsey and colleagues at Indiana University. Kinsey had studied human sexual behavior but had relied on subjects' self-reports. Masters decided to actually observe subjects engaging in sexual behavior in his lab. He started this work after he had established his reputation in the field of infertility at Washington University in Saint Louis. He eventually partnered with Virginia Johnson.

Virginia Johnson dropped out of college and became a country music band singer. After several divorces, she found herself working full time as a single mother trying to raise her children. She felt stuck in life, so she decided to "better" herself. She enrolled at Washington University, intending to study sociology. However, she had to continue working to be able to support herself and her children. She looked for work at the university and found a position as a research assistant to Dr. Masters. He hired her and immediately saw that she had great potential because of her native intelligence and superior interpersonal skills. Virginia started out doing secretarial work in Master's office, which included taking personal histories from Master's subjects who had agreed to participate in his sexual behavior research. She became increasingly motivated and more involved in Master's research. He decided it would be best if he worked with a female

collaborator. He taught Virginia basic science as well as provided her with advanced training in the biological sciences. Before long, he took her on as an equal partner in his research, and they eventually coauthored a book on human sexual response for which they became famous.

Masters and Johnson came to understand that many couples, in fact, had unhappy relationships and the sexual life of one or both couples contributed substantially to their distress. They began to view it as their mission to work with couples who were unhappy with their sexual relationship and spent a lot of time, basically doing couples therapy. They went on to write a book addressing these issues from their perspective using their specialized approach.<sup>5</sup>

Therefore, because there is not much scientific literature on psychiatrists expanding their practice to include marital therapy, in this lesson I will describe my experiences so that others can get a sense of my approach should they choose to “take the leap.” That is not to say that this lesson lacks any emphasis on evidence-based practice. There is a large body of scientific knowledge about marital therapy and how to improve the functioning of couples in general, which I will selectively describe, and which is highly evidence-based.

## **Are All Couples Salvageable?**

Most marital therapy is performed by psychologists or other therapists who may or may not be certified in this specialty. However, the outcome is often not great. Although some couples are helped, many are not. Even the best trained have lots of disappointing outcomes, and one of the main reasons for this is that often by the time couples come in for therapy, their marriages are on the brink of death, and even heroic efforts can’t rescue them.

However, one should be aware that sometimes even seemingly doomed couples can be rescued. Let me provide an example from my clinical practice. This was one of my first attempts at marital therapy and a case that inspired me to continue.

The patient is a 35-year-old male who had come to me for help with “depression and emotional turmoil.” Two weeks ago, he had found his wife in bed with his best friend and found out they

had been having an affair. He had been crying uncontrollably and was having nightmares. He decided he was done with the relationship and had filed for dissolution. However, he also informed me that his wife did not want to end the marriage. I asked him if I could meet with her individually before I decided on a treatment plan for him. Despite a high degree of skepticism, he agreed, and she did then, in fact, come to see me individually. At our meeting, she was distraught, tearful, genuinely remorseful, and said she would do anything she could to save the marriage. I next brought my patient back in and told him I didn’t blame him for wanting to end the marriage. However, I suggested to him that in my opinion, it would be better for his mental health in the end if he and his wife tried to work on their marriage to see if there was some hope of rescue. After undergoing additional emotional turmoil trying to make up his mind, he decided to give it a try. I saw the two of them together for a while, and slowly the marriage was rebuilt. My patient’s mental health also greatly improved. That was two years ago, and the marriage is still enduring to this day, and both are glad they gave it another try.

## **Discovering and Treating the Pathogenesis of Psychiatric Syndromes**

In seeing many patients over the years, both inpatient and outpatient, I have noticed, as I’m sure have many of you, that a lot of psychiatric symptomatology is brought on by our patients’ relationship struggles. This perspective has been discussed by Levine.<sup>6</sup> Our patients’ sufferings are commonly brought about by fights and disappointments in their conflict-ridden relationships, and Levine describes this perspective as the “pathogenesis,” or clinical pathway, of their symptom complex, as opposed to “etiology,” (mostly based on biological causes of illnesses), and which psychiatrists tend to have more familiarity with. Along the same lines, I was trained in my residency in the perspectives of psychiatry, which emphasizes the

wisdom of considering patients from several different perspectives when developing a treatment plan.<sup>7</sup> The essence of this approach is that our patients can be viewed through the following four clinical lenses: a biological perspective, through the perspective of their personalities, through the perspective of their drives and addictions, or through the perspective of their life stories. At any particular time, we may choose to view our patients through and emphasize one or more of these perspectives, and our judgment of what is contributing to their symptoms and distress may change from one encounter to the next. The more time I have spent in practice, I have come to appreciate the complexity of our clinical cases and to be humble in forming hypotheses of what is driving my patient's distress. Thus, it is helpful to be flexible on our approach to best address the needs of our patients. Oftentimes, as noted in this lesson, this may involve seeing patients through the lens of their marital struggles.

## **Barriers to Viewing the Complexities of Our Patients**

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Apparently, times have changed. When I was in training, we were taught to try to understand our patients through the lens of the biopsychosocial model.<sup>8</sup> While clinicians still pay lip service to this paradigm, it seems to be an afterthought for many and does not guide practice or research in our field at this time.<sup>9</sup> Instead, contemporary psychiatrists seem to have embraced the “bio-bio-bio” model.<sup>10</sup> This paradigm shift and its consequences are nicely explained and summarized by Paris.<sup>11</sup> Also, the modern crop of psychiatrists tend to be employees of healthcare organizations, hospitals, and clinics who have embraced the “med evaluation and med check” as the role of psychiatrists, and they encourage psychiatrists to see as many patients as they can for brief visits. Seeing more patients briefly also helps to provide ready “access” for referrals from primary care doctors, who often don't know what to with psychiatric patients.

## **Divorce**

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According to a broad survey of couples (over 70,000 worldwide,<sup>12</sup> roughly 25% of couples are anywhere from

unhappy to extremely unhappy in their relationships. Further, more than a third of responders say they think about breaking up all the time or often. Among unhappy couples, 87% contemplate leaving their relationship.

It was previously thought that over a lifetime, about 50% of marriages in the United States ended in divorce, but this view has changed in the past 3 decades. According to Luscombe, experts now put the rate at about 39%.<sup>13</sup> The higher rates reflected a time during the 1970s when divorce rates were at their peak. There have been numerous societal changes leading to the decline, including couples marrying later in life and being more cautious in marrying after experiencing the break-ups of their parents. Also, many couples are choosing to cohabit rather than marry.

There is much suffering brought about by unhappy and unfulfilling relationships, and many individuals suffering from depression and anxiety brought about by their marital difficulties are going to present to you. You may decide to treat their symptoms with medication, but why not get to the root cause of their suffering as another tool to help relieve it?

## **It is Good Clinical Practice to Obtain Collateral Information**

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Obtaining collateral information was considered to be mandatory when presenting a case during rounds to our chief of psychiatry. This was also hugely important in my forensic psychiatry training. Subsequently, having embraced this ideal, during my private practice, I often have found it helpful to have a patient bring in a spouse or other family member to provide collateral information. Such persons often add a helpful perspective and more objective observations about my patient's difficulties. Often it became evident that, in fact, marital conflict lay at the heart of many of my patients' symptoms. In time, I found myself trying to help my patient and his or her spouse resolve some of their differences to help alleviate the distress of my patient, and, to my amazement, sometimes my interventions really helped!

I have found that when my interventions bring about peace in what had been a stormy marriage, and when I found I could help restore a valued connection between couples, it was a very exciting and satisfying experience. Further, my patient's symptoms, which were

only partially relieved with medication management, inevitably improved further when the patient achieved greater relationship harmony. So, I became determined to learn more about couples, their conflicts, and the techniques of helping couples. I read a great deal, learned a lot, and then practiced skills. I found out that producing a good outcome and improving the quality of life for my patients was a very professionally satisfying and rewarding experience.

## **It is Best to Catch Marital Problems Early**

I also learned that it is much better to catch couples early in their difficulties. The usual course is for unhappy couples to wait an average 6 years of being unhappy before they try to get help.<sup>2</sup> By catching couples earlier, while there is still optimism about the future of their relationship, you have a much better chance of succeeding in making a positive impact on the marriage. If couples slog through 6 or more years of misery, and the marriage has mostly self-destructed, then a positive outcome of marital therapy is much harder to achieve. At that point, marital therapy often ends up being “divorce” therapy. Consequently, I have been very proactive in having patients bring in their spouse at the earliest signs of trouble to perform a “tune-up,” rather than trying to rebuild the relationship from ground zero.

## **Do You Need to be an Expert Before Attempting Couples Therapy?**

The other thing I learned was that I only needed to learn a few techniques to be effective and that these techniques worked both for heterosexual and gay couples. I did not have to have an encyclopedic knowledge of couples’ techniques to produce a good outcome. Of course, there are couples who are hopelessly complicated and whose marriage is already in ruins. At that point, you tell them that their problems are beyond your expertise, and then you refer them on to a certified marital and family therapist.

## **Start by Providing Education: What is Scientifically Known About Successful and Unsuccessful Couples and What Accurately Predicts the Doom of a Relationship**

I usually start by providing couples with education, informed by the research literature, especially the scientific studies of John Gottman, PhD. Couples typically find this information helpful, especially when it is supported by scientific studies of large numbers of couples. Gottman is one of the world’s leading experts on marital therapy, having studied scientifically more than 3000 couples and their interactions in his “Love Lab” at the University of Washington in Seattle. He has studied both happy and unhappy couples and has followed many of them for over 20 years in his lab, bringing them back repeatedly and following their progress. Based on his studies and resulting expertise, Gottman is able to predict divorce with 91% accuracy, and further able to predict whether a couple will divorce after watching or listening to them for just fifteen minutes discussing an area of disagreement. Gottman’s method and expertise are described in Malcom Gladwell’s “Blink,”<sup>14</sup> a book about how experts can make “snap judgments” or draw rapid conclusions based on prior extensive learning and integration of the complex relationships between ideas. This deep learning develops a part of their brain, known as the adaptive unconscious. Of Interest, John Gottman received a mathematics degree from M.I.T. before he branched out into the field of psychology. He has been the recipient of numerous prestigious research scientist awards. His research on couples outcomes and the subsequent interventions he and his wife, Julie Schwartz Gottman, PhD, developed are based on his extensive controlled studies and are evidence-based.<sup>2</sup>

During my educational introduction at the start of therapy, based on findings by Gottman, I explain that some couples, whether intuitively or by way of hard work, are the “masters” and other couples the “disasters” of relationships. If couples nourish the patterns that predict a happy relationship, there are many benefits. Many studies have shown that a higher quality relationship predicts not only better health but also a stronger recovery from illness



and a longer life span.<sup>15</sup> And the opposite is true when people are in unhappy relationships. I then explain that if they continue following the destructive patterns that the disasters of relationships follow, then there is an extremely high statistical likelihood that either their relationship will fail or that they can expect to live in misery for the foreseeable future, as shown by the scientific literature.

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**Table 1:**  
**Differences Between Healthy and Unhealthy Relationships<sup>2</sup>**

**Healthy Relationships:**

- High quality friendship
- More frequently (86% of the time or more) responding to spouse's bids for connection (turning toward)
- Avoiding resorting to the "Four Horsemen" during disagreements\*
- Make repair attempts after regrettable incidents and then processing the incidents\*
- Ratio of positive to negative interactions during conflict is at least five to one
- "Soft startups" when voicing a complaint\*
- The husband accepts influence from his wife
- Frequent emotional engagement
- Maintaining a state of "positive sentiment Override" \*\*

**Unhealthy Relationships:**

- Poor quality friendship
- Less frequently (33% of the time or less) responding to spouse's bids for connection (silence or turning away)
- Frequent use of the "Four Horsemen" during disagreements\*
- Infrequent repair attempts after regrettable incidents \*
- Ratio of positive to negative interactions during conflict is 0.8 to 1
- "Harsh startups" when voicing a complaint\*
- The husband fails to accept influence from his wife
- Tendency toward emotional disengagement
- Maintaining a state of "negative sentiment Override"

**Explained subsequently in the text**

\*\* Positive – interpreting a behavior of the spouse in the best positive light

\* Negative – interpreting a behavior of the spouse in the worst positive light

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## Solvable Vs Perpetual Conflicts

I explain that all couples, even healthy ones, have a variety of issues and conflicts which come up between them. Marital conflicts can be grouped into either solvable or perpetual conflicts.<sup>16</sup> Examples of perpetual conflicts

include differences in sharing chores and housework and differences of frequency of desire for sexual relations. Gottman's studies have shown that 69% of conflicts fall into the perpetual conflict category. The difference between the masters and the disasters is not in the number or seriousness of conflicts, and whether or not couples are able to resolve their differences, but rather in the WAY they manage their conflicts. There are ways of starting a conversation about disagreements which are more benign and called "soft-start-ups" vs more hurtful "harsh" start-ups, which can cause emotional damage, and which can be alienating. Further, harsh startups generally lead to diffuse physiological arousal, also known as the fight or flight response.<sup>2,17</sup> After the start-up, other patterns start to emerge, either helpful or damaging. This emphasizes the importance of the nature of communication in a marriage or other committed relationship.

## References to Evolutionary Theory

In addition to providing education and teaching communication skills, I also teach couples some basics of evolutionary psychology and biology. I teach them how the two genders have evolved differently. Thus the average woman evolved to be a "connection machine," who craves *emotional attunement* from her husband (he accepts her bids for attention; he listens and tries to understand; he empathizes).<sup>16</sup> Being able to connect with their partner and their tribe helped women to survive the harsh ancestral environment and pass on her genes to a future generation after mating. Those women who did not learn how to connect often failed to survive long enough to mate or were less successful in mating. Men, on the other hand, were evolutionarily designed to be problem-solvers, providers and defenders. They learned how to solve practical problems such as hunting or providing shelter. If they failed at this, men had more difficulties finding a mate and thus were less likely to pass on their genes to future generations (see Buss<sup>18</sup> for an excellent and readable introduction to evolutionary psychology as it relates to mating behavior). Also, men developed a more finely tuned danger response system to help fight off predators. Men are quicker to activate an adrenaline rush known as the "fight or flight" mode, and to stay in this mode longer to ensure safety. This system worked well

when it came to fighting lions, tigers, and marauders, but is less adaptive when it comes to being confronted with an angry and critical mate.<sup>2</sup>

## Communication

When asked, a substantial percentage of both men and women worldwide said that communication problems caused stress and unhappiness in their relationships.<sup>12</sup> Among unhappy women, 40% listed a wish for better communication as their number one priority, followed by a wish for more affection. Recently divorced individuals listed lack of communication as the number one reason why their relationship ended.

On the other hand, good communication helps relationships prosper. In the Northrup et al. study<sup>12</sup> the happiest couples said that the most fulfilling thing about their relationship was good communication, which even trumped friendship in importance (#2) and affection (#3). As stated by one participant in the Northrup et al. study (p 96):

*"We are best friends, passionate lovers; we focus on communication and make a point of making time for each other." – female, 42, married 21 years with kids.*

*Another said, "We communicate well, and when there is a conflict, we are able to resolve the problem. I feel that I am one of the most important things in his life and I feel the same way about him." – female, 30, in a 2-year-relationship, no kids*

Thus, communication is of key importance in keeping a relationship sound and healthy, and this is what I have found to be true in countless examples of problem couples, as well as often happy ones.

I focus a great deal on helping couples improve their communication skills (note: these are in fact skills which can improve with practice). I teach couples a highly structured way of communicating to be used when there are problems, which I will describe below and which is detailed in several books written by John Gottman and others (this stylized method is not always necessary when things are going well).

## The "Four Horsemen of the Apocalypse"

*"Never go to bed mad. Stay up and fight."  
– Phyllis Diller*

As mentioned, Gottman can assess the health of a relationship in 15 minutes of listening to couples. He has them discuss an issue of conflict to see how they treat each other during conflicts and their communication methods, either healthy or unhealthy. He has found that there are 4 communication responses which are relationship killers, which he calls the "Four Horsemen of the Apocalypse." The four horsemen alone predict divorce with an 82% accuracy rate, and when you add something called failure of repair attempts, he can predict divorce with over 90% accuracy.<sup>2</sup> Repair attempts refer to efforts the couple makes to de-escalate the tension during arguments. It is any statement or action, such as apologizing or lightening the tone and using humor to prevent negativity from escalating out of control.<sup>16</sup>

### The Four Horsemen:

- **Criticism – focusing on a partner's perceived character flaws (e.g., "Why can't you ever remember anything?" or "You're so selfish.")**
- **Contempt – showing contempt, acting superior, mocking, using sarcasm (e.g.: name calling such as "Why are you so stupid?"). This is the #1 relationship killer of all the 4 Horsemen.**
- **Defensiveness (e.g., "Why are you picking on me? Why don't we look at how you mess things up for me.")**
- **Stonewalling (turning away and tuning out).**

These destructive patterns have a way of escalating conflicts, making them more and more bitter. Once these patterns get established, they lead to couples living in what Gottman calls the "Roach Motel" of unhappy couples. He has found that when couples are stuck in



these destructive communication cycles, they divorce on average after 5 or 6 years.<sup>2</sup>

## Teaching Structured Communication Skills

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First, one of the main problems in couples' heated disagreements is that they often occur *quickly*. So, my first task is to "slow things down." Sometimes you have to *really* slow things down and take it one step at a time in small increments, often depending on the emotional intelligence of the couple you're working with. One sentence at a time, keeping things simple. One partner is then given the first chance to air a grievance. The grievance should be stated in terms of a SPECIFIC event (not general, such as "*you never do the laundry*"), and, importantly, how this event affected the partner emotionally. For example, "*When you didn't wash the laundry yesterday like you said you would, it made me feel like you don't care about me. It also affected my trust in you.*" The next step is to make sure that the partner has *heard* what their spouse has said. While it seems common sense to think that partners would hear what the spouse has said, in fact, many spouses are so busy coming up with a retort, or counterattack, that they only listen vaguely and can't repeat what they just heard, especially the part about how it made their partner feel. So, then you, as the "referee" who makes the rules, stop the process and repeat the speaker and listener technique until the listener gets it right. The listener then asks his partner, "*Did I get it right?*" You then see if you can get some empathic response from the listener to indicate to his partner some level of understanding of how it makes sense that his partner would feel that way. This process is a way to not only teach communication skills but empathy skills.<sup>2</sup>

One of the things that can get in the way of this process is when one partner (typically the male) becomes overly reactive, or "flooded." Men can easily have a response to their wives in which he reacts the same way as his ancestors did when they were being threatened by a saber-toothed tiger. They go into fight or flight mode, their breathing increases, their heart rate and blood pressure increase, they develop tunnel vision and hearing, and their blood gets rerouted from the higher parts of the brain that engage in problem-solving to the parts of the brain that control the limbs to start moving. Nothing

productive in the way of problem-solving can occur under these conditions until the man calms down and his blood supply gets rerouted. When feeling flooded, the man needs to ask for a time out, but with a promise that this discussion will continue after he has an opportunity to calm himself down, say in 20 minutes.<sup>2</sup>

## Solving Solvable Problems

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Then, at a later time, when things are calmer, the couple can be taught how to try to start addressing problem solving. If it is a solvable problem, then the first thing is to teach the couple how to have a "soft" vs a "harsh" start-up. Harsh start-ups often lead to a response which calls up one of the "Four Horsemen," which then stops a productive conversation in its tracks. Examples of a soft start-up, which may include using a sense of humor and acceptance of one's ownership in the conflict as well as an action plan. Such an approach may look like this: "*You know me. I can be thoughtless at times when I'm focusing on my work, and then I forget to do things I had promised. I usually get to the laundry, but when I have a work deadline like I did yesterday, everything else seems to go out the window. Let's see if we can come up with a plan for days like that so that I remember to do the things I had promised.*" Such an opening likely leads to a productive discussion that doesn't escalate and leads to a peaceful resolution.

I have often found that one positive improvement in the relationship leading to an improved system of communication often turns things around dynamically so that the couples can maintain and continue practicing their new-found skills. Sometimes just a few sessions can turn things around. Other times it takes repeated similar sessions.

## Addressing Perpetual Conflicts

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As mentioned previously, the majority of conflicts couples face are actually perpetual and not easily resolved. Such perpetual conflicts often shine a light on differences in values and expectations, ways in which individuals differ because of the ways they were raised and their different personalities. In solving perpetual problems, the same communication skills apply, and it is essential to emphasize the importance of beginning with a soft vs a harsh startup. There tends to be a greater likelihood of

such conflicts escalating into the use of one of the Four Horsemen. When discussions don't seem to be getting anywhere, there can be a tendency to "turn up the volume" to make a point. Further, it is important to practice acceptance. Partners must accept that they are not likely to resolve things in their favor and get their spouse to change their opinions and values. Instead, couples must work hard on negotiating and compromising. You must accept that your partner is a unique individual and is not likely to change. It helps to have a sense of humor and to view one's partner as having endearing quirks, rather than seeing them as stubborn and unlikeable for sticking to their opinion and point of view. In this, it greatly helps if the couple has fostered a healthy "bank account" of good will over time.

## Building a Bank Account of Good Will

There are many things couples can do to build a bank account of good will. It helps to consistently show your partner that she (or he) is your number one priority and that she comes before your work, your hobbies, and the children. It helps to develop a solid friendship, spending lots of quality time together, doing fun things together, attuning regularly, showing respect, and repeatedly communicating your "fondness and admiration" for your spouse. It helps to practice forbearance - restraint, and tolerance. Forbearance is a gift you offer your partner out of love. You don't harp on every little error they make, point out an irrationality, get irritated when they forget something important. Instead, you perhaps ignore something that is your prerogative to point out. Instead, you tell yourself that you also are not perfect and hope that your partner will not emphasize your shortcomings.

## Additional Issues

A further note is that studies have shown that the actions of specifically the man in relationship makes the difference in whether a relationship succeeds or fails. Unfortunately, men often fail to understand women, even very highly intelligent and professionally accomplished men. They tend to be clueless about how men and women are emotionally different (by way of their evolutionary heritage, brain wiring and hormonal makeup) and

are often ill-equipped to deal with the strong emotional life of women. Even otherwise intelligent men can be confounded by their inability to understand women. Thus, the following quotes (Thanks to John Gottman):<sup>16</sup>

*"The great question that has never been answered and which I have not yet been able to answer, despite my 30 years of research into the feminine soul, is 'What does a woman want?'"*

— Sigmund Freud

*When asked what scientific puzzle confounded him the most, Stephen Hawking answered, "Women. They are a complete mystery."*

Thus, I often find myself recommending the following book to men: "The Man's Guide to Women."<sup>17</sup>

## Human Sexuality:

If you are going to do couples therapy, then you also have to be knowledgeable about human sexuality. A more in-depth discussion of this issue within the context of marital therapy would require a separate lesson. However, it has been a remarkable experience in my clinical practice to observe some of the following:

I had a spouse attend a collateral session in which the focus was my client's depression when, out of the blue, the spouse complains and emphasizes the unhappy state of their sexual life from her perspective. Sometimes a patient's sexual life is the most crucial issue they bring up when I start to see him or her for common complaints such as depression and anxiety. Of note, sexual issues may be at the forefront of the problems that present when a couple is in distress and facing a relationship crisis. Often the complaint is that the spouse refuses to have sex with my patient, they have not had sex in years, and my patient finds it highly upsetting.

For example, I had the spouse of one of my faculty colleagues referred to me for evaluation of "seasonal mood swings, r/o bipolar II." However, within a few minutes, she focused instead on the fact that she and her husband had been married for decades and had not enjoyed sexual relations in at least 25 years. She thought he had no interest in a sexual life. She lashed out at him at times because of her frustration. In a subsequent collateral session, her husband acknowledged the problem but had

difficulty explaining it. Only after gaining their trust in several subsequent sessions did the husband reveal, for the first time in their marriage, that, in fact, he had a private sexual life which involved some fantasy which he could not reveal. His wife wanted to know, but he just could not get himself to tell of his private sexual life. Of note, I have found it relatively common in my practice to hear a woman complain that her husband refuses to have sex with her, and this often causes tremendous suffering for my female patient, who commonly comes to view herself as unlovable and unattractive.<sup>19</sup>

The topic of sexual life and the research literature associated with it, as well as strongly-held opinions of many sexologists, makes for fascinating reading, and the scope of writing is vast. A good place to start is Levine et al's book.<sup>1</sup> For further information on specific issues involved in male sexuality, see Zilbergeld.<sup>20</sup> For a compelling view of women's sexuality, a good introduction is Nagoski.<sup>21</sup> A very worthwhile resource, descriptions of a research project which includes many clinical vignettes on sexual relations is ZilberGeld & Zilbergeld.<sup>22</sup> The book looks at sexuality over a lifespan. Zilbergeld studied a convenience sample (rather than a random sample, he interviewed friends, friends of friends, some of their relatives, volunteers who answered an advertisement looking for people who were willing to talk about their sex lives and volunteers obtained during some public talks) of 145 men and women, 80 of whom reported gratifying sexual sex lives, and compared them to those who reported having unhappy sexual lives. He also explores the general relationship dynamics of what make for couples with fulfilling sexual experiences.

The budding marital therapist should also be familiar with the topic of love and the evolution of love and how it shaped our species over time. An interesting cross-cultural exploration is by Helen Fisher, an anthropological anthropologist.<sup>23</sup> A more opinionated introduction is Levine.<sup>5</sup> It is also fun to read about the clinical pathologies of love. For this, I recommend Tallis.<sup>24</sup>

Note that the above process of teaching relationship skills works just as well for gay couples as for heterosexual partners. It turns out they have the same conflicts centered around housekeeping and chores, extended family dynamics, needs for closeness versus distance, and sexual frequency differences.

## **Stepfamilies:**

Psychiatrists seeing couples will also become aware of differences of opinion about child rearing and the complex world of stepfamilies. A review of the complexities of this topic is beyond the scope of this lesson. However, some general principles apply. As always, good communication using soft startups is key. Also, the psychiatrist should emphasize the importance of teamwork. Whenever there is a difficult problem involving children, such as defiance, a child splitting his parents trying to play one against another, and when a child's behavior gets out of control, it is vitally important that partners present a united front and stick together, however imperfect their approach. Also, the parents need to find ways to sooth themselves so that the child's behavior does not cause the parents to become emotionally reactive. It may help to involve the child in a behavioral contract. So, for example, asking the child's opinion of what a fair consequence might be for a particular infraction.

## **The “Stay In Your Lane” Phenomenon**

I should caution the psychiatrist interested in pursuing adding marital therapy to his practice that this ambition is viewed as not fitting by some patients. Because of the paradigm shift in psychiatric practice in recent decades, in which psychiatrists have commonly come to view their role as prescribers whose mission is to treat illness,<sup>11</sup> many of our patients have embraced this view of psychiatry. I have had patients be incredulous when I tell them that I also treat couples, and many of them are reluctant to trust their relationships to me. All they often want is a pill for their distress.

## **Billing and Coding:**

A final note about billing and coding. As mentioned, I often start by seeing a patient for some psychiatric problem, and typically prescribe medication for some set of symptoms. Then I learn that there is a marital problem and ask my patient to bring his partner in. The couple's sessions are then billed using E&M codes. I ask some basic questions about how my patient is doing with their symptoms and/or medications, and then spend the rest of the time in couples therapy. The time spent in therapy is

then billed as an “add on” code. There is no requirement for any specific therapy when using the add on code. Another serious but related issue is a large number of “no-shows” and cancellations in our practice. It is much easier to financially absorb a no-show often consisting of a 15-minute medication check, rather than to suffer through an hour you have set aside for a marital session when the couple doesn’t show up.

## Summary

This lesson has addressed a common pathway to clinical distress, the often-unhappy marriages, or other committed relationships of our patients. While most psychiatrists tend to “farm out” such problems to psychotherapists, this lesson has tried to persuade psychiatrists that they

can do this work themselves in a competent, though not necessarily expert manner by understanding some of the factors which create successful and unsuccessful relationships. This lesson has reviewed the importance of effective communication and have provided a structured approach to encourage better communication and develop empathy. I have reviewed the most destructive communication patterns that commonly lead to the end of relationships in a predictable manner and further provided the beginnings of a problem-solving approach that can help couples manage their conflicts. Our wide reading in related areas adds significant breadth to our knowledge base of human nature, which may have inspired many psychiatrists to choose psychiatry as a specialty. This practical lesson is intended to encourage psychiatrists to consider adding marital therapy into their practices. ■

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L003446

## Multiple-Choice Questions

**13. The pathogenesis of symptom complexes refers to biological causes. This statement is:**

- A. True
- B. False

**14. Psychiatrists need to have certification in marital and family therapy to become competent to practice marital therapy. This statement is:**

- A. True
- B. False

**15. Scientific studies have shown that most marital conflicts are solvable if one chooses the right approach. This statement is:**

- A. True
- B. False

**16. The “Four Horsemen of the Apocalypse,” the most destructive of communication patterns, as described by the scientific studies of John Gottman, include all of the following, *except*:**

- A. Contempt
- B. Stonewalling
- C. Criticism
- D. Belligerence

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# Best Practices in Continuing Medical Education

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## You Too Can Do Marital Therapy: Expanding Psychiatric Practice to Include Marital Therapy

By Otto Kausch, MD

ID#: L003446

**This valuable take-home reference translates evidence-based, continuing medical education (CME) research and theory, acquired from reading the associated CME lesson, into a stepwise approach that reviews key learning points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

This lesson provides guidance to psychiatrists who are considering expanding their practice to include marital therapy. Scientific studies have shown that there are definable differences between a successful and unsuccessful relationship and communication patterns that can predict the death—or success—of a marriage. In the author's experience, marital difficulties have often been shown to be the basis for symptoms of psychiatric disorders. This lesson encourages psychiatrists to consider adding marital therapy to their practice to help their patients achieve symptom relief.

#### **Key Point 1: Address the Totality of Factors That Lead to a Patient's Symptoms, and the Psychiatrist is in a Good Position to Address Them All**

**The pathogenesis of the symptom complexes we see in our patients can be challenging. An unhappy marriage can be an important component of that complexity. By addressing our patients' marital issues, we can find patterns of behavior that may have contributed to the presenting symptoms. By exploring interventions that may help change those behaviors, we may help relieve our patients' distress.**

#### **Key Point 2: We Can Predict the Success or Failure of Relationships Based on Scientific Research**

**John Gottman and colleagues have documented factors that can lead to the success or failure of a relationship. These factors include communication patterns, which can be destructive or helpful. Learning the basics of this research can help the psychiatrist learn how to predict, with a high level of confidence, whether a marriage will succeed or fail.**

#### **Key Point 3: There is Treatment for Unhappy Couples**

**Once we have identified the factors that can be used to predict whether a relationship will be successful or unsuccessful, we can teach couples the skills that favor a positive outcome.**

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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**Key Point 4: Psychiatrists Without This Expertise Can Acquire a Sufficient Understanding of the Research and Learn Enough Basic Skills to Assist Couples in Their Struggle to Achieve a Happier Relationship**

Experience has shown that basic interventions by psychiatrists can help couples along their journey toward a happier relationship. By providing education about the factors that predict relationship failure vs success, we can also help couples gain insight into the steps they need to take to improve the quality of their relationships. Doing so often leads to symptomatic relief from their clinical distress.

**Key Point 5: Read Widely About a Broad Array of Topics That May Affect Our Understanding of Those Relationships Which Adds Important Breadth to Our Knowledge of Human Nature**

It is prudent for the psychiatrist to read about subjects other than psychiatry that affect intimate human relationships, such as human sexuality, love, and the theory of evolution. This extended learning can keep our love of learning alive. Also, spending time with our patients in exploring the nuances of their relationships helps us value our ability, as an expected part of our practice, to get to know our patients on a very human level.

# Prevention of Mental Health Disorders Using Internet- and Mobile-Based Interventions: A Narrative Review and Recommendations for Future Research

## Part 1: An Overview

David Daniel Ebert, PhD; Pim Cuijpers, PhD; Ricardo F. Muñoz, PhD;  
Harald Baumeister, PhD

*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Mental health • Self-help • E-health • M-Health • Internet interventions • Depression • Anxiety • Prevention

**LEARNING OBJECTIVES:** Upon reading this lesson, readers will be introduced to the subject, narrative reviews and available evidence for the effectiveness of *internet- and mobile-based interventions* (IMIs); review how they may aid in the prevention of mental health disorders, and recognize the challenges and need for future research using this modality in the field.

**LESSON ABSTRACT:** Although psychological interventions might have a tremendous potential for the prevention of *mental health disorders* (MHD), their current impact on the reduction of disease burden is questionable. Possible reasons include that it is not practical to deliver those interventions to the community *en masse* due to limited health care resources and the limited availability of evidence-based interventions and clinicians in routine practice, especially in rural areas. Therefore, new approaches are needed to maximize the impact of psychological preventive interventions. Limitations of traditional prevention programs could potentially be overcome by providing *Internet- and mobile-based interventions* (IMIs). This relatively new medium for promoting mental health and preventing MHD introduces a fresh array of possibilities, including the provision of evidence-based psychological interventions that are free from the restraints of travel and time and allow reaching participants for whom traditional opportunities are not an option. This article provides an introduction to the subject and narratively reviews the available evidence for the effectiveness of IMIs with regard to the prevention of MHD onsets. The number of randomized controlled trials that have been conducted to date is very limited and so far it is not possible to draw definite conclusions about the potential of IMIs for the prevention of MHD for specific disorders. Only for the indicated prevention of depression there is consistent evidence across four different randomized trial trials. The only trial on the prevention of general anxiety did not result in positive findings in terms of *eating disorders* (EDs), effects were only found in *post hoc* subgroup analyses, indicating that it might be possible to prevent ED onset for subpopulations of people at risk of developing EDs. Future studies need to identify those subpopulations likely to profit from preventive. Disorders not examined so far include substance use disorders, bipolar disorders, stress-related disorders, phobic disorders and panic disorder, obsessive-compulsive disorder, impulse-control disorders, somatic symptom disorder, and insomnia. In summary, there is a need for more rigorously conducted large scale randomized controlled trials using standard clinical diagnostic instruments for the selection of participants without MHD at baseline and the assessment of MHD onset. Subsequently, we discuss future directions for the field in order to fully exploit the potential of IMI for the prevention of MHD.



**COMPETENCY AREAS:** This lesson provides knowledge as it reviews the evidence and potential for utilizing internet- and mobile-based interventions in the prevention of mental health disorders. The lesson applies quality improvement as it explores treatment strategies concerning the patient and community needs and how the implantation of IMIs shows promise to prevent the onset of mental health disorders. Lastly, the lesson covers the need for further research in this field to address various populations, mental health disorders that have not been tested, among other barriers to implementation of this modality.

## Introduction

*Mental health disorders* (MHD) are highly prevalent, with estimated lifetime and 12 month-prevalence rates, ranging across countries between 18.1–36.1 and 9.8–19.1%, respectively.<sup>1</sup> MHD are one of the leading causes of disability<sup>2</sup> and associated with an immense disease burden such as poorer quality of life of sufferers and their loved ones, an increased risk of developing chronic physical conditions and related mortality.<sup>3–5</sup> The economic burden of these disorders is enormous, including substantial economic costs, reduced work-force participation, occupational impairment, and lost productivity.<sup>6–8</sup>

In the past decades, a variety of interventions have been developed to treat MHD for which efficacy has been demonstrated in a large number of randomized trials.<sup>9,10</sup> However, even assuming the hypothetical scenario of 100% coverage and compliance to evidence-based treatments, approximately only 28% of the disease burden attributable to MHD could be averted.<sup>11</sup> In fact, less than half of the individuals with a MHD are recognized and treated.<sup>12</sup> Therefore, attention has increasingly been focused on the prevention of MHD.

Preventive interventions can be classified as universal interventions, directed at the whole population; selective interventions, directed at individuals with specific risk factors for the development of a MHD; or as indicated preventive interventions, directed at individuals in the prodromal stage of a disorder, who do not yet fulfill the criteria for a full blown disorder but experience subclinical symptoms.<sup>13</sup>

Emerging evidence indicates the potential of psychological interventions for the prevention of MHD. For example, in a recent meta-analysis, van Zoonen and colleagues found psychological interventions aiming to prevent *major depressive disorders* (MDDs) to reduce the incidence by approximately 22%.<sup>14</sup> Results from another review found that cognitive behavioral indicated

preventive interventions reduced the transition to psychosis with a risk ratio of 0.54 (95%-CI: 0.34–0.86);<sup>15</sup> encouraging evidence from a limited number of randomized controlled trials is also available, for example, for the prevention of *eating disorders* (EDs)<sup>16</sup> and tobacco use,<sup>17</sup> whereas the efficacy for other disorders such as interventions to prevent anxiety<sup>18</sup> is not yet established.

Although psychological interventions might have a tremendous potential for the prevention of MHD, their current impact on the reduction of disease burden is questionable. Possible reasons include that it is not practical to deliver those interventions to the community *en masse* due to limited health care resources and the limited availability of evidence-based interventions and clinicians in routine practice, especially in rural areas. Therefore, new approaches are needed to maximize the impact of psychological preventive interventions.

Limitations of traditional prevention programs could potentially be overcome by providing *Internet- and mobile-based interventions* (IMIs). This relatively new medium for promoting mental health and preventing MHD introduces a fresh array of possibilities, including the provision of evidence-based psychological interventions that are free from the restraints of travel and time and allow reaching participants for whom traditional opportunities are not an option.

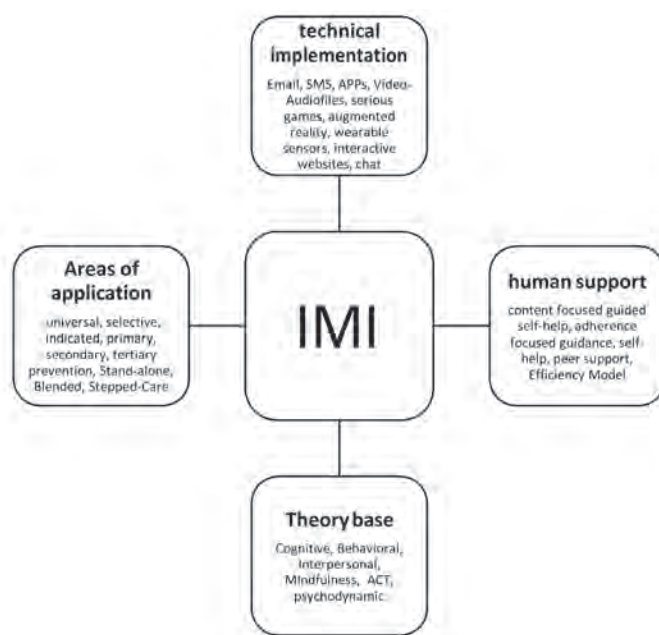
**Internet- and mobile-based interventions have been shown to be effective in clinical populations, including the treatment of depression<sup>19–21</sup> anxiety,<sup>20, 22, 23</sup> alcohol use,<sup>24</sup> and sleep disorders.<sup>25</sup>** However, evidence for their effectiveness in preventing the incidence of MHD is much less documented.

This article provides an introduction to the subject and narratively reviews the available evidence for the effectiveness of IMIs with regard to the prevention of MHD onsets. Subsequently, we will offer some suggestions regarding the direction of future research in this field.

## Characterizing IMIs

The possibilities to use IMIs for the prevention of MHD range from mobile-based apps for the monitoring of health behavior and stand-alone self-help interventions to supplemental elements integrated in conventional on-site psychological interventions (blended concepts). One common element of such interventions is that emotional, cognitive, and behavioral processes are modified and their generalizations to users' daily lives promoted using established psychological techniques.<sup>26</sup> **IMIs can be categorized in regard to their use of technology, the extent of human support, the theoretical basis, and with respect to their areas of applications and indications (Figure 1).**

**Figure 1:**  
**Characteristics of Internet- and Mobile-based Interventions (IMIs)**



## Technical Implementation

For the implementation of IMIs, numerous technical possibilities are applicable. These range from (1) the provision of evidence-based strategies as interactive self-help lessons; (2) e-mail, chat, or video-based sessions;<sup>27</sup> (3) virtual reality for exposure interventions;<sup>28</sup> (4) serious-games, in

which psychological strategies are trained in the context of a computer game;<sup>29</sup> (5) the use of automated memory, feedback, and reinforcement interventions, for example, through apps, e-mails, text messages, or short prompts, which support the participant in incorporating intervention content into everyday life; to (6) sensors and apps for monitoring health behavior such as physical activity, which can be used to support the learning process.<sup>30</sup>

## Theoretical Basis

**Due to their distinctive structured nature, standardization, and focus on the training of strategies and specific behavior, IMIs are particularly suited for techniques that target changes in thoughts and behaviors.**<sup>26</sup> These include well-researched cognitive, behavioral, and interpersonal interventions. Approaches such as mindfulness-based methods, acceptance and commitment therapy, or psychodynamic approaches, which are already used within some clinical IMIs,<sup>31-35</sup> also have the potential for application to preventive IMIs.

## Human Support

As a basic principle, **IMIs can be implemented with varying degrees of human support. The current most commonly used method is the so-called “guided self-help,” in which evidence-based content is usually provided as self-help material so that the participants can perform most tasks independently.** An accompanying coach then regularly gives feedback on the completed exercises. Fostering adherence to the content of the intervention is usually the main aim of human support, rather than the delivery of new therapeutic techniques that go beyond the content of the current lesson.<sup>36,37</sup> **The main task of the coach is to clarify any comprehension questions, provide feedback on solved problems and progress, and to encourage participants to continue to work on themselves.** For this to happen, communication can happen either synchronously (per chat or video) or asynchronously (for example, per e-mail), the latter of which is more commonly used, and normally takes a few minutes to a few hours (1–3h) per participant and intervention. For the participant, the processing of self-help material, execution and repetition of exercises, as well as correspondence with a coach can, however, be very intense

and require a much greater time investment than that of the supporting coach.<sup>38</sup> The combination of self-help material with minimal human support via the Internet thereby increases empowerment of the participants and the degree of self-directed coping while maximizing the efficiency of the accompanying coach. Irrespective of location, asynchronous contact and time-independent communication results in increased flexibility and autonomy for both participants and prevention workers.

An “Efficiency Model of Support”<sup>39</sup> has been recently put forward to contribute to the development of a taxonomy of elements involved in guided interventions, such as type, quantity, timing, quality, and cost of human support. A commentary on that article<sup>40</sup> suggests that it may be useful to categorize contemporary interventions into four major types: traditional *face-to-face* (FTF) interventions, FTF interventions augmented by *behavior intervention technologies* (BITs), BITs augmented by human support, and BITs that are fully automated.

Applications of IMIs range from mental health promotion and mental disorder prevention to full treatment of mental disorders and interventions to reduce relapse or recurrence. In the fields of psychological health promotion and prevention, IMIs are considered a promising approach for increasing the accessibility of evidence-based psychological techniques to people on a larger scale due to their low threshold for accessibility, location and time independence, and anonymous usability.<sup>41</sup> IMIs can be used in the prevention of mental disorders either as a stand-alone approach, as part of a stepped-care approach or as an integrated element of a preventive intervention consisting of online and conventional on-site sessions (blended).

As a *stand-alone measure*, IMIs increase the reach of effective psychological interventions. Telehealth interventions (live therapy online) can transcend space. IMIs can transcend space and time. For example, the temporal and spatial independence of IMIs facilitates access to evidence-based interventions for individuals with limited mobility or those who live in areas with low access to preventive interventions. Populations who are not able to attend appointments during usual visiting hours and, therefore, are not able to attend other on-site FTF options, would then also be able to participate in interventions in the evenings or on the weekend at their

own pace. Persons who would have not sought to participate in a preventive intervention due to other individual reasons, such as fear of stigma, would also have access to IMIs. Despite increasing social acceptance of psychological interventions, everything that might be associated with mental problems produce for some individuals a sense of shame, which in itself creates a barrier to the actual use of preventive interventions.<sup>39, 40</sup> Moreover, a general problem with preventive interventions lies in the fact that, by definition, the impairment people appropriate for preventive interventions are experiencing is low or not noticeable to them, diminishing their willingness to “invest” into mental health interventions. Hence, the lower the threshold and effort associated with participating in a preventive intervention, the likelier it is that the target group makes actual use of it.

In the combination of IMIs and personal FTF interventions, the so-called *Blended-Concept*, IMIs take over areas that need not necessarily be mediated by a prevention worker, allowing more time during the sessions for FTF psychological process work.<sup>26</sup> Prevention workers could, for example, delegate time-consuming routine aspects of the intervention, such as the delivery of psychoeducation to digital tools. In principle, IMIs could also be used to improve FTF interventions by providing exercises for the participant to work on in between the intervention sessions, thereby increasing intervention intensity. Another way in which IMIs could be used to improve the outcome of FTF interventions is by supporting the integration of behavior changes or training of techniques into routine life, thus extending the reach of the psychological intervention into the daily lives of participants. This can be achieved through methods, such as smartphone-based behavioral diaries, sending of messages with ultra-short prompts aimed at training-specific strategies in daily life, or smartphone-based coaches that lead patients through potential anxiety-provoking or other difficult situations.

Furthermore, the objective of most psychological interventions is that participants actively try to integrate new behavior into their daily life and maintain these changes in the long term. IMIs emphasize the active role of the person concerned in this process, thus promoting a sense of empowerment through encouraging them to use their own resources to solve problems. IMIs could

be used by people much before there is any need to seek FTF mental health services (and hopefully prevent the need to do so), during times when they are receiving treatment, as adjuncts to FTF care, and after treatment ends, to maintain gains, continue to progress in terms of reaching ever sturdier mental health levels, and to reduce relapse and recurrence.

Within *stepped-care approaches*, the degree of support participants receive are designed according to their actual individual need. In step-up interventions (guided) preventive approaches can be offered, for example, to individuals in the prodromal disease stage (indicated prevention) as a first element in the chain of treatment in order to prevent the transition to the full blown disorder. Further intensive therapeutic support, such as outpatient psychotherapy, then occurs should the patient respond insufficiently to the self-help intervention. Similarly, step-down interventions supplement more intensive therapeutic measures with lower intensity support. For example, IMI-relapse prevention concepts could be offered to patients following an acute treatment in order to stabilize acute treatment effects and thereby prevent relapse and recurrence.<sup>42-46</sup>

## Effectiveness of IMI in Preventing the Onset of MHD

While there are currently well over 100 randomized controlled studies on Internet- and mobile-based concepts fostering mental health, only few studies to date have investigated their potential in preventing the incidence or onset of a MHD. In the following section, we will review these studies and thereby only focus on studies that assessed the effects of an IMI on MHD onset (assessed according to diagnostic and statistical manual of mental disorders/ICD criteria) in a sample of adults, adolescents, or children, who is free from an acute mental disorder at baseline. There are further studies on mental health IMIs evaluated in samples with subthreshold mental health conditions. However, these studies were often planned for other purposes than examining disorder onset and limited in their methodological quality.<sup>47</sup> Table 1 gives an overview of the reviewed studies, and Tables 2 and 3 are about the characteristics of the reviewed studies and interventions.

## Indicated Prevention

### Depression:

Three studies have evaluated the effects of Internet-based approaches with regard to the primary prevention of depression. Buntrock et al. recently published a trial on the effects of an Internet-based indicated prevention stand-alone intervention.<sup>41, 48, 60</sup> They randomized 406 adults with subclinical symptoms of depression who did not fulfill the criteria for MDD in the last 6 months to either a 6-week guided Internet-based cognitive behavioral intervention or to an online passive psycho-education intervention. The *intervention group* (IG) included behavioral activation and problem solving as core intervention components; in addition, participants were able to choose among several different optional modules (e.g., sleep hygiene/sleep restriction, progressive muscle relaxation, and rumination techniques). In addition to the Internet-based self-help module, a text message coach sent a set of “tiny tasks” to the participant’s mobile phone in order to foster the application of intervention techniques in daily life. In the IG, 32% of the participants experienced a MDD during the 12 months of follow up, whereas 47% in the *control group* (CG) did. Cox regression analyses controlling for baseline depressive symptom severity showed a *hazard ratio* (HR) of 0.59 indicating a 41% reduction in the risk for developing a MDD with a number need to treat to avoid one new case of MDD of 5.9. It is important to note that, in this trial, it was not assessed whether participants had a prior history of MDD. Hence, future studies are needed to investigate whether the effects count both for first incidence and subsequent onset of MDD.

**Table 1:**  
**Summary of Included Randomized Controlled Trials that Assessed MHD Onset Using Categorical ICD/DSM Diagnostic Criteria**

| Study                     | Prevention type | Disorder   | Target group   | Program type | Program   | Conditions  | N                  | Follow-up | Instru-ment                    | Results   |
|---------------------------|-----------------|------------|--|--------------|---|---|--------------------|-----------|--------------------------------|---|
| Buntrock et al. (48)      | Indicated       | Depression | Adults, sub-threshold depression (CES-D > 16)<br>No MDD  | Stand-alone  | GET.ON mood enhancer<br>6 weeks CBT, guided self-help for subthreshold depressive symptoms  | IG: intervention<br>CG: online-psychoeducation  | 406                | 12 months | SCID                           | MDD onset within 12 months<br>IG: 32%<br>CG: 47%<br>RRR = 39%<br>HR = 0.59<br>( $p = 0.002$ )<br>NNT = 5.9            |
| Christensen et al. (49)   | Selective       | Depression | Adults, primary insomnia (MINI) and depressive symptoms (PHQ > 3 < 20)<br>No MDD   | Stand-alone  | SHUTi<br>6 weeks unguided self-help for insomnia symptoms   | IG: intervention<br>CG: attention control   | 1,149              | 6 months  | MINI                           | MDD onset within 6 months<br>IG: 0.78%<br>CG: 1.13%<br>ns   |
| Christensen et al. (50)   | Indicated       | GAD        | Adults 18–30, GAD symptoms (GAD-7 > 5)<br>No PD, SP, BDP, schizophrenia, psychosis<br>Not undergoing psychiatric treatment | Stand-alone  | iChill<br>10 weeks unguided iCBT for anxiety symptoms   | IG1: unguided iChill<br>IG2: iChill + phone reminders<br>IG3: iChill + e-mail reminders<br>CG1: attention control website<br>CG2: attention control website + phone reminders | 558                | 6 months  | MINI                           | GAD onset within 6 months<br>Across all IG: 6.7%<br>Across all CG: 4.5%<br>ns   |
| Imamura et al. (51)       | Indicated       | Depression | Adult workers with self-identified subthreshold depressive symptoms (WHO-CIDI 3.0, self-administered)<br>No MDD            | Stand-alone  | 6 weeks unguided iCBT, manga comic-based intervention for depression, feedback on demand  | IG: unguided iCBT<br>CG: e-mail with non-CBT stress-management tips   | 822                | 12 months | WHO-CIDI 3.0 self-administered | MDD onset within 6 months<br>IG: 0.8%<br>CG: 3.9%<br>HR = 0.22<br>RRR = 0.20<br>( $p = 0.009$ )<br>NNT = 32           |
| Lindenberg and Kordy (52) | Universal       | EDs        | Secondary education students (13–16)<br>No ED diagnosis<br>Not undergoing treatment (ED)                                   | Stepped care | Young E[s]prit stepped guided intervention (ranging from unguided feedback and self-help, though peer support to individual counseling) | IG: intervention<br>CG: online-psychoeducation  | 1,667 <sup>a</sup> | 12 months | LIFE                           | Any ED onset within 12 months, IG1: 5.9%<br>CG1: 9.6%<br>( $p = 0.038$ )<br>HR = 1.67<br>IG2: 5.6%<br>CG2: 4.8%<br>ns |
| Taylor et al. (53)        | Selective       | EDs        | College-age women, weight shape concern<br>No diagnosed ED   | Stand-alone  | Student bodies<br>8 weeks guided CBT-based self-help treatment  | IG: intervention<br>CG: wait list control   | 480                | 24 months | EDE                            | Any ED onset within 24 months<br>IG: 10%<br>CG: 5%<br>ns  |



| Study                      | Prevention type               | Disorder        | Target group  | Program type | Program  | Conditions                             | N   | Follow-up       | Instru-ment | Results  |
|----------------------------|-------------------------------|-----------------|---|--------------|--|--|-----|-----------------|-------------|--|
| Thompson et al. (54)       | Indicated                     | Depression      | Adult epilepsy patients, subthreshold depression (CES-D > 8, < 27, PHQ-9)   | Stand-alone  | UPLIFT 8 weeks Internet-/ telephone-delivered mindfulness cognitive therapy-based intervention | IG: UPLIFT CG: wait list control       | 128 | 8 weeks         | PHQ-9       | MDD onset within 8 weeks<br>IG: 0%<br>CG: 10.7%<br>( $p = 0.028$ )   |
| Holländare et al. (55, 56) | Indicated, relapse prevention | Depression      | Adults, MDE in the past 5 years, subthreshold depression (MADRS-S > 7, < 19)<br>Not undergoing treatment<br>No BDP, psychosis, addiction                | Stand-alone  | 10 weeks guided Internet-based CBT self-help intervention for depressive symptoms              | IG: intervention CG: TAU CG            | 84  | 6 and 24 months | SCID        | MDD onset within 6 months<br>IG: 10.5%<br>CG: 37.8%<br>within 24 months IG: 13.7%<br>CG: 60.9%<br>( $p = 0.001$ )<br>HR = 0.16 |
| Bauer et al. (57)          | Selective, relapse prevention | Transdiagnostic | Adult discharged stationary patients<br>No psychotic symptoms   | Stepped-care | 12–15 weeks Internet-based guided non-manualized chat intervention                             | IG: chat intervention CG: TAU CG       | 152 | 12 months       | LIFE        | Any DSM disorder onset within 52 weeks<br>IG: 22.2%<br>CG: 46.5%<br>( $p < 0.1$ )  |
| Taylor et al. (58)         | Selective                     | EDs             | Young adult women, weight/ shape concerns (WCS $\geq 47$ ), eating-related teasing, depression or non-clinical compensatory behavior<br>No diagnosed ED | Stand-alone  | Image and mood 10 weeks guided CBT-based self-help treatment                                   | IG: intervention CG: wait list control | 185 | 24 months       | EDE         | ED onset within 24 months<br>IG: 24%<br>CG: 31%<br>ns<br>HR = 0.73   |

*Universal—universal prevention. Interventions directed at the whole population; selective—selective prevention. Interventions directed at individuals with specific risk factors for the development of a MHD; indicated—indicated prevention. Interventions directed at individuals in the prodromal stage of a disorder; relapse prevention—interventions aiming to reduce relapse and recurrences after first onset.*

<sup>a</sup>Two waves (wave 1:  $N = 896$ , wave 2:  $N = 771$ ).

CES-D, Center for Epidemiological Studies Depression Scale; CBT, cognitive behavioral therapy; IG, intervention group; CG, control group; SCID, structured clinical interview for DSM disorders; MDD, major depressive disorder; RRR, relative risk reduction; HR, hazard ratio;  $p$ , level of significance; NNT, number needed to treat; MHD, mental health disorders; MINI, Mini-International Neuropsychiatric Interview; PHQ, patient health questionnaire; GAD, generalized anxiety disorder; PD, panic disease; SP, social phobia; BDP, borderline personality disorder; WHO-CIDI, World Mental Health Composite international Diagnostic Interview; EDs, eating disorders; LIFE, longitudinal interval follow-up evaluation; TAU, treatment as usual; DSM, diagnostic and statistical manual of mental disorders.



**Table 2:**  
**Target Conditions Addressed by Studies Investigating the Effectiveness of Internet- and Mobile-based Interventions on Mental Health Disorders Onset**

| Study                      | Unipolar depression | Bipolar | Eating disorders | Psychosis | Addiction | Stress-related disorders | Phobic disorders | Panic disorders | Obsessive-compulsive disorders | Generalized anxiety | Impulse control disorders | Insomnia | Transdiagnostic |
|----------------------------|---------------------|---------|------------------|-----------|-----------|--------------------------|------------------|-----------------|--------------------------------|---------------------|---------------------------|----------|-----------------|
| Buntrock et al. (48)       | X                   |         |                  |           |           |                          |                  |                 |                                |                     |                           |          |                 |
| Christensen et al. (49)    | X                   |         |                  |           |           |                          |                  |                 |                                |                     |                           |          |                 |
| Christensen et al. (50)    |                     |         |                  |           |           |                          |                  |                 |                                | X                   |                           |          |                 |
| Imamura et al. (51)        | X                   |         |                  |           |           |                          |                  |                 |                                |                     |                           |          |                 |
| Lindenberg and Kordy (52)  |                     |         | X                |           |           |                          |                  |                 |                                |                     |                           |          |                 |
| Taylor et al. (53)         |                     |         | X                |           |           |                          |                  |                 |                                |                     |                           |          |                 |
| Thompson et al. (54)       | X                   |         |                  |           |           |                          |                  |                 |                                |                     |                           |          |                 |
| Holländare et al. (55, 56) | X                   |         |                  |           |           |                          |                  |                 |                                |                     |                           |          |                 |
| Bauer et al. (57)          |                     |         |                  |           |           |                          |                  |                 |                                |                     |                           |          | X               |
| Taylor et al. (58)         |                     |         | X                |           |           |                          |                  |                 |                                |                     |                           |          |                 |
| Total number of studies    | 5                   | 0       | 3                | 0         | 0         | 0                        | 0                | 0               | 0                              | 1                   | 0                         | 0        | 1               |

**Table 3:**  
**Characteristics of Studies and Interventions that Investigated the Effectiveness of Internet- and Mobile-based Interventions on Mental Health Disorders Onset**

| Study                      | Target group |            |        | Prevention type |           |           | Media type |        | Program features |           |            | Cost-effectiveness evaluated | Reported potential negative effects | Type of human support |          |
|----------------------------|--------------|------------|--------|-----------------|-----------|-----------|------------|--------|------------------|-----------|------------|------------------------------|-------------------------------------|-----------------------|----------|
|                            | Children     | Adolescent | Adults | Universal       | Selective | Indicated | Internet   | Mobile | Sensors          | Wearables | Algorithms |                              |                                     | Guided                | Unguided |
| Buntrock et al. (48, 59)   |              |            | X      |                 |           | X         | X          | X      |                  |           |            | X                            |                                     | X                     |          |
| Christensen et al. (49)    |              |            | X      |                 | X         |           | X          |        |                  |           |            |                              |                                     |                       | X        |
| Christensen et al. (50)    |              |            | X      |                 |           | X         | X          |        |                  |           |            |                              |                                     |                       | X        |
| Imamura et al. (51)        |              |            | X      |                 |           | X         | X          |        |                  |           |            |                              |                                     |                       | X        |
| Lindenberg and Kordy (52)  |              | X          |        | X               |           |           | X          |        |                  |           |            |                              |                                     | X                     |          |
| Taylor et al. (53)         |              |            | X      |                 | X         |           | X          |        |                  |           |            |                              |                                     | X                     |          |
| Thompson et al. (54)       |              |            | X      |                 |           | X         | X          |        |                  |           |            |                              |                                     | X                     |          |
| Holländare et al. (55, 56) |              |            | X      |                 |           | X         | X          |        |                  |           |            |                              |                                     | X                     |          |
| Bauer et al. (57)          |              |            | X      |                 | X         |           | X          |        |                  |           |            |                              |                                     | X                     |          |
| Taylor et al. (58)         |              |            | X      |                 | X         |           | X          |        |                  |           |            |                              |                                     | X                     |          |
| Total number of studies    | 0            | 1          |        |                 |           |           |            |        |                  |           |            |                              |                                     |                       |          |

In a randomized crossover trial, Thompson and colleagues evaluated an 8-week Internet or telephone-delivered mindfulness-based stand-alone intervention in 64 adult epilepsy patients with subthreshold depressive symptoms. They found that the incidence of MDD episodes, assessed *via* self-report from baseline to interim assessment was significantly lower in the intervention condition (0.0%) than in *treatment as usual* (TAU) (10.7%) condition 8 weeks following randomization. Half of the participants were assigned to receive the intervention *via* web, half *via* telephone, but the authors did not find any differences between the two different forms. Although future studies with longer follow-up periods, larger sample sizes and observer-based clinical interviews are clearly needed to determine the potential of the approach for the prevention of depression, this trial is an example of the potential of Internet-based approaches.

Imamura and colleagues<sup>51</sup> evaluated an Internet-based indicated prevention program with workers who self-identified as having depressive symptoms but not fulfilling the diagnostic criteria for MDD. They randomized 822 workers either to a 6-week, Internet-based cognitive-behavioral program delivered in a comic-form or to a wait list CG. The CBT components of the program included self-monitoring, cognitive restructuring, assertiveness, problem-solving, and relaxation. Results showed significantly lower incidence of MDE at the 12-month follow-up, with 0.8 and 3.9% of the experimental and control participants, respectively, experiencing a MDE. This corresponds to a HR of 0.22 and a numbers needed to be treated of 32 in order to prevent one case of major depression. However, the results need to be interpreted with caution as the diagnosis of MDD had been established only on the basis of a self-report instrument [*World Mental Health Composite International Diagnostic Interview* (WHO-CIDI) self-administered] and not using standard clinician/expert-based diagnostic instruments.

### Anxiety Disorders:

The only trial we are aware of that evaluated the effects of an IMI on anxiety disorder onset is an indicated prevention of general anxiety disorder trial conducted by Christensen et al.<sup>50</sup> They evaluated three different versions of iChill, a 10-week Internet-based-cognitive behavioral intervention for anxiety symptoms (without any reminders, phone reminders, and e-mail reminders) compared to two

attention placebo CG (interactive, attention-matched, Internet-based placebo control program “Healthwatch” with/without phone reminders) in 558 young adults (age 18–30) with general anxiety symptoms who did not meet the criteria for an anxiety disorder.

Generalized anxiety disorder onset at 6-month follow up was 6.7% across all IGs, and 4.5% across both CGs, a difference that was not statistically significant.

## Selective Prevention

### Depression:

Christensen and colleagues evaluated the effects of a 6-week unguided fully automated Internet-based intervention for sleeping problems (SHUTi) with regard to the prevention of major depressive episodes<sup>49, 61</sup> They randomized 1,149 adults with primary insomnia and depressive complaints who did not fulfill the criteria for a major depression to either SHUTi or to Healthwatch. Although large effects in the SHUTi group on insomnia complaints and a lower depression symptoms on the patient health questionnaire-9 at 6 weeks and 6 months compared with Healthwatch were found, the intervention was not superior with regard to the effect on diagnosis of MDD assessed with the Mini-International Neuropsychiatric Interview. However, only ~4% percent of the total sample developed a major depression during the 6-month follow up, making it difficult to detect any preventive effects, even at such a large sample size. Hence, future studies on the longer term follow-up data of this trial (12/18 months) are needed in order to conclude whether this approach is indeed promising with regard to the prevention of major depressive episodes.

### Eating Disorders:

At least two randomized trials have been conducted to date that focused on the selective prevention of ED onset. Taylor and colleagues evaluated the effects of an online cognitive behavioral selective preventive intervention (StudentBodies) on ED incidence compared with a wait list control condition over 3 years in a sample of women with a body mass index >24 and any baseline compensatory behaviors.<sup>53</sup> Although they found the intervention to be efficacious in reducing high weight/shape concerns over a period of 24 months and lower ED incidence rates

in the intervention (5%) group compared to controls (10%), the difference in ED onset was only significant in a subgroup of individuals, recruited and treated at one particular trial site. However, they identified in subsequent analyses specific risk factors associated with ED onset [i.e., comments/teasing about eating from a teacher, coach, or sibling and lifetime depression].<sup>62</sup> Based on these findings, they adapted the IMI to target these specific risk factors and subsequently evaluated this intervention (image and mood) in 185 young adult women (age 18–25) with elevated weight/body shape concerns, eating-related teasing, depression and compensatory behavior compared to a wait list-CG. Although ED onset rates within a 24-month follow up was 27% lower in the intervention compared to the CG, this did not reach the level of statistical significance. Significant lower onset rates were, however, found in a subgroup with the highest body shape concerns, onset (20 vs. 42%, number needed to treat = 5), indicating that it is possible to prevent EDs in very high-risk samples. Another study on StudentBodies showed promising effects on subthreshold ED onset, but did not investigate the effects on full blown disorder onset.<sup>63</sup>

## Universal Prevention

To the best of our knowledge, only one study has been published to date evaluating a universal prevention approach with regard to MHD onset. Lindenberg and Kordy<sup>52</sup> evaluated a universal approach for the prevention of EDs in secondary education students (age 13–16) with no prior ED diagnosis and not undergoing treatment for any ED. Young E[s]sprit is a stepped program tailored to the individual risk of the participant, with elements ranging from screening and tailored risk feedback plus recommendations for specific self-help modules, through monitoring of risk behavior and symptoms and synchronous group and individual online chats up to individual

FTF counseling. Schools including a total of 1,667 adolescents were cluster-randomized in two waves to receive either Young E[s]sprit or an online-psychoeducation intervention. Results showed significantly reduced ED onset rates in the IG compared to control schools in the first wave (intervention: 5.6%, controls: 9.6%) but the second wave (intervention: 5.6%, controls: 4.8%) did not yield significant differences in the overall analyses.

## Relapse Prevention

By now, quite a few studies have investigated the effects of IMI as a relapse prevention intervention,<sup>42-45, 64, 65</sup> and at least two of these also investigated the effects of an IMI on the prevention of MHD relapse.

Holländare and colleagues<sup>55, 56</sup> evaluated a 10-week guided self-help cognitive behavioral intervention for the prevention of relapse in 84 partially remitted depressed adults with at least one previous depressive episode in the past 5 years compared to a no-treatment CG. Six (intervention 5%, controls: 37.8%) and 24 months (intervention: 13.7%, controls: 60.9%) following randomization they found lower rates of relapse in the IG compared to the CG with a HR for time to relapse within 24 months of HR 0.16 in favor of the IG.

Bauer and colleagues<sup>57</sup> investigated the effects of a synchronous transdiagnostic non-manualized Internet-chat group as a stepped-care intervention following inpatient psychotherapy of MHD compared to TAU in 152 adults. They found the chat group to significantly reduce the risk for relapse with 46.5 and 22.2% of the participants experiencing a relapse within 1 year of inpatient discharge in the control and IG, respectively.

**Editor's Note:** Part 2 of this lesson will continue the discussion on IMIs and future directions for the field, possible adverse effects of MHD prevention IMIs, and strategies to increase the reach and utilization of available interventions. ■

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## Multiple-Choice Questions

17. Less than \_\_\_\_\_ of the individuals with a *mental health disorder* (MHD) are recognized and treated.
- A. 10%
  - B. 30%
  - C. 50%
  - D. 70%
18. According to the lesson, internet- and mobile-based interventions have been shown to be effective in clinical populations including the treatment of all, *except*:
- A. Depression
  - B. Schizophrenia
  - C. Alcohol use
  - D. Sleep disorders
19. *Internet- and mobile-based interventions* (IMIs) can be categorized in regard to:
- A. Their use of technology
  - B. The extent of human support
  - C. The theoretical basis
  - D. All of the above
20. Due to their distinctive structured nature, standardization, and focus on the training of strategies and specific behavior, IMIs are particularly suited for techniques that target changes in thoughts and behaviors
- A. True
  - B. False

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# Best Practices in Continuing Medical Education

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## Prevention of Mental Health Disorders Using Internet- and Mobile-Based Interventions: A Narrative Review and Recommendations for Future Research

David Daniel Ebert, PhD; Pim Cuijpers, PhD; Ricardo F. Muñoz, PhD; Harald Baumeister, PhD

ID#: L003447

**This valuable take-home reference translates evidence-based, *continuing medical education* (CME) research and theory, acquired from reading the associated CME lesson, into a stepwise approach that reviews key learning points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

Although psychological interventions might have a tremendous potential for the prevention of *mental health disorders* (MHD), their current impact on the reduction of disease burden is questionable. This article introduces the subject and narratively reviews the available evidence for the effectiveness of *internet- and mobile-based interventions* (IMIs) with regard to the prevention of MHD onsets. Disorders not examined so far include substance use disorders, bipolar disorders, stress-related disorders, phobic disorders and panic disorder, obsessive–compulsive disorder, impulse-control disorders, somatic symptom disorder, and insomnia. In summary, there is a need for more rigorously conducted large scale randomized controlled trials using standard clinical diagnostic instruments for the selection of participants without MHD at baseline and the assessment of MHD onset.

#### Key Point 1: Background

**Less than half of the individuals with a MHD are recognized and treated. Therefore, attention has increasingly been focused on the prevention of MHD. Preventive interventions can be classified as universal interventions, directed at the whole population; selective interventions, directed at individuals with specific risk factors for the development of a MHD; or as indicated preventive interventions, directed at individuals in the prodromal stage of a disorder, who do not yet fulfill the criteria for a full blown disorder but experience subclinical symptoms.**

#### Key Point 2: Current Use of IMIs

**Although internet- and mobile-based interventions have been shown to be effective in clinical populations, including the treatment of depression anxiety, alcohol use, and sleep disorders, evidence for their effectiveness in preventing the incidence of MHD is much less documented.**

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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### **Key Point 3: Technical Implementation**

For the implementation of IMIs, numerous technical possibilities are applicable. These range from (1) the provision of evidence-based strategies as interactive self-help lessons; (2) e-mail, chat, or video-based sessions;<sup>27</sup> (3) virtual reality for exposure interventions;<sup>28</sup> (4) serious-games, in which psychological strategies are trained in the context of a computer game;<sup>29</sup> (5) the use of automated memory, feedback, and reinforcement interventions, for example, through apps, e-mails, text messages, or short prompts, which support the participant in incorporating intervention content into everyday life; to (6) sensors and apps for monitoring health behavior such as physical activity.

### **Key Point 4: Need for More Rigorously Conducted Large-Scale Randomized-Controlled Trials**

Future studies need to identify those subpopulations likely to profit from preventive IMIs. Given that ~75% of all MHD have their onset before the age of 25, future studies should explore the potential of IMIs for preventing the first incidence in children, adolescents, and young adults. There is a need also for more large-scale randomized controlled trials using standard clinical diagnostic instruments for the selection of participants without MHD at baseline and the assessment of MHD onset.

# Telepsychiatry in the Time of COVID-19

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*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Telehealth • Pandemic • COVID-19 • Telemedicine • Telepsychiatry • Limitations

**LEARNING OBJECTIVES:** On completion of this lesson, psychiatrists and other clinicians will be able to (1) delineate the advantages of using telehealth/telepsychiatry as means of healthcare delivery in COVID-19 infection settings; (2) describe recent changes in policies regarding reimbursement, technology use, and licensure at the state and federal level to facilitate the use of telehealth in the United States; and (3) explain limitations in the provision of care associated with this system of healthcare delivery. Additional limitations are added in the last section pertaining to the use of telehealth in the current COVID-19 era.

**LESSON ABSTRACT:** Now that COVID-19 infections have reached pandemic proportions, the use of telehealth to provide psychiatric services has been expanded. To facilitate the extensive use of these services, existing policies have been altered at both federal and state levels of government. The goals of this lesson are to (1) help psychiatrists understand the importance of telepsychiatry/telemental health during this pandemic; and (2) review recent changes in regulations affecting reimbursement, licensure, and the use of technology that were made to support the expansion of this modality. Specifically, this lesson reviews various technological modalities that can be used to ensure compliance with regulations regarding healthcare portals (other than those covered by the Health Insurance Portability and Accountability Act) to ensure confidentiality when carrying out patient evaluations. It also highlights nontraditional methods of interacting with patients that were recently approved by the Center for Medicare and Medicaid Services to facilitate patient care. Case vignettes are provided to illustrate these changes. This lesson also highlights recent changes in methods of prescribing controlled substances. Last, limitations in access to technology and patient safety issues that may be associated with them are described.

**COMPETENCY AREAS:** This lesson addresses the gap in understanding by psychiatrists and other clinicians of how telepsychiatry/telehealth can be used effectively during the current COVID-19 pandemic. It provides psychiatrists with updates on telehealth policy changes, informs them about the basics of incorporating telehealth services into their practices, and reviews changes in licensing requirements which are made rapidly on a daily basis by each state, and what they need to know to facilitate the use of these services. The reader will also learn about new billing codes that have been introduced for reimbursement. After reading this lesson, psychiatrists will have a better understanding of the usefulness—and limitations—of telepsychiatry under current pandemic conditions and gain confidence in their ability to incorporate telepsychiatry into their practices to enhance the effectiveness of patient care while minimizing in-person visits to help prevent the spread of this infection.

## Introduction

The entire world has been challenged by the sudden and rapid development of a devastating viral infection that has come to be known as COVID-19. Caused by a novel respiratory coronavirus named SARS-CoV-2,<sup>1</sup> this disease eventually acquired the name “coronavirus disease 2019,” abbreviated COVID-19.<sup>1</sup> On January 30, 2020, the *World Health Organization* (WHO) declared the COVID-19 infection to be a *public health emergency* (PHE) of global concern.<sup>1</sup> On March 11, 2020, WHO declared COVID-19 to be a pandemic.<sup>2</sup> WHO and other public health authorities throughout the world have been working diligently to control this pandemic by issuing guidelines intended to minimize the spread of this disease.<sup>1</sup> According to the July 10, 2020, updates by the *US Center for Disease Control and Prevention* (CDC), 3,106,931 cases of COVID-19 and 132,855 COVID-19-related deaths had been confirmed in the United States alone.<sup>3</sup>

The outbreak of this disease occurred in Wuhan, China in early December 2019.<sup>4</sup> Since then, the number of cases has increased exponentially worldwide.<sup>3</sup> COVID-19 not only affects the physical health of the patient, but the mental health of the individual as well, particularly in terms of emotions and cognition.<sup>5</sup> Negative emotions (e.g., aversion, anxiety, depression) are most likely to be expressed and are likely to be accompanied by a negative cognitive assessment.<sup>5</sup> For self-protection, people have adapted avoidant behaviors and obey social norms strictly.<sup>5</sup> Prolonged negative emotions can reduce immune function, making the individuals more vulnerable for infection.<sup>5</sup> An online study carried out in China using the “Sina Weibo” social networking tool identified an increase in negative emotions—particularly anxiety, depression, and indignation—within 2 weeks after COVID-19 was identified. This was accompanied by a decrease in positive emotions and life satisfaction.<sup>5</sup> People with a confirmed or suspected case of COVID-19 experience fear of the severe consequences of this disease and its contagion.<sup>4</sup> The sense of loneliness that can develop while in quarantine may also lead to depression, anxiety, insomnia, aggression, and suicidal thoughts.<sup>4</sup> Obsessive-compulsive behaviors have also appeared, taking the form of repeated temperature checks and sterilizations resulting in repeated hand washing. Strict quarantine and contact tracing can

lead to societal rejection, financial loss, discrimination, and stigmatization.<sup>4</sup> The policy of social distancing and sheltering-in-place to avoid the spread of this contagious disease has compelled healthcare organizations to explore alternatives to traditional face-to-face (FTF in-person) modalities of delivering health care.

**The telehealth platform has been proven to be the most appropriate modality to address the healthcare needs of patients with low acuity while effectively minimizing the number of patient visits to emergency rooms, urgent care centers, and the primary care office.<sup>6</sup> Among telehealth services, telemental health/telepsychiatry seems to be ideal for providing mental health care in community settings, particularly at this crucial moment in time.<sup>7</sup> It can be used to provide effective mental health services to people in self-isolation or quarantine or who are at high risk for infection and complications of infection. It also helps reduce the risk of exposure to clinical staff while allowing them to continue to provide services.<sup>7</sup>** Since the current pandemic began, both federal and state laws have gradually been altered to facilitate the use of telehealth platforms to provide patient care. Legal and regulatory changes have included the relaxation of state and federal policies regarding reimbursement, use of technology, and licensure requirements to widen the use of this modality during this pandemic.<sup>6</sup> Telepsychiatry is as effective as FTF in-person evaluations in terms of patient’s/provider’s satisfaction, inter-rater/intermethod reliability, and treatment outcome.<sup>8,9</sup> In one study that included (n=167) Hispanic patients with major depression, (n=80) were treated using telepsychiatry, and (n=87) received usual FTF in-person consultation.<sup>10</sup> The patients treated with telepsychiatry reported better therapeutic alliance, visit satisfaction, and adherence to treatment in comparison to patients treated in person.<sup>10</sup> Further, the depression severity decreased faster among patients treated with telepsychiatry. However, the overall depression rating scales scores were the same in the two groups.<sup>10</sup> Studies have shown similar treatment outcomes for mental health services (medication management and psychotherapy) delivered via telepsychiatry in comparison to FTF in-person treatment.<sup>9</sup>

## Telepsychiatry Encounter

### Case Vignette I:

*Mr. J, a 35-year-old man with a history of bipolar disorder type 1, is scheduled for a 3-month follow-up visit. He is stabilized on risperidone 4 mg at bedtime and lithium carbonate 300 mg in the morning and 600 mg at bedtime. He is currently in remission. Because of the recent COVID-19 pandemic, his outpatient psychiatrist is transitioning his appointments to a virtual platform. He is enrolled in the electronic medical record (EMR) MyChart, which gives him access to telehealth services. Mr. J has a laptop with a built-in camera. He spends most of his time surfing the internet and understands how to operate a computer.*

Telehealth serves as an important means of reducing the risk of exposure of clinicians to disease while caring for patients who are contagious or symptomatic and minimizing the risk of exposure of other patients during clinic visits.<sup>11</sup> The CDC is encouraging healthcare providers to explore alternatives to in-person visits for patients with COVID-19 using such portals as telephone and telehealth video applications.<sup>11</sup> Virtual visits include face-to-face-video visits, which have been classified by the *Center for Medicare and Medicaid Services* (CMS) as “telehealth” visits, and non-face-to-face visits through such modalities as telephone *evaluation and management* (E/M) services, online digital E/M communication (also called e-visits), brief virtual check-ins (e.g., using the phone or other telecommunication devices), and remote evaluations (stored and forwarded).<sup>11</sup>

Telehealth, telemedicine, and telepsychiatry are related terms referring to the transfer of medical information from one site to another electronically using audio and visual modalities in the course of providing health care services.<sup>12</sup> During this current pandemic, there has been an urgent need to expand telehealth services. The CMS is expanding them on an emergent and temporary basis under the 1135 Waiver Authority and Coronavirus Preparedness and Response Supplemental Appropriations Act.<sup>12</sup> Since March 6, 2020, the 1135 Waiver has allowed practitioners to arrange telehealth visits in the patient’s home (designated by the CMS as the “originating site”);

the Waiver remains in effect through the end of the pandemic.<sup>13</sup> Previously, this service was only available for patients with end-stage renal disease on dialysis or patients with a substance use disorder.<sup>11</sup> Various video conferencing applications are available that comply with the safety and security standards established for telehealth services by the American Telehealth Association.<sup>8</sup> Clinicians who want to provide telehealth services for prolonged periods of time must sign a *Health Insurance Probability and Accountability Act* (HIPPA)-compliant Business Associate Agreement with a software company. Many Zoom-based HIPPA-compliant software packages—including Mega Meeting, Telemedicine, Vsee, and Doxyme—can be used for telehealth purposes.<sup>14</sup> Medicare reimburses providers who use such software for *physician’s fee for services* (PFS). The PFS may include the origination fee if the patient is seen in a healthcare facility, in which case the origination fee is paid to the healthcare facility as reimbursement for the use of their technology. Non-facility reimbursement includes a single payment to the practitioner for services provided in his/her office.<sup>1</sup> Telehealth services use the same codes that are used for in-person visits, such as office visits (CPT 99201-99205; 99211-99215) and transitional care management (CPT 99495-99496).<sup>11</sup> The provider should use the *place-of-service* (POS) code s/he would have used if the services were provided in person,<sup>15</sup> along with the modifier 95 to indicate the use of telehealth.<sup>11</sup> Any service reported with POS 02 (telehealth) will be paid at the facility rate.<sup>15</sup> Telehealth services are now available for both new and established patients.<sup>11</sup> Out of pocket payments may apply as the use of telehealth does change out-of-pocket costs for Medicare beneficiaries.<sup>16</sup> The beneficiaries are liable for both the deductible and the coinsurance.<sup>16</sup> The Office of the Inspector General (Health & Human Services) is providing flexibility for health care providers to reduce or waive the cost-sharing for telehealth visits paid for by (Medicare).<sup>16</sup> Written or verbal consent is required from the patient and must be documented in the chart by clinic staff or the provider.<sup>11</sup>

## Can I Use Non-HIPPA-Compliant Platforms for Telepsychiatry?

### Case Vignette 2:

*Mr. K, a 75-year-old man with a history of major depressive disorder without psychotic features, generalized anxiety disorder, and posttraumatic stress syndrome, lives in Houston, Texas. He is stabilized with sertraline 150 mg, and he has been tolerating it well. Mr. K is scheduled for routine outpatient follow-up. Because of COVID-19, the clinic where he has been seen for psychiatric care is trying to minimize patient in-person visits and offered him a telepsychiatry evaluation. The clinic uses an EMR system with the option for telehealth visits through MyChart. The clinic also uses other HIPPA-compliant virtual apps that can be accessed on Apple and android smart phones. Mr. K lives alone and has only minimal family support. Additionally, he is not computer savvy and, consequently, has not signed in for MyChart or installed any phone apps for virtual visits. He knows how to use Skype, however, and has installed it on his phone to stay in contact with his son, who lives in California. He has asked his psychiatrist, Dr. E, for either a phone visit or a visit using Skype. Mr. K is feeling anxious and does not want to reschedule his appointment. **Because of recent changes in the policy about using non-HIPPA-compliant platforms, Dr. E was able to select Skype to conduct follow-up visits with Mr. K.***

The Office of Civil Rights (OCR) at the Department of Health and Human Services is responsible for enforcing HIPAA 1996.<sup>17</sup> During the COVID-19 pandemic, OCR will not enforce penalties for noncompliance with any HIPAA rules when it is carried out under the good faith provision of telehealth services.<sup>17</sup> Under this rule, the healthcare provider may use popular applications to provide telehealth services—including Apple's Facetime, Facebook Messenger video chat, Google Hangouts video, Zoom, or Skype—without being penalized.<sup>17</sup> This rule does not allow the use of Facebook Live, Twitch, or TikTok for telehealth services.<sup>17</sup> While the patient is giving consent, s/he should be informed about the potential

risk for a privacy breach when using these third party applications.<sup>17</sup>

## Virtual Non-Face-To-Face Services Beyond TelehealthMy Patients Want to be Evaluated by Phone: What Should I Do?

### Case Vignette 3:

*Ms. E, a 66-year-old woman with a history of schizophrenia that is currently stabilized with olanzapine 20 mg at bedtime, is scheduled for a follow-up visit with Dr. S. She lives alone in an apartment. Ms. E has a daughter who lives in the neighborhood and is in self-quarantine after recently traveling overseas. She used to bring Ms. E for her appointments. Ms. E was offered a telepsychiatry follow-up, but she insists on being evaluated by phone because she does not have a smart phone or access to a computer. Her psychiatrist recently implemented telehealth services in his clinic, which has limited rules and billing options.*

*Because of the COVID-19 pandemic, CMS recently approved the temporary expansion of non-face-to-face virtual visits (e.g., telephone visits) for patient care. Initially, such visits were not included under the umbrella of "telehealth."<sup>11</sup> They now include telephone E/M services, online digital E/M e-visits, virtual check-ins, and remote evaluations.*

### Telephone Evaluation and Management (E/M) Services:

Physicians who are treating patients remotely for the first time may find it difficult to determine what kind of services should be used and how to bill for reimbursement. Telephone E/M services are allowed for new or established patients during the current pandemic.<sup>11</sup> **Telephone-only visits are being reimbursed by Medicare and by many private payers during the pandemic.**<sup>18</sup> Most payers reimburse for this service at the same rate as for in-person services.<sup>18</sup> **The codes used for this service are 99441 (5-10 min with a 0.25 relative value unit [rvu]),<sup>11</sup> 99442 (10-20 min with 0.50 rvu), 99443 (21-30 min**



**with 0.75 rvu).**<sup>15</sup> Documentation for reimbursement must show the reason for the communication, pertinent data that were reviewed, and an assessment plan.<sup>11</sup> **In order to bill this encounter the E/M services provided should not be related / orientated from E/M services provided in the previous 7 days, nor should it lead to E/M services or procedure in next 24 hours.**<sup>11,18</sup> **According to the interim final rule of the new CMS policy, dated March 31, 2020, these codes can be used to bill payers retrospectively from March 1, 2020.**<sup>18</sup> Telephone E/M services include the diagnosis and management of a problem over the phone without face-to-face interactions.<sup>11</sup> As a result of this recent change, Dr. S can be reimbursed for the period of time during which these services were provided.

#### Case Vignette 4:

*Ms. T, 37-year-old woman with a history of bipolar disorder, endometriosis, and infertility, sent the following EMR message to Dr. Z:*

*“Dear Dr. Z:*

*For the last week I have been experiencing bouts of increased energy despite sleeping for just 4 hours at night. I wake up in the middle of the night and start cleaning my house. I lost my job last week, as my store is closed due to shelter-in-place orders. My mood has been great, and I am handling the stress of this virus pretty well. I am taking lamotrigine 100 mg, which is working great. I saw Dr. N, my OB-GYN, for treatment of endometriosis, and she started me on the pill. My husband is concerned that I am very active these days and suggested that I should consult you. Don't worry I am not suicidal hahaha.”*

*Dr. Z reviewed Ms. T's chart along with chart notes from Dr. N, who had prescribed extended-cycle levonorgestrel/ethylene estradiol oral contraceptive pills for her during an in-person visit 2 weeks before for treatment of endometriosis. He also touched based with Dr. N to discuss her potential treatments for endometriosis. Reviewing her medication list, Dr. Z found that Ms. T was also taking ibuprofen as needed for pelvic pain and has been taking lamotrigine 100 mg for last 6 months.*

*She was last seen in the clinic 6 weeks ago, at which time her symptoms were at baseline levels. Her recent lab results were within normal limits. After reviewing all the clinical data, Dr. Z concluded that Ms. T is experiencing a hypomanic episode that may be related to a drug interaction. Given that levonorgestrel and ethylene estradiol can reduce lamotrigine levels, Dr. Z suggested increasing her lamotrigine dose to 125 mg and scheduling a follow-up visit in 2 weeks to monitor her response. He wrote a detailed message to Ms. T about his recommendations and sent a new prescription to her pharmacy. Six days later, Ms. T sent an EMR message to Dr. Z informing him that she had been tolerating the increased dose of lamotrigine well. She also asked whether she should continue taking the contraceptive pills. Dr. Z had already discussed this plan with Dr. N, who recommended that Ms. T continue taking the pills. Dr. Z responded to Ms. T by explaining the treatment plan. He took 50 minutes to make his medical decision, which was documented in Ms. T's EMR as occurring 7 days after the first message he received from Ms. T. Dr. Z documented her e-visit note, along with the initial message he received from her indicating that she had kept her appointment. He billed for his services using the 99423 code.*

## Online Digital E/M Services E-visits

On January 1, 2020, new CPT codes were added for online digital E/M services. This took place before the pandemic became known.<sup>11</sup> They include codes for asynchronous (i.e., not real-time) communication with patients through HIPPA-compliant platforms, including the EMR patient portal or a secure email. These are patient-initiated services that require medical decision making that would otherwise be provided during an office visit.<sup>11</sup> The physician's response to a message a patient sent through an EMR portal or by secure email is not considered a service that qualifies for billing.<sup>11</sup> The codes used for billing this service include 99421 (5-10 min with 0.25 rvu), 99422 (11-20 min with 0.5 rvu), and 99423 (21+ min with 0.8 rvu). These codes are billed



for cumulative time spend over seven days period which should not be related to E/M services provided in the last seven days, and cannot be separately billed if it results in a subsequent E/M face-to-face visit within the next 7 days.<sup>11</sup> Thus, the 7-day period begins when the physician first receives an inquiry from the patient. The total time spent responding to patient inquiries/medical decision making during those 7 days should be documented in a separate e-visit note, along with the patient's messages.<sup>11</sup> It should not include the time spent communicating test results, appointment scheduling, or any other information that is not part of E/M.<sup>11</sup>

### Virtual Check-Ins:

Patients usually initiate virtual check-ins, which are brief technology-based services enabling them to communicate with their providers to avoid unnecessary office visits. This check-in is only for existing patients. Communication should not be related to an office visit from the previous seven days; and it should also not lead to an office visit in the following 24 hours.<sup>13</sup> Check-ins include a brief (5 to 10 minutes) check via telephone (or other another telecommunication device) and can be billed with code HCPCS G2012.<sup>11,13</sup> CMS approved this service before the current pandemic in an attempt to treat health care problems in their initial phase.<sup>13</sup> It also helps providers ensure that patients follow the health care plan at home, especially patients with mental health issues. This tool can be beneficial in providing effective care by minimizing patients' visits and limiting their exposure at this time.

### Remote Evaluations (Store and Forward):

Remote evaluations include the interpretation of recorded videos or images submitted for an established patient (store and forward technique) with a follow-up response within 24 business hours. This remote evaluation should not be related to E/M services provided in the previous seven days and should also not lead to E/M services or procedures in the next 24 hours.<sup>11</sup> This evaluation is billed by the code (HCPCS G2010),<sup>13</sup> and could be an effective way for the patients to get timely input from several specialists. This asynchronous telehealth tool can be effectively used in an integrated care model, which involves the care managers coordinating services between the primary care provider and the psychiatrist.<sup>19</sup>

### Consent for Non-Face-To-Face Encounters:

Obtaining informed consent is the first step in establishing a therapeutic alliance with the patient. This is as true for a virtual "tele" consult as it is for a physical encounter. As the use of telehealth services (including telepsychiatry) continues to grow, a thorough explanation of this service can reduce any anxiety over its use and allow the doctor-patient relationship to be established quickly.

While obtaining patient consent for non-face to face encounters, the clinician must inform the patient about risks associated with the use of such modalities for treatment, especially the issue of privacy when using platforms that do not comply with HIPPA regulations. During this process, the patient should be told if s/he has to pay for any portion of the services provided.<sup>1</sup> Informed consent is required by state law. Consent can be obtained either by auxiliary staff under supervision or directly by the billing provider. It should not result in any delay in the provision of services. Consent must be obtained annually; it can be obtained at the time services are provided or before.<sup>15</sup>

## Changes in Licensure Requirements

### Case Vignette 5:

*Ms. I is a 22-year-old female with a history of generalized anxiety disorder with panic attacks. She is a senior at a university in New Jersey and majoring in business administration. Her psychiatrist, Dr. P, is also located in New Jersey and is only licensed to practice in that state. Ms. I is legally a resident of Pittsburgh, PA but had been living in a dormitory at the university in New Jersey. She had been visiting her family in Pennsylvania when the COVID-19 pandemic struck. Since then, she has enrolled in a distant learning program. She is stabilized on paroxetine 20 mg daily, but her anxiety has worsened. Ms. I requested a consultation via telepsychiatry, because she feels that her medication is no longer working. Dr. P is not sure if he can evaluate her remotely, because she now lives in a state in which he does not have a license to practice.*

Several states have temporarily relaxed their physician licensing requirements to allow clinicians to practice medicine in states other than those in which they are licensed and to allow retired physicians and those with an inactive license to treat patients via telehealth modalities in order to provide effective care for as many patients as possible during the COVID-19 pandemic.<sup>20</sup> This involves waiving licensing requirements or offering temporary expedited licenses for out-of-state providers.<sup>20</sup> CMS has temporarily waived the requirement to be licensed in the state in which the physician practices to allow physicians to provide telehealth services across state lines.<sup>20</sup> At this time, Connecticut, Delaware, Iowa, New York, Pennsylvania, Tennessee, Maryland, Mississippi, and West Virginia are allowing out-of-state physicians to provide telehealth services across state lines.<sup>21</sup> The State of New Jersey has implemented accelerated temporary licensure by reciprocity, thereby waiving background checks, fees, and proof of malpractice insurance to allow physicians to provide telemedicine/mental health services across state lines.<sup>21</sup> Alabama, Arizona, California, Colorado, Florida, Georgia, Hawaii, Idaho, Illinois, New Hampshire, New Mexico, North Carolina, North Dakota, and Oklahoma have also implemented changes in licensing requirements,<sup>21</sup> whereas Alaska, Arkansas, Maine, Michigan, Minnesota, Missouri, Montana, Nebraska, Nevada, Ohio, South Dakota, Utah, Vermont, Virginia and Wisconsin have not.<sup>21</sup> The licensing requirements of state medical boards are being updated on a day-to-day basis. Providers are encouraged to contact their state medical boards or the *Federation of State Medical Boards* (FSMB)<sup>22</sup> frequently for current information.<sup>20</sup>

Thus, Dr. P can provide services to Ms. I, because the State of Pennsylvania is allowing providers licensed in other states to provide telehealth services across the state line.<sup>21</sup>

### Case Vignette 6:

*A is a 15-year-old male who moved to the United States from the United Kingdom with his parents 3 months ago. He was diagnosed with attention-deficit hyperactive disorder and was stabilized on methylphenidate long-acting 30 mg daily. He was scheduled to see Dr. D, but his appointment was cancelled because the clinic was closed for in-person*

*visits due to the COVID-19 pandemic. A's mother had brought her son's medical record from his UK provider and sent them by fax to Dr. D. The clinic at which Dr. D provides services is in the process of developing telehealth services, and A was offered a telehealth appointment. Based on his remote evaluation and review of A's medical records, Dr. D restarted A's prescription for methylphenidate, with which he was stabilized. A is now enrolled in on-line classes but struggling to concentrate.*

According to the Ryan Haight Act, the provider must do an in-person initial evaluation before prescribing controlled substances electronically. On March 17, 2020, the *Drug Enforcement Agency* (DEA) suspended this requirement.<sup>14</sup> As a result, DEA-registered practitioners can prescribe controlled substances without performing an in-person evaluation. As long as the prescription has been written for a legitimate medical purpose and the practitioner is acting in accordance with applicable federal and state laws, the practitioner can carry out telehealth visits using real-time audio-video modalities that include a two-way interactive communication system.<sup>23</sup> Thus, Dr. D was able to electronically prescribe stimulants for A without seeing him in person. Since March 31, 2020, providers have been allowed to prescribe buprenorphine for new and existing patients with opiate use disorder by phone as long as the clinician is registered with the DEA as an opioid treatment provider. The DEA is of the opinion that patients can be evaluated adequately over the phone by such "data-waived" practitioners.<sup>23</sup>

## How Can I Use Telepsychiatry To Handle Crisis Situations?

### Case Vignette 7:

*Dr. M runs a telepsychiatry service. In the wake of the COVID-19 epidemic, his service has been receiving requests for psychiatric evaluations of new patients. Dr. M is located in Florida and is licensed to practice there and in several other states, including New Jersey. Dr. M did an intake on Mr. K, a 35-year-old male with a history of major depressive disorder and alcohol use disorder*

*who has been stabilized with fluoxetine 20 mg. Mr. K, who currently resides in Galloway, NJ, has been hospitalized four times and attempted suicide twice by taking an overdose of pills. He was working in a restaurant as a waiter but recently lost his job because of the COVID-19 pandemic. He is experiencing financial problems and has reported a worsening of his depressive symptoms. He lives alone and has only limited family support. He has a brother who lives in New York, and his parents are deceased. Since he lost his job, he has been drinking heavily and on a daily basis. Dr. M evaluated Mr. K using a HIPPA-compliant videoconferencing app. During the intake, Mr. K achieved a score of 22 on the Patient Health Questionnaire (PHQ-9). He has reported passive death wishes but denies having active suicidal thoughts. His fluoxetine dose was increased to 40 mg, and hydroxyzine 50 mg at bedtime was prescribed as needed for insomnia. He was also advised to cut down on his drinking. Dr. M developed a crisis and safety plan with Mr. K that called for Mr. K to call 911 or a suicide hotline if he felt that his symptoms were getting worse or he was having active suicidal thoughts. Dr. M also obtained the phone number of the Galloway Township Police Department for Mr. K so that he could call them whenever a crisis situation arose. Given the severity of Mr. K's symptoms, Dr. M scheduled a follow-up appointment for the following week. During the follow-up visit, Mr. K reported having active suicidal thoughts involving an overdose of pills. He reported stockpiling pills, which showed an intent to carry out his plan. Using a secure messaging system, Dr. M informed his staff to call the local police department. He continued to engage Mr. K in conversation until the police and EMS arrived at his home. Mr. K was taken to a local hospital emergency room.*

Telepsychiatry is associated with a number of limitations and challenges besides licensing, credentialing, reimbursement, malpractice, boundary violations, the use of technology, and the settings in which these services are provided. Because of the ongoing pandemic, most regulations governing the use of technology, as well as professional licensing and reimbursement, have been

relaxed, at least temporarily. Technology-related barriers are significant at the time of this pandemic, which includes patients' limited access to webcams and smartphones, their inability to use technology, especially among the elderly population, and the arrangement of computer hardware for healthcare facilities in a short timeframe.<sup>24</sup> Transitioning of the traditional face-to-face evaluation to a virtual visit in outpatient clinics is challenging and requires training of staff and providers. System overload is a common problem when using HIPPA-protected EMR services such as MyChart.<sup>25</sup> Information technology (IT) support is required to ensure adequate bandwidth and secure connections.<sup>25</sup> A valid concern and limitation is cybersecurity when using commercially available video conferencing software.<sup>25</sup> For example, the popular video conferencing software, Zoom, has been a victim of hacking during this pandemic resulting in interruption of educational sessions.<sup>25</sup> Video conferencing to provide services in unsupervised settings (e.g., the patient's home) presents challenges in terms of boundary violations and patient safety issues in crisis situations that are usually not encountered in supervised settings (e.g., health care facilities).<sup>26</sup> To overcome these challenges, the psychiatrist must develop an emergency protocol and procedures. The psychiatrist must also demonstrate the availability of emergency psychiatric services at the patient's location<sup>26</sup> and indicate how these services can be activated at the time of a crisis.<sup>26</sup> This may involve demonstrating the ability to obtain contact information for a family member who would be available when a crisis arises and contact information for the local law enforcement agency. In this vignette, the psychiatrist demonstrated such planning by obtaining contact information for law enforcement in his patient's hometown and reminding the patient to call 911 when necessary. Given that Mr. K does not have family support, this information could be vital in a crisis situation.

## Conclusion

Telehealth/telepsychiatry had been used effectively to provide patient care well before this current public health emergency. Because of the high rate of infection seen with the novel coronavirus, social distancing and self-isolation are important components of the strategy to minimize the morbidity and mortality associated with this disease.

Telepsychiatry can be used to provide mental health services effectively in communities that can abide by social distancing precautions. The relaxation in the rules to widen the use of telehealth/telepsychiatry, coupled with improved confidence of providers in taking advantage of this technology, will result in mental health services being available at the patient's doorstep. It is particularly needed in rural and underserved areas. Current efforts

to facilitate the use of this mode of patient care may encourage changes in state and federal laws to allow it to remain in use beyond the current public health crisis. There should also be an effort to continue to improve the technology to develop user-friendly software while expanding access through broadband internet throughout the country, especially in rural areas. ▮

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## Multiple-Choice Questions

**21. Telepsychiatry can effectively deliver health services during the COVID-19 pandemic because:**

- A. It can help minimize disease spread by preventing patients from visiting clinics or other health care facilities, where face-to-face contact puts both patients and practitioners at risk.
- B. It is widely available at reduced cost.
- C. It can be easily used by the patients with limited technical skills.
- D. Results are better than through a face-to-face in-person evaluation.

**22. In Vignette 2, the psychiatrist evaluated the patient via Skype because:**

- A. It can be used on patient's request.
- B. Skype for business is HIPPA compliant.
- C. Skype can be used if no other options are available routinely.
- D. According to recent OCR guidelines, it can be used to evaluate patients remotely without the risk of penalty.

**23. During the ongoing pandemic, providers can bill their healthcare facility for reimbursement for telephone E/M services *except*:**

- A. Telephone only visits are reimbursable by Medicare as well as many private payers during this COVID-19 PHE.
- B. It is billed by using specific CBT codes
- C. It can be separately billed to previous E/M services provided in the preceding seven days.
- D. As per the CMS new policy based on interim final rule dated 3/31/2020 these codes can be billed retrospectively from March 1st 2020.

**24. Online digital E/M services include all of the following *except*:**

- A. On January 1<sup>st</sup> 2020 new CPT codes were added to bill online digital E/M services.
- B. It can be done through non HIPPA compliant platforms
- C. It includes asynchronous not real time communication with a patient.
- D. It should be initiated by the patient.

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# Best Practices in Continuing Medical Education

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## Telepsychiatry in the Time of COVID-19

By Syed Z. Iqbal, MD; Ali Hashmi, MD; Asim A. Shah, MD

ID#: L003448

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

This lesson provides guidance to psychiatrists who are planning to switch from traditional face-to-face clinical encounters to telemental health. Telemental health is an effective way to deliver mental health services during a pandemic in which social distancing, sheltering in place, and improved personal hygiene practices are the main tools for preventing the spread of infection. Policies regulating medical practices have been relaxed on both state and federal government levels to facilitate the use of this modality where possible. This lesson highlights recent changes that have been made to allow the use of varied technologies and methods of reimbursement and licensure to facilitate the use of telehealth for patient care.

#### **Key Point 1: Telehealth Services Can Be Provided Temporarily Using Non-HIPPA-Complaint Platforms Without Penalty For the Duration of the COVID-19 Pandemic**

Providers who are considering switching from in-person clinical encounters to telemental health should preferably use HIPPA-compliant platforms, which include various android- and Apple-compatible apps. They can also activate telehealth options in existing EMRs, if available. Patients who have never been evaluated using HIPPA-complaint platforms can be evaluated using popular non-HIPPA-compliant apps, such as Skype or Facetime, without facing any penalties.

#### **Key Point 2: Telemental (Audio and Video) Health Encounters Are Billed Using the Same Codes for E/M and Psychotherapy Visits As In-Person Visits With a Modifier<sup>9</sup>**

Providers are particularly curious about billing and reimbursement codes used with this service. Telehealth services can be billed using the same codes that are used for in-person services, with a modifier. Reimbursement for such evaluations are equivalent in amounts to reimbursements for in-person evaluations.<sup>8</sup>

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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**Key Point 3: CMS Has Waived Its Requirements for Site Reimbursement: Services that Are Provided in the Patient's Home Will Now Be Reimbursed**

In light of the COVID-19 pandemic, CMS has relaxed its rules to allow the provider to evaluate patients in their homes using telepsychiatry. These provider will be reimbursed for these services at the same level as they are for providing services to home-bound Medicare patients. This has allowed the expansion of the scope of the telehealth encounters at this difficult time.

**Key Point 4: Telephonic-Only Encounters Can Be Used to Provide E/M Services: These Can Be Reimbursed By Using Special Codes**

Clinicians are allowed to provide E/M services through telephone-only encounters during this COVID-19 pandemic. These services can be used to do assessments of new and established patients. Providers can bill for reimbursement using the special codes 99441, 99442, and 99443.

**Key Point 5: Online Digital E/M Services Are Permitted: They Are Reimbursed As Non-Face-To-Face Encounters**

Online digital E/M services are permitted without requiring face-to-face encounters. Only HIPPA-compliant patient portals can be used for this purpose. These services must be initiated by the patient and can be billed for 7-day periods. The codes for reimbursement vary with the total amount of time spent providing services during each 7-day period.

**Key Point 6: Controlled Substances Can Be Prescribed Without an Initial Face-To-Face Evaluation**

The DEA has waived the Ryan Height ACT temporarily during this COVID-19 PHE. Thus, controlled substances can now be prescribed online without a one-time, face-to-face evaluation to establish a doctor-patient relationship.

**Key Point 7: State Licensing Requirements Have Been Relaxed to Allow Practitioners to Provide Telehealth Services Across State Lines**

State medical boards are working diligently to alter state regulations in order to facilitate the use of telehealth across state lines. Many states have waived the requirement of state-specific licensure to provide telehealth services. Others are in the process of expediting and accelerating the licensure process for those who intend to provide care using telehealth procedures. These rules are being changed on a day-to-day basis. Providers are advised to contact their respective state medical boards to get the latest updates.

**Key Point 8: Safety Issues and Other Limitations**

Recent healthcare policy changes have helped eliminate barriers to the use of telemental health services. Most address limitations in access to these services and the required amount of knowledge about the technology and safety issues involved in evaluating patients using these services. First, patient should be educated about the risks (especially regarding privacy) involved in using telehealth platforms. Second, clinicians should have a plan in place before providing such services, with a focus on the availability of contact information for patient support systems that must be activated in case of a crisis. This is especially important for providers who are seeing patients across state lines.

**Professional Development Series**

# You Too Can Do Marital Therapy: Expanding Psychiatric Practice to Include Marital Therapy, Part 2

Otto Kausch, MD

*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Marital therapy • Successful and unsuccessful relationships • COVID-19 pandemic

**LEARNING OBJECTIVES:** Upon completion of this program, psychiatrists and other clinicians will be able to: (1) delineate the basic principles of marital therapy; (2) explain the difficulty in determining whether a marriage is sufficiently troubled to require intervention; (3) describe the challenges involved in getting couples to agree to marital therapy when it is recommended by their psychiatrist; (4) identify basic factors and strategies that can facilitate the success of a relationship, including positive sentiment override and repair attempts; (5) describe the potential effects of stress due to lifestyle changes associated with the current COVID-19 pandemic on marital relationships; and (6) express confidence in his/her ability to conduct marital therapy despite the complexities involved.

**LESSON ABSTRACT:** This lesson is a supplement to an earlier lesson on how psychiatrists can expand their practice to include marital therapy. It is also a beneficial supplement for any clinician providing therapy for patients whose marriages are under stress due to mental illness. The author reviews basic factors that should be considered to determine the appropriateness of marital therapy and the barriers and challenges involved in starting the process. He includes a discussion of the effect of the COVID-19 pandemic on marriage and reviews suggestions for addressing marital conflict during the crisis.

**COMPETENCY AREAS:** This lesson addresses gaps in learning related to understanding how the marriages of our patients affect their mental health and how their mental health impacts their marriage. Many clinicians lack the knowledge and understanding needed to address dysfunctional marital dynamics. Similarly, many psychiatrists lack an understanding of how to provide marital therapy as an adjunct to other psychiatric treatments. This lesson will facilitate the ability of these healthcare professionals to understand the basics of marital therapy and how it should be conducted.



## Introduction

In a previous lesson, I outlined the general principles of conducting marital therapy for psychiatrists who wish to expand their practice.<sup>1</sup> Specifically, I provided guidance on conducting marital therapy when our patients reveal that they are experiencing difficulty in their marriages. The purpose of this lesson is to expand on those topics, further clarifying specific terms and approaches, and providing additional material related to the practice of marital therapy. Again, I admit to my biases in the material I present.

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### *Author's Note:*

*I found myself writing this lesson as the world we once knew was changing rapidly because of the COVID-19 pandemic, and it appeared that we were going to be living with these changes for quite a long time. The pandemic is changing many aspects of our lives, including our mental health and the dynamics of marital relationships. Therapists who are trying to help their patients cope with the effects of the pandemic, as well as those already practicing marital therapy, are finding themselves assisting couples whose relationships have changed, often for the worse because of “too much togetherness.” Both stable marriages and marriages marked by long-standing problems are being adversely affected. In the latter part of this lesson, some of these issues will be addressed.*

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## A Brief Review of My Method of Adding Marital Therapy to Psychiatric Practice

After determining that some of my patients were experiencing marital problems, I started asking the patient's spouse to join us for a session during which I could obtain collateral information. I would bring up the topic of marriage as a natural component of my history taking and subsequently ask the spouse questions that could reveal problems in the relationship. If the spouse did not acknowledge any relationship problems, I would then ask specific questions such as: “*Were you aware that your spouse is unhappy in your marriage?*” I might then encourage my patient to generally describe the unhappiness s/he was experiencing, indicate how long this has been an issue, and explain how this made that individual feel.

I usually found that the spouse was likely to work on marital issues after attending this session, which indicated

some degree of caring and concern and a willingness to be involved. Once the spouse acknowledged problems in the marriage, I hoped that the couple would agree to marital therapy. If so, I would use marital therapy techniques that are based on substantial scientific evidence to help the spouses improve their marriage. Using such interventions, I was often successful in helping to relieve my patients' mental health symptoms while assisting them in improving their marriage. I usually achieved greater success using this technique than traditional marital therapy tactics because it allowed me to catch problems early enough to help my patient and his/her spouse turn things around. This differs from the usual pattern of couples seeking marital therapy, in which the spouses come in together seeking marital therapy after years of unhappiness and when they are on the verge of divorce. It is much harder to turn the tide when the marriage is already in shambles.

In this lesson, I offer a brief review of my method of engaging established patients in marital therapy. I will examine the common difficulty of determining whether the patient is unhappy enough to require intervention and the challenge of getting partners to agree to marital therapy. I will review basic principles governing the process of marital therapy and examine certain important dynamics in relationships such as positive versus negative sentiment override, and explain how such dynamics can determine the success or failure of a relationship. **I will also emphasize the importance of repair attempts, which have been found to predict strong marriages and can be taught to partners in a troubled marriage to improve their relationship.** Further, I will elaborate on the concept of having a “bank account of good will” to demonstrate to the spouse that s/he and their marriage are valued. I will also touch on the effect of quarantine on marriages in the age of the coronavirus and provide recommendations for couples during this time of heightened stress.

## How Difficult Is It to Determine Whether Your Patient Is in a Troubled Marriage?

Patients generally do not come to see me with a chief complaint of marital unhappiness, because I am not primarily a marital therapist. Rather, I see patients for individual mental health issues. I have found, however,

that identifying marital unhappiness is an important clue to the reason for the patient's distress at any given time and display of psychiatric symptoms. Identifying problem marriages can be complicated, however. For example, if you simply ask the patient, "*How is your marriage?*" you often get a superficial answer, such as "*fine*." This can be very misleading. I can't tell you how many patients respond "*fine*" or "*OK*"; yet when I delve a little deeper, they reveal that the marriage is a source of much unhappiness and dissatisfaction in their life. The following are some factors to consider when attempting to determine the state of a patient's marriage:

- Many patients are very guarded when answering. They may not trust you enough to reveal something so personal—at least not until they get to know you better.
- Patients may believe this is none of your business. As their psychiatrist, you may "only" be seen as a medication prescriber, and they are just not going to get into it with you.
- Patients often see psychiatrists because they want a quick fix with medication so they can avoid time-consuming work on any underlying issues (marital or otherwise).
- If things have been going smoothly for a while, they may be in denial or may have forgotten how miserable they were just a short time ago.
- It is common, especially for men, to say that everything is fine when their partner is very unhappy, even when their partner has complained bitterly about how unhappy she is in the relationship. A lot of people don't want to acknowledge any "failures"; they believe that they must present the psychiatrist with a picture-perfect view of their marital relationship.
- I have often found that the couple is happy in their companionate relationship but very unhappy with a specific area of their

**relationship—such as sexual intimacy—which greatly distresses one or both partners.**

### **Clinical Example:**

The patient is a 62-year-old woman who started treatment in an intensive outpatient program to work on symptoms of depression, anxiety, and anger. Upon reviewing the onset of her symptoms, it became clear to me that her lack of sexual relations with her husband contributed in large part to her distress. They had been married for 40 years and raised several children, who were now living on their own. The patient described her husband as a great guy who was very caring and had been a good father and provider. She described the two of them as good companions who previously really enjoyed doing things together. In recent years, however, he had been avoiding having sexual relations with her. In addition to his full-time job, he had also taken on volunteer activities at their church. It seemed that he was always busy and frequently exhausted when he was home. They had talked about their lack of intimacy, but it seemed he could never find the time and/or energy to be intimate with her. She had started to feel that her husband did not find her attractive anymore, and her sense of self-worth had started to suffer. Her preoccupation with these beliefs seemed to precipitate many of her symptoms of depression and anxiety. She also became angry with her husband sometimes and had become more critical because of her disappointment in the lack of affection in her life, given that affection and physical closeness had played an important part in her well-being and previously helped her cope with the stresses of life. During marital therapy, it was determined that her husband had developed erection problems and was ashamed to reveal this to his wife. It was very difficult for him to admit the sense of "failure" brought about by his inability to have an erection.

## Getting the Couple to Agree to Marital Therapy Can Be Challenging

A successful marital outcome is difficult to achieve even in the best of times, i.e., when both partners agree to work on their marriage. Not only do both partners have to put forth a great deal of effort to change their dysfunctional patterns of thinking, but the therapist must work hard to gain their trust. Getting both partners to agree to work on their marriage is often the initial challenge. The “chief complaint” can be an important clue that the issue is a marital problem. This can then be confirmed by taking the time to gather a comprehensive psychosocial history.

### Clinical Example:

**The patient is a 47-year-old man who worked as a specialized police officer. He was accompanied on this visit by his wife, a nurse, who provided collateral information. They both agreed that he had serious anger problems. The wife felt that her husband’s “bipolar disorder” was out of control and that his meds “weren’t working.” He had been seeing another psychiatrist, who had changed his medication numerous times, only to find that none of the medications seemed to help. On further inquiry, I found that the patient had been married for 14 years and that the marriage had been very rocky. Their fighting increased greatly after she allowed her son from a previous relationship to live in their home (against the objections of her husband, my new patient). She wanted her son to live with them, because he had become unemployed and needed a place to stay. The wife seemed to enable her son’s bad behavior at home and was supporting him financially (using the couple’s earnings) while he spent most of his time playing video games rather than looking for another job. Whenever my patient accused her of “coddling” her son instead of setting limits, she would yell at him and accuse him of lacking empathy and always being controlling. He, in turn, would lose his temper and start throwing things around the house. The patient admitted that his**

**anger was worse when he had been drinking, and he admitted he had been drinking more lately. His wife also noted that she had found sexually provocative texts from a woman at his job on his cell phone.**

You will note that in the above paragraph, the sixth sentence begins with “on further inquiry . . .” I have found that many of my peers go straight from a chief complaint to a review of diagnostic criteria in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) for various disorders and then work through a differential diagnosis to try to establish the final diagnosis. The next step is usually the development of a “treatment plan” that involves the prescription of a certain medication. Many psychiatrists nowadays hear “anger” and right think “bipolar” or “bipolar spectrum” disorders. Their attention is then focused almost exclusively on medication management for this diagnosis. In the initial evaluation, they often provide a perfunctory review of psychosocial issues, but their attention is mostly focused on which medication they are going to prescribe. I have found it helpful to inquire more closely about other things, such as relationship dynamics. In the case just described, I had to draw the spouse out to gain information that I found helpful; this involved asking numerous relevant questions.

In my approach, as described in my earlier lesson,<sup>1</sup> the patient may not reflect the true nature and complexity of the problems that need to be addressed. After completing my evaluation, I decided that the couple was the most significant “patient.” Further, both the husband and wife had personality issues that needed attention. The husband also needed to work on his dysfunctional drinking. I did prescribe a medication that would help him with his anger problems, but I explained very clearly to both of them that at best, the medication would only provide some relief but would not significantly improve the quality of their lives. That would require them to address their marital issues. Getting them to agree to work on the marriage was a challenge, because the wife really believed that if I would only prescribe the “right” medication for her husband, everything would be better. As far as she was concerned, the main problem was her husband—he needed to be “fixed” if the marriage was ever going to improve.

## Factors to Consider When Providing Marital Therapy

One must learn to get a sense early on whether marital therapy is going to succeed with each couple. Sometimes the psychiatrist who is functioning as a marital therapist must make the difficult decision that the marriage is beyond repair. Gottman<sup>2</sup> provides guidelines to determine when a marriage is better off ending. He notes that in such marriages, love has turned to hate, and there is much bitterness. Additionally, the couple's narrative of their marital history has become pervasively negative. Marriages that may be considered doomed include those in which (1) one partner is very narcissistic and lacks empathy; (2) there has been an affair, and the partner involved in the affair refuses to stop communicating with the person with whom s/he is having an affair (the specifics about how to manage a relationship tainted by an affair is beyond the scope of this lesson); (3) one or both spouses has an addiction (or severe mental illness) and refuses to get help; or (4) one or both spouses refuses to accept any responsibility for changing his or her pattern of behavior.

### Clinical Example:

The patient is a 61-year-old married man whom I had been treating for schizophrenia. He had been married for 29 years. During a collateral session, his wife indicated that he sometimes didn't take his medicines and would then become extremely paranoid. She said that he drank excessively. He often complained about not getting enough sex in the marriage and used pornography frequently. I briefly attempted a course of marital therapy, but the patient made it known that he was not going to change at all and that his wife needed to make herself sexually available more often. After expressing my pessimism about the marriage, I stopped marital therapy, and the couple subsequently divorced.

Additional factors of importance to emphasize when providing marital therapy include:

- The therapist has to constantly remind the couple of the dysfunctional *patterns of interaction* between them, patterns that

have become established and habitual. The therapist also needs to frequently reinforce the notion that his or her job is not to “fix” the other partner or prove that one partner is right. Rather, the couple needs to see the partner as clearly and objectively as possible, and each of them must learn to understand the other's strengths and limitations. Most of their efforts and attention should be focused on reversing their dysfunctional patterns.

- The therapist must help the marriage partners understand that progress requires a certain amount of humility on each person's part and an acknowledgment that their previous patterns of interaction have not worked well. Both partners need to accept responsibility for the role they play in these patterns. It can be difficult for one person to change any pattern of behavior; it can be particularly challenging when two people are involved.
- A couple must understand the need to make a considerable effort to improve their marriage when children are involved because this dramatically raises the stakes. Marital therapists are well advised to have a basic understanding of good parenting practices, given that many of the conflicts between couples with children center on different approaches to parenting. The presence of stepchildren makes the job of the marital therapist exponentially more difficult. I have had great difficulty making any progress in the area of divided loyalties among stepfamilies.

### Clinical Example:

The patient is a 47-year-old construction foreman with a long history of depression and anxiety, as well as anger problems. He had difficulty identifying the conditions that triggered his symptoms. I asked his wife, a nurse, to join us to provide collateral information. She



indicated that his 16-year-old daughter from his first marriage precipitated many of his emotional outbursts. His daughter sometimes acted lovingly toward her father but, at other times, ignored his texts or said hurtful things to him. His emotions during periods of perceived rejection got out of hand, to the point that he threatened to commit suicide. His wife was distraught by the fact that he seemed to devote more attention to his daughter than to their marriage. During marital therapy, I spent a lot of time trying to get him to reorient his priorities. He needed to make his wife and her feelings a priority, rather than furthering his unhealthy preoccupation with his teenaged daughter.

One of the main jobs of the therapist is to facilitate effective communication between partners, and sometimes communication issues must be worked on immediately. In my previous lesson, I indicated that I usually start marital therapy by educating the couple about what is known scientifically about successful couples. There are times, however, when other things need even more immediate attention. In such cases, I usually alter my approach.

### **Clinical Example:**

The patient is a 26-year-old woman who sought treatment for depression and anxiety. She and her husband had two young children. Their marriage had deteriorated to the point that they were living in separate parts of the house. My patient believed that divorce was inevitable. They had tried marital therapy previously, but her husband walked out during the second session after the therapist told him that he needed individual help for his problems before there could be any hope for improving the marriage. The husband was not keen on trying marital therapy again. I convinced her to bring in her husband for a collateral session. When he came, I spent the initial portion of the session speaking to him in a respectful tone and getting to know his views about his wife and her emotional difficulties. He subsequently agreed there were problems in the marriage, but he didn't want

the marriage to end. I immediately started a communication exercise, teaching them both how to communicate with each other in a structured way. I had them focus on a recent fight and interrupted any attempt by either spouse to demonize the other. I had them focus instead on describing their hurt feelings and how each one felt betrayed and rejected by the other. At the end of the session, the husband said he felt better. He believed that she had heard him. He expressed a new willingness to engage in another attempt at marital therapy.

Hopefully, the therapist will inspire confidence in his or her approach by demonstrating an understanding of and ability to communicate clearly and simply the relevant scientific findings for a successful relationship (more on this in my previous lesson). Once the therapist has gained their trust, s/he will find that the couple is more likely to follow his or her recommendations.

When each partner makes an effort and shows the other partner some consideration, compassion, and patience, they will help inspire in each other the positive qualities that support a healthy relationship.

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## **Positive vs Negative Sentiment Override**

In his extensive research on marriage, carried out by closely and objectively following a large number of couples over many years, John Gottman developed a formula for predicting both a successful and unsuccessful marriage.<sup>3</sup> He called the successful couples the “masters” of relationships and unsuccessful couples the “disasters” of relationships. When he analyzed the interactions of spouses whose marriages worked well despite the everyday strains of a relationship—whom he described as being in emotionally intelligent marriages—he discovered several universal traits. He found that at the heart of a sound marriage is a deep friendship, which he believes is the foundation for a loving relationship. **Gottman found that the ability to maintain a loving, positive relationship offered the best protection against the development of adversarial feelings during the inevitable disagreements and irritations of married life. He termed the ability to maintain**

such a relationship, even under adverse conditions, a *positive sentiment override* (POS).

A POS consists of developing positive thoughts about one's spouse and the marriage that are so pervasive they supersede any negative thoughts. It takes an extremely significant conflict to overcome a POS, one that would cause the spouse to lose his or her equilibrium in the relationship. Spouses with this override have positive expectations from their life together and tend to give their spouse the benefit of the doubt. When faced with an ambiguous situation, emotionally intelligent spouses manage to give the situation a positive spin.

Alternatively, once the couple's relationship starts to unravel and slide into dysfunction, the partners start to view each other and their relationship as going through a negative sentiment override and typically become adversarial. Once this pattern sets in, it becomes self-propagating and deeply entrenched, making it difficult to salvage the marriage. Note that this "switch" can be turned on at any point in the marriage, even after a lengthy period of tranquility. Indeed, spouses often say that they don't understand why their "partner changed" and fail to recognize that it was the dynamics of the relationship that changed, not the partner.

I explain to each couple that it can be trying to maintain a positive sentiment override even under normal circumstances. Once problems crop up, it becomes more difficult. Perhaps the best protection against losing this override is for both partners to make regular contributions to their "bank account of good will."

## How Does One Build a Bank Account of Good Will?

In my previous lesson,<sup>1</sup> I provided a table that listed the factors that can be used to distinguish between a healthy and unhealthy relationship. These factors are listed here in more detail:

- **Maintain a high-quality friendship.** Go out of your way to engage in behaviors that can be used to help build and maintain a high-quality friendship (see reference 2 for ways to accomplish this).
- **Respond to your spouse's bids for connection.** Go out of your way to pay attention

and respond to your spouse's bids for connection (turning toward). For example, put down the newspaper and pay attention when your partner wants to talk, no matter how trivial the topic may seem at the moment.

- **Avoid the "Four Horsemen of the Apocalypse" during disagreements.** As explained by John Gottman,<sup>2</sup> and reviewed in my previous lesson,<sup>1</sup> there are four communication responses which are relationship killers such as *criticism*—focusing on a partner's perceived character flaws; (2) *contempt*—showing contempt, acting superior, mocking, using sarcasm; (3) *defensiveness*—deflecting by pointing out the spouse's flaws rather than accepting responsibility for your behavior; and (4) *stonewalling*—turning away and tuning out . . . totally avoiding your partner's concerns.

Be particularly mindful of your voice tone and word choice when responding to your spouse during a disagreement. Words—and the way they are said—can be very powerful. Make every effort not to show any contempt (the most deadly of the Four Horsemen), and be mindful to avoid sarcasm.

- **Make repair attempts after regrettable incidents and then try to process them.** In his research on successful and unsuccessful couples,<sup>3</sup> Gottman found that repair attempts and how well they are received are among the most important factors in determining the success or failure of a marriage. A repair attempt is any effort to de-escalate the tension that builds during an argument. It may be a statement or action that can prevent any negativity from getting out of control. Such attempts include apologizing, lightening the tone, and using humor. An example of a repair attempt is as follows: *"My reaction was too extreme.*



*Sorry. Let me try again.*” Hopefully, with extra effort, regrettable incidents will be avoided. When they occur, however, each partner should make a conscientious effort to offer a repair attempt at the earliest opportunity. Even if your spouse doesn’t respond right away, continue to make repair attempts while maintaining a positive attitude.

- Make sure the ratio of positive to negative interactions in the relationship is at least five to one. I advise spouses to do their best to keep that ratio as high as possible. Negative interactions include using the “Four Horsemen” during conflicts and being dismissive of the partner’s concerns. Positive interactions include the use of humor and affection (such as holding hands when discussing a difficult topic).
- Use “soft start-ups” when voicing a complaint. Try hard to avoid a harsh start-up. Keep a close eye on your tone of voice (not just the volume).
- Soft start-ups consist of the following: One partner gently raises an issue so that it does not become a criticism (one of the “Four Horsemen”). That partner should focus on how an action or lack of action affects his or her feelings. Here’s an example of a soft start-up: *“I’m upset that you forgot to sweep the kitchen last night as you promised you would. Can you please get to it as soon as possible to make my day easier?”* By contrast, a harsh start-up results in negative and accusatory statements reflecting global judgments about the partner’s character. For example, *“Why are you always forgetting to do things that you promised to do? You are such a jerk!”* Avoid using absolutes such as “always” or “never,” as well as name-calling.
- Allow your partner to influence you. Gottman found that the actions of the

husband play a considerable part in the success—or failure—of a marriage. He noted that men, in general, are more likely to escalate marital disputes into negativity using one of the Four Horsemen. When they do, they put the marriage at risk (3, chapter 7). One way to counter this tendency is for men to be willing to share power with their wives, thereby accepting their influence. The husband should solicit his wife’s opinion on matters that involve running the household, finances, and family matters and then show a willingness to compromise.

- When simple compromises are not possible, then it is essential to have a strategy to avoid gridlock. Gridlock occurs when partners can’t agree on issues important to them, and these continuing disagreements threaten the couple’s sense of cohesion and intimacy. Arguments centering on significant issues can generate many hurt feelings. When gridlock seems to be present or inevitable, communication is vital. Perpetual conflicts are often grounded in different values, which are a product of each partner’s early life and also their temperament. Spouses should explain to one another how their upbringing and temperament have developed them into the person they are. For example, one partner may like frequent socializing and parties or sporting events, whereas the other is more of a homebody who prefers to read or watch movies. Sometimes couples can make partial compromises as a way to show good faith.
- Extend frequent emotional engagement. Thank your partner for every small kindness s/he shows you. Show your appreciation.

Additionally, I suggest a little romance. In a major international survey,<sup>4</sup> both men and women throughout the

world stated that they wished their partner was more romantic. Examples of ways in which they wanted their partner to be more romantic included giving romantic gifts on special occasions, having a regular date night, giving (and accepting) back rubs, and passionate kissing. Other ways in which they felt a partner could be romantic was by saying, “*I love you*” sincerely, giving frequent compliments on the spouse’s appearance, and frequent positive body contact such as “*cuddling*.” As the therapist working with a symptomatic patient, consider emphasizing these behaviors as a sure way to build a bank account of goodwill.

### **The Overlap Between Positive Sentiment Override and Gratitude**

Gottman found that PSO is a powerful factor in determining whether a marriage would be successful and happy. PSO is a pervasive positive cognitive distortion in which one spouse focuses on all the positive traits of the other, frequently gives the other spouse the benefit of the doubt, and minimizes all the quirks and less-than-admirable qualities of the other spouse. Research in the area of gratitude in marriage dovetails nicely with the findings on PSO. One researcher noted that gratitude involves an appreciation of both the kind acts of the partner and the positive qualities and best traits of their partner. “Moments of gratitude help people recognize the value of their partners, and a valuable partner is a partner worth holding on to.”<sup>5</sup> Research on gratitude in couples has revealed that therapists should encourage their marital therapy patients to record the nice things they did for their partner that day and how they felt about doing them. At the next visit, the therapist can ask each spouse how the partner’s kind deeds affected their views of the spouse, how this affected their perception of the marriage, and whether it increased their feelings of love. I encourage the spouse who has benefited from an act of lovingkindness to express gratitude for that kindness. Exercises such as these, which encourage expressions of gratitude, can help increase the PSO in the marriage.

### **Not All Couples Need to Address Conflict and Dysfunction During Therapy, but Bringing the Spouse for a Collateral Session May Reveal Unexpected Problems**

There have been numerous instances in which I have had both partners come to the same session to offer assistance to each individual and to the couple. Couples often undergo numerous stressors that can affect not only the partner who is your patient but also your patient’s spouse. For example, if your patient tells you that he suffered a job loss, and it is causing him distress, I recommend that you ask how this stress is affecting his wife. It may be prudent to ask your patient to bring the spouse to a therapy session to help your patient process this stressor, as well as to obtain collateral information on the effect of the job loss on the financial security and psychological well-being of the family. If the husband is the primary breadwinner, for example, you may want to see how empathetic the wife is to his stress. If she is empathetic, you can teach your patient that seeking empathy from his wife may be a beneficial way to cope. This type of collateral session may also reveal that the wife is really struggling because of the husband’s job loss, even though she has not said this to him out of fear or to avoid revealing the extent of her disappointment and stress. This revelation will allow you to develop a course of marital therapy that addresses each partner’s distress and helps them understand each other better. On the other hand, if their marriage is rockier than your patient led you to believe, you may need to consider the issue of unemployment and the financial complications that can result, serving as significant stressors in a marriage, while developing your therapeutic approach.<sup>6</sup> The distress caused by job loss can put a couple on the road toward divorce.<sup>7</sup> In the words of Tumin and Quian:<sup>8</sup> “Job loss by either the husband or wife may strain the marriage because it forces the couple to make do with fewer resources, upsets the ‘bargain’ over what each spouse contributes to the relationship, and makes the unemployed spouse less attractive as a partner.”

Psychiatrists interested in couples therapy are likely to see more examples of marital distress being caused by unemployment due to the aftershocks of the coronavirus

pandemic. The effects of the pandemic on couples will be discussed in the next section.

## The Effect of the COVID-19 Pandemic on Marriage

Relationships are being increasingly affected by the pandemic, often in a negative way<sup>9</sup> as a result of partners spending “too much” time together. Issues that were simmering before the pandemic are likely to be magnified and multiplied. One very worrying concern is a reported increase in domestic violence and even pet violence.<sup>10</sup> Campbell summarized some of the more worrisome trends and outcomes for marriage as a result of previous natural disasters.<sup>10</sup>

In a recent news post, the manager of a marriage registry in a province of southeast China reported that more than 300 couples had scheduled appointments to get a divorce.<sup>11</sup> He stated further that “The divorce rate [in the district] has soared compared to before [the coronavirus outbreak].” He also explained that “Young people are spending a lot of time at home. They tend to get into heated arguments because of something petty and rush into getting a divorce.” Some natural disasters have been followed by an increased birth rate, but this pandemic will more likely lead to an increased divorce rate.<sup>12</sup> One contributing factor may be heightened anxiety, leading to marital tension. According to Julie Swartz Gottman, wife and professional collaborator with John Gottman: “Anxiety is rampant [during this pandemic], and people are potentially taking some of that anxiety out on each other. So, the relationships that are perhaps a bit unsteady, uncomfortable, perhaps have some tension and don’t have ways of dealing with stress together, can spiral downwards.”<sup>13</sup>

Thus, we psychiatrists will likely see more of our patients’ marriages becoming dysfunctional. This trend can be a further motivating factor for us to learn some of the basics of marital therapy.

### Recommendations for Couples During the Pandemic:

Aside from the steps recommended for building a bank account of good will (described in a preceding section), I would offer some advice to couples during the pandemic that is recommended by the Gottmans:<sup>13</sup>

1. **Make an appointment (at a specific date and time) for arguments that could lead to a fight.**<sup>13</sup> When a spat gets out of hand, partners can become “flooded” in the heat of the moment, which makes conflict resolution almost impossible.<sup>3</sup> This scenario is particularly likely to happen during periods of heightened stress, such as this pandemic.
2. **Make a point of preventing children from witnessing arguments—even if it means that parents hide away from the children with a “do not disturb” sign on the door.**
3. **Respect boundaries.**
4. **Use your sense of humor to ease tension.**

In another article about relationships in the time of the coronavirus,<sup>14</sup> the following recommendations were made:

1. **Don’t feel obligated to interact more just because couples are both at home more. I think it is worth emphasizing here that boundaries are essential—especially if one partner prefers peace and solitude. The couple can always come together to talk intimately at the end of the day.**
2. **Be mindful not to overreact to little annoyances. It is easy for annoyances to pile up more quickly when couples are seeing each other so much.**
3. **Given all the togetherness, it may be necessary to reevaluate the usual frequency and quality of sexual relations.**
4. **Remember: “*This, too, shall pass.*”**

## Summary

As a psychiatrist, you may want to help their patients improve their marriages as a means of resolving mental health issues. To this end, it is important to determine how the mental health of your patient is being affected by a dysfunctional marriage, to understand key dynamics

in relationships that commonly determine the success or failure of a marriage and offer specific steps a couple can take to improve their marriages. These include

lifestyle changes that have been recommended to help preserve marital harmony during the current coronavirus pandemic. 📖

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## Multiple-Choice Questions

**25. According to John Gottman, husbands dismiss their wives' emotions every time they:**

- A. Try to fix them or distract her from them.
- B. Minimize them or ignore them.
- C. Mock them.
- D. All the Above

**26. Negative sentiment override refers to a tendency to be positive in the face of marital problem. This statement is:**

- A. True.
- B. False.

**27. *"I'm upset that you forgot to sweep the kitchen last night as you had promised you would. Can you please get to it as soon as possible in order to make my day easier?"* This is an example of a:**

- A. "Harsh" start-up.
- B. "Soft" start-up.
- C. Neither.
- D. Can't tell.

**28. Research shows that using words like "always" or "never" in complaining about your partner is likely to:**

- A. Improve your relationship.
- B. Worsen your relationship.
- C. Have no effect on the relationship.
- D. Be irrelevant to the outcome of the relationship.

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# Best Practices in Continuing Medical Education

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## You Too Can Do Marital Therapy: Expanding Psychiatric Practice to Include Marital Therapy, Part 2

By Otto Kausch, MD

ID#: L003449

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

This lesson reviews the basic approach to conducting marital therapy when psychiatrists determine that marital conflict is an underlying factor in the symptoms and distress of their patients. This lesson augments a previous introductory lesson with additional details and strategic recommendations that may improve the chance of a successful outcome. Carriers and challenges resulting in marital distress are identified, along with specific factors and strategies that can help marriages succeed. The research underlying these principles is emphasized. Preliminary evidence of the influence of the coronavirus pandemic on marriage is reviewed, along with suggestions for preventing them from causing the marriage relationship to deteriorate.

#### **Key Point 1: By Viewing the Distress of Our Patients Through the Lens of Pathogenesis, We Can Understand and Appreciate the Importance of Marital Distress in Their Symptoms**

Research indicates that our patients' symptoms, especially symptoms of depression, are often associated with marital unhappiness. It is preferable to address the root causes of this distress, rather than just focus on the presenting symptoms to generate a treatment plan.

#### **Key Point 2: The Positive Changes Required to Overcome Dysfunctional Relationship Patterns in a Marriage Require Considerable Effort and Practice**

Clinical experience demonstrates that the work required to change dysfunctional patterns in a relationship can be extensive and involve much effort, both on the part of the individuals in a couple and on the part of the therapist. Once such patterns become established, they are difficult to reverse. It is worth emphasizing that the patterns in the relationship need to be changed, rather than the unwanted behaviors of one spouse or the other. The reward for making these efforts can be substantial and can significantly improve the quality of the marriage.

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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**Key Point 3: Positive Sentiment Override and Effective Repair Attempts Are Defining Characteristics of a Successful Marriage**

These factors and strategies have been shown by research to improve marriages. While each is important, the combination of the two greatly improves the likelihood that the marriage will survive and enhances the couples' happiness.

**Key Point 4: Marriage Partners Should Be Encouraged to Use Additional Factors (e.g., Positive: Negative Interactions Ratio and Soft Startups) Frequently to Try to Stabilize and Improve Their Marriage**

These relationship tools have been scientifically proven through the research of John Gottman to be useful in distinguishing the “masters” of relationships from the “disasters” of relationships. It is best to use as many tools as possible to improve the quality of a marriage.

**Key Point 5: Preliminary Reports Suggest That Marital Relationships Are Affected—Often Negatively—by the COVID-19 Pandemic**

It is advisable that psychiatrists and other clinicians keep these issues in mind when seeing patients during this time in our history. While some couples will become more resilient because of their ability to grow from the challenges imposed on them by this pandemic, others will be negatively affected. It will be prudent for clinicians to inquire about the state of a patient's marriages as a part of our clinical inquiries, and then provide appropriate interventions.

# Clinically Relevant Psychotropic Drug Interactions in the Geriatric Population

Mujeeb U. Shad, MD, MSCS; Vimal M. Aga, MD

*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Psychotropic • Drug • Interactions • Geriatric • Older adults

**LEARNING OBJECTIVES:** On completing this lesson, the practitioner will be able to (1) identify adverse interactions among psychotropic drugs and other substances that are most likely to be seen in US geriatric populations; (2) explain basic pharmacological concepts underlying these interactions; and (3) describe methods of diagnosis, treatment, and prevention for these disorders in older individuals.

**LESSON ABSTRACT:** Individuals aged 65 years and older are at significantly higher risk for the adverse effects of drug-drug interactions primarily because of polypharmacy, age-related changes in *the pharmacokinetics* (PK) and *pharmacodynamics* (PD) of drugs, and psychiatric and medical comorbidities. PK and PD interactions can occur among drugs, herbs, dietary factors, and other substances. Interactions that result in the metabolism of one drug being altered by another concomitantly administered substance are the most common and clinically relevant interactions seen in geriatric populations. Additionally, the response to and/or tolerance of a particular drug may be adversely affected in the presence of genetic polymorphisms that alter the PK and/or PD of the drug in the absence of polypharmacy. Our discussion of basic pharmacological concepts may facilitate the clinician's understanding of various types of drug interactions, the mechanisms underlying those interactions, and the psychiatric and medical implications of those interactions in vulnerable geriatric populations.

**COMPETENCY STATEMENT:** Upon the conclusion of this lesson, readers will have gained increased knowledge about basic pharmacological concepts underlying different types of drug interactions in the geriatric population. The readers will know the clinically relevant drug interactions between psychotropic drugs as well as other commonly used drugs in this population.



## Introduction

Individuals older than 65 years are at increased risk for the adverse effects of drug interactions primarily because of the prevalence of polypharmacy, comorbid psychiatric and medical conditions, and increased age-related vulnerabilities in this population. A direct correlation between polypharmacy and *adverse drug reactions* (ADRs) has been seen in this age range is indicated by a 3.4-fold increase in ADRs with the use of four to six drugs, a 4.6-fold increase with the use of seven to nine drugs, and a 5.9-fold increase with the use of 10 or more drugs compared with three or fewer drugs.<sup>1</sup> A large number of drug interactions may be misdiagnosed as ADRs because of a lack of awareness of the complex mechanisms underlying drug interactions.<sup>2</sup> *Drug-drug interactions* (DDIs) are somewhat simplistically and rather arbitrarily divided into *pharmacokinetic* (PK) and *pharmacodynamic* (PD) interactions, despite the fact that PK and PD interactions are not mutually exclusive, given that any change in the concentration of a drug can alter its PK and, thus, also alter its effect (i.e., the PD) at its site of action. Both PK and PD interactions occur when one drug interacts with another drug, as well as when a drug interacts with the genetics of a cell, a disease process, or another substance, including foods and herbs. The PK of a drug is most likely to be affected when the concentration of the drug at its site of action is altered by the concomitantly ingested substance. Alterations in PK can result in changes in the absorption, metabolism, distribution, or elimination of the drug. These possibilities are at the root of the fact that interactions affecting the metabolism of drugs are among the most commonly researched biochemical interactions today.

The result of a drug-gene interaction is frequently referred to as the “genetic biomarker” of the response to and tolerance of a drug. Commonly known as pharmacogenomics, these interactions are considered clinically relevant to the management and treatment of refractory disorders in older individuals. Drug-gene interactions can compromise the patient’s response to or tolerability of a drug. Because they can occur without polypharmacy, however, drug-gene interactions can easily be overlooked in older adults. The focus of this review is primarily metabolic and gene-drug interactions, although other interactions will be briefly described.

## Basic Pharmacological Concepts

The clinical response to a pharmacological agent is determined by its PK (which determines the concentration of the drug at its site of action) and PD (which determines the affinity of the drug for its site of action). A “PK interaction” may be defined as an interaction in which the concentration of a drug at its site of action is altered by a concurrently administered drug, herb, substance, or food; a PD interaction can be defined as one in which the mechanism of action of the drug at its site of action is altered by a concomitantly administered drug, herb, substance, or food item. In practice, the clinical response to a pharmacological agent also depends on the biological makeup of the patient, including the patient’s age, gender, race, organ function, diagnosis, environment, and genetics.

### Pharmacokinetic Drug Interactions:

**The PK of a drug depends on its absorption, distribution, metabolism, and elimination; its PK interactions have been classified accordingly. The rate of absorption, for example, can change with the age-related increase in gastric pH, coupled with polypharmacy, which becomes increasingly common as the patient grows older.**<sup>3</sup> A common form of polypharmacy among the elderly involves an increased intake of sucralfate for relief from duodenal ulcer pain and antacids to neutralize excess gastric acid. Ionized drugs can bind to the divalent cations of antacids and sucralfate, forming complexes that are poorly absorbed. Additionally, the increase in gastric acid pH that results from the action of these particular drugs reduces the absorption of drugs that are weak bases and enhances the absorption of drugs that are weak acids.<sup>4</sup> Additionally, **the absorption, distribution, and elimination of a drug is influenced by the transporter protein *P-glycoprotein* (P-gp). This protein, which regulates the efflux of substances from body cells, is found primarily on the apical surface of epithelial cells, including those lining portions of the gastrointestinal tract. Any compromise in the function of this protein can put the patient at risk for undesirable drug effects. P-gp activity can be reduced through the concurrent administration of a P-gp inhibitor (e.g., grapefruit juice, calcium channel blockers, or macrolide antibiotics),<sup>5</sup> which results in the accumulation of**

**drugs in the body. Conversely, a P-gp inducer (e.g., St John's Wort, carbamazepine, rifampicin, or phenytoin) can increase the efflux of drugs from the body, thereby reducing drug activity.<sup>6-9</sup>**

PK DDIs that affect drug distribution, commonly known as protein displacement reactions, may have a greater effect in older adults due to age-related changes in the volume of the drug being distributed, metabolized, and eliminated. Highly protein-bound drugs, which include antidepressants, antipsychotics, mood stabilizers, and benzodiazepines, can displace more weakly bound drugs from their binding sites. This may take on clinical significance when the displaced drug has an extremely narrow therapeutic index, such as warfarin.<sup>10</sup> The highly protein-bound drug *valproate* (VPA), for example, reportedly saturates its own protein-binding sites at concentrations of at least 50 mcg/mL;<sup>11</sup> the resulting increase in the unbound fraction compromises the patient's response to and tolerance of this drug.<sup>11</sup> The unbound VPA fraction is increased in patients with hypoalbuminemia; this may occur during acute medical conditions.<sup>12</sup> When it does, it has similar clinical effects in older adults.

**Metabolic DDIs occur when the concentration of a drug at its site of action is altered during the concurrent intake of another drug or an herb, substance, or a food item. Metabolic drug interactions can be mediated both by phase I and phase II enzyme systems, although the most clinically relevant metabolic drug interactions are associated with the phase 1 *cytochrome P450* (CYP) enzyme system. These enzymes may affect older adults disproportionately as a result of the impact of aging on CYP enzyme activity, especially CYP2C19.<sup>13</sup>**

Drug interactions affecting elimination occur less frequently than those affecting the metabolism of drugs and occur only when the renal clearance of a drug is compromised. A good example of DDIs of this is seen with thiazide diuretics (e.g., chlorthalidone, hydrochlorothiazide, chlorthalidone), which can increase plasma levels of lithium by increasing the rate of drug reabsorption in the proximal tubules.<sup>14</sup>

### **Pharmacodynamic Drug Interactions:**

PD interactions vary with the mechanism of action of the drug. In a recently published study, PD drug interactions were found to occur as frequently as PK drug interactions.<sup>15</sup> Drugs with multiple mechanisms of action are most likely

to induce PD interactions and, thus, have serious clinical implications in geriatric populations. Drug interactions that have relatively mild effects in younger individuals may have clinically adverse effects in the elderly. A good example of this is seen with the potentiation of the anticholinergic, antihistaminic, antiadrenergic, and membrane-stabilizing effects of antipsychotic drugs (e.g., chlorpromazine, thioridazine, clozapine) when they are administered with a tertiary amine tricyclic antidepressant such as amitriptyline, doxepin, imipramine.

## **Drug-Drug Interactions Involving Antidepressants**

### **Pharmacokinetic Drug-Drug Interactions:**

**Selective-serotonin reuptake inhibitors (SSRIs) led the way to our awareness of PK drug interactions in psychiatry through their inhibitory effect on CYP enzymes. Theirs is not a class effect, however, given that some SSRIs inhibit CYP enzymes more strongly than others. The SSRI fluoxetine is considered a “pan inhibitor” of the most clinically relevant cytochrome P450 enzymes. It inhibits CYP2D6 and CYP2C9/10 substantially and CYP2C19 moderately, and its active metabolite norfluoxetine inhibits CYP3A3/4 to a moderate degree. Paroxetine is a potent inhibitor of CYP2D6, whereas sertraline, citalopram, and escitalopram (within their recommended dosing ranges) are weak inhibitors of CYP2D6, and, thus, their effect is not clinically significant.<sup>16,17</sup>**

Metabolic DDIs can occur when an SSRI or a *serotonin norepinephrine reuptake inhibitor* (SNRI) is administered with a psychotropic. The risk for this combination is relatively high among older adults, given the frequency of both ischemic heart disease and depression in this age group.  $\beta$ -blockers are commonly prescribed for older individuals with arrhythmias and hypertension. Several of these agents—including carvedilol, metoprolol, and timolol—are strongly metabolized by CYP2D6. **SSRIs, some of which are prescribed as antidepressants, are potent inhibitors of CYP2D6. Thus, the simultaneous administration of a  $\beta$ -blocker and an SSRI can reduce CYP2D6 levels and prevent the breakdown of the  $\beta$ -blocker. As a result,  $\beta$ -blockers can reach concentrations high enough to cause bradycardia and heart**

**block.**<sup>18</sup> Fortunately, some  $\beta$ -blockers are not completely reliant on CYP2D6. Instead, they are metabolized by multiple cytochrome P450 enzymes (e.g., propranolol) or are excreted mainly unchanged through the kidneys (e.g., atenolol) and, thus, are less strongly activated by CYP2D6.<sup>18</sup> These agents may be safer choices for patients who require both an antihypertensive or anti-arrhythmia agent and an antidepressant. Conversely, an alternative agent can be selected to control depression. This must be done with care, however. For example, bupropion, a commonly used antidepressant, is not a SSRI, but strongly blocks CYP2D6. Therefore, it must be used with caution in combination with drugs that serve as substrates for this enzyme.<sup>19</sup>

**The SSRI antidepressant fluvoxamine inhibits multiple CYP enzymes, including CYP1A2, CYP2C19, and CYP3A4. Its greatest effect is on CYP1A2, which metabolizes two important second-generation antipsychotic drugs—olanzapine and clozapine—as well as caffeine.**<sup>20</sup> Its most clinically significant DDI, however, involves caffeine. This is important to note for patients with psychiatric disorders, because they tend to consume much more coffee than the general population<sup>21</sup> and, thus, are at increased risk for significant drug-caffeine interactions. Approximately 95% of caffeine is metabolized in the presence of CYP1A2.<sup>22</sup> Caffeine has a low affinity for CYP1A2 itself, but is metabolized by its inducible \*1F allele. In the absence of inducible allele, caffeine can reach concentrations high enough to displace clozapine from CYP1A2.<sup>23</sup> Theoretically, olanzapine, metabolized by CYP1A2, can also be displaced by high caffeine concentrations. Caffeine also increases the renal clearance of lithium; conversely, caffeine withdrawal can precipitate lithium toxicity.<sup>24</sup>

Among the SNRIs, duloxetine is a moderate inhibitor of CYP2D6,<sup>25</sup> and venlafaxine and its metabolite, desvenlafaxine, are weak inhibitors of CYP2D6.<sup>26,27</sup> Desvenlafaxine is metabolized primarily by phase II enzymes (e.g., *uridine diphosphate glucuronyl transferase* [UDPGT]), and almost half of it is eliminated through the kidneys. Having a relatively low risk for CYP-mediated interactions,<sup>28</sup> desvenlafaxine should be safer than other SNRIs in older adults. The SNRI levomilnacipran is metabolized by CYP3A4; thus, any drug that inhibits CYP3A4 (e.g., ketoconazole) can increase plasma levels

of levomilnacipran.<sup>29</sup> Sertraline, citalopram, and escitalopram are the safest SSRIs to use in older adults due to a lower risk for clinically significant metabolic DDIs.

**Concomitant use of some over-the-counter<sup>30</sup> (OTC) drugs with prescription drugs, including certain psychotropics, can also cause clinically significant DDIs.** For example, omeprazole—a proton pump inhibitor that is currently available OTC—inhibits CYP2C19 and induces CYP1A2 in the presence of the inducible allele CYP1A2\*1F.<sup>31</sup> As such, it has the potential to increase the concentration of drugs metabolized by CYP2C19 (e.g., citalopram, escitalopram, and diazepam) while decreasing the concentration of drugs metabolized by CYP1A2 (e.g., clozapine and olanzapine).<sup>31</sup>

## Pharmacodynamic Drug-Drug Interactions:

The concomitant administration of markedly anticholinergic antidepressants (e.g., protriptyline and amitriptyline) with other anticholinergic drugs (e.g., benztrapine or trihexphenidyl) can induce toxicity and may prove to be fatal.<sup>32,33</sup> The concurrent use of drugs that are not known to be anticholinergic (e.g., digoxin, prednisone, captopril, or warfarin)<sup>33</sup> can significantly increase the anticholinergic load in older individuals. The sedative effect of histamine receptor-1 receptor blockade that occurs with tertiary amine *tricyclic antidepressants* (TCAs) and low-potency first-generation antipsychotics may be potentiated by an antihistamine (e.g., diphenhydramine or hydroxyzine), which can boost the anticholinergic effects of these drugs. The concomitant use of an  $\alpha$ 1-antagonist—these are commonly used to manage hypertension (e.g., doxazosin), posttraumatic stress disorder (e.g., prazosin) and benign prostatic hyperplasia (tamsulosin)—with an  $\alpha$ 1-blocking psychotropic drug (e.g., iloperidone, quetiapine, clozapine, or trazodone) can increase the risk for dizziness and orthostatic hypotension.

The most significant safety issue, particularly in older adults, is posed by an increase in QT interval. This has been reported with most first- and second-generation antipsychotics, with both secondary and tertiary amine TCAs, and with at least two SSRIs (citalopram and escitalopram).<sup>34</sup> This risk may be exaggerated when two or more drugs that cause QTc prolongation are prescribed together.<sup>35</sup> SSRI-induced hyponatremia can be potentiated through the concurrent use of diuretics, such as

furosemide and the mood stabilizer carbamazepine, which are both known for their hyponatremic effects.<sup>36</sup> The weight gain that has been reported with second-generation antipsychotic drugs (e.g., clozapine and olanzapine) and mood stabilizers (e.g., valproic acid and lithium), can be potentiated with specific SSRIs, such as paroxetine.<sup>37</sup>

*Monoamine oxidase inhibitors* (MAOIs), which are known for PK interactions with tyramine-containing foods that result in a hypertensive crisis, also have the potential to trigger PD interactions resulting in such conditions as serotonin syndrome when administered with serotonergic drugs (such as SSRIs, SNRIs, buspirone, and the triptans). One exception is the combination of the MAO-B inhibitor rasagiline in therapeutic doses with an SSRI; this combination is not uncommon in patients with depression and idiopathic Parkinson's disease.<sup>38</sup> Non-MAOI drugs can exhibit potent MAOI-like drug-drug reactions when administered with agents such as the antibiotic linezolid.<sup>39</sup> Some opioid analgesics function as weak serotonin agonists (meperidine, tramadol, methadone, dextromethorphan, and propoxyphene) or have no serotonergic activity (morphine, codeine, oxycodone, and buprenorphine). Even though all opioids are thought to be contraindicated for concurrent administration with MAOIs or SSRIs, the latter can be used safely.<sup>40</sup>

OTC<sup>30</sup> drugs can result in a PD DDI when taken with prescription drugs. In the survey mentioned previously,<sup>41</sup> aspirin was the most commonly used OTC agent (taken by 40% of older adults between 2010 and 2011). Antiplatelet therapy is well known to increase the risk of bleeding; the addition of an SSRI<sup>42</sup> to the treatment plan further potentiates that risk through a PD interaction.

## Drug-Drug Interactions Involving Antipsychotics

### Pharmacokinetic Drug-Drug Interactions:

Unlike SSRIs, most antipsychotic drugs do not have a significant inhibitory effect on CYP enzymes. They are frequently involved in DDIs in which one or more of their metabolic pathways is altered (inhibited or induced) by a concomitantly administered drug. Several first- and second-generation antipsychotics are metabolized by CYP2D6, which means that caution is required when

co-administering any of these drugs with a CYP2D6 inhibitor (e.g., fluoxetine, paroxetine, or bupropion).

### Pharmacodynamic Drug-Drug Interactions:

**Antipsychotic medications are not recommended for older adults primarily because of a relative lack of beneficial effects in bipolar disorder and major depression, along with an increased risk for QTc prolongation, extrapyramidal symptoms, hyperprolactinemia, and cognitive blunting effects.** The potent anticholinergic, antihistaminic, and alpha-1-blocking effects of first- and second-generation antipsychotic drugs add to their highly undesirable effects in older patients. **Antipsychotic drugs now come with a black box warning that they are not indicated for individuals with dementia-related psychosis based on the findings of a meta-analysis that revealed an increased mortality rate with these drugs compared with placebo.**<sup>43</sup> If the *US Food and Drug Administration* (FDA) approves several relatively new antipsychotic drugs—including lurasidone, quetiapine, and cariprazine—for patients with bipolar depression, treatment-refractory older adults may have safer options than the older antipsychotic medications.

As stated above, the increase in body weight observed with some second-generation antipsychotic drugs (e.g., clozapine and olanzapine) is further potentiated with antidepressants (especially amitriptyline, mirtazapine, and paroxetine),<sup>37,44</sup> certain antihistaminic drugs (especially cyproheptadine), and certain mood stabilizers, including lithium and valproic acid. Hyperprolactinemia induced by high doses of haloperidol, fluphenazine, or risperidone can further contribute to weight gain through some of the metabolic interactions described herein.

## Drug-Drug Interactions Involving Mood Stabilizers/Antiepileptics

### Pharmacokinetic Drug-Drug Interactions:

SSRIs, SNRIs, and antipsychotic drugs do not induce CYP enzyme activity, but some mood stabilizers have a potent effect on these enzymes. The most studied class of CYP enzyme inducers consists of *antiepileptic drugs* (AEDs),<sup>45</sup> which include carbamazepine. A frequently used mood stabilizer, carbamazepine, is known to induce



CYP 3A4 activity, which, in turn, metabolizes this drug to increase its metabolic activity. When a drug acts as both a substrate and an inducer, it is said to carry out autoinduction. Frequent monitoring of the initial plasma levels of carbamazepine is recommended because its clearance rate is 300% faster during the initial 30 days of therapy than when it reaches a steady state. Thus, it could take 2 to 3 weeks to achieve a stable concentration.<sup>46</sup> Carbamazepine, along with other older enzyme-inducing AEDs (including phenytoin, phenobarbital, and the phenobarbital pro-drug, primidone), reduces the levels of many psychotropic and nonpsychotropic drugs by inducing the activity of CYP3A4, as well as CYP1A2, CYP2C9, and CYP2C19, along with several UDPGT agents.<sup>47</sup> AEDs also induce P-gp activity, which may further reduce plasma levels of P-gp substrates<sup>48</sup> that are commonly used in older subjects, including antihypertensives (diltiazem and verapamil), antidepressants (amitriptyline), azole antifungals (ketoconazole, itraconazole), and macrolide antibiotics (erythromycin, clarithromycin).<sup>49,50</sup>

## Drug-Drug Interactions Involving Antidementia Drugs

### Pharmacokinetic Drug-Drug Interactions:

Donepezil and galantamine are commonly used in patients with dementia. Both of these drugs are metabolized extensively by CYP2D6 and CYP3A4.<sup>51,52</sup> Inhibition of either of these enzymes can have adverse cholinergic effects. Caution should be exercised when prescribing donepezil or galantamine concomitantly with any drug that is a substrate for either of these CYP enzymes. Farlow (2003)<sup>52</sup> reported a 40% increase in galantamine bioavailability when taken with paroxetine (which inhibits CYP2D6) and a 30% and 12% increase in galantamine bioavailability when it was administered with the CYP3A4 inhibitors ketoconazole and erythromycin, respectively.<sup>52</sup> By contrast, rivastigmine is inactivated through its inhibition of acetylcholinesterase; in this manner, its involvement in drug interactions mediated by CYP enzymes can be reduced.<sup>53</sup> Another antidementia drug—memantine—only inhibits CYP2B6 and is unlikely to inhibit other CYP enzymes at clinically relevant plasma levels.<sup>54</sup> Therefore, it should be used cautiously with CYP2B6 substrates (e.g.,

bupropion, ketamine, pethidine, propofol, methadone, nevirapine, and efavirenz).

### Pharmacodynamic Drug-Drug Interactions:

As cholinesterase inhibitors, antidementia drugs can become involved in significant PD DDIs. Because they enhance acetylcholine activity, these drugs can cause bradycardia, which, in turn, can be potentiated by other drugs with a similar negative chronotropic effect, such as  $\beta$ -blockers. Post-marketing data for a common antidementia drug—donepezil—show the potential for further prolongation of the QT interval, which increases the risk for torsades-de-pointes. This effect was not supported in a meta-analysis of cholinesterase drugs, however.<sup>55</sup> Some antipsychotics (e.g., thioridazine and ziprasidone) and antidepressants (e.g., imipramine and citalopram) extend the QT interval and should be used with extreme caution in elderly patients with dementia. Memantine is a glutamate *N-methyl-D-aspartate* (NMDA) receptor antagonist that may enhance the effects of anti-parkinsonian treatments (e.g., levodopa, dopamine agonists) and anticholinergic agents while reducing the effects of barbiturates and neuroleptics.<sup>56</sup>

## Drug-Gene Interactions/Genetic Biomarkers

Pharmacogenomics (the study of genes involved in response to and tolerability of a drug) is being used with increased frequency to optimize the efficacy and tolerability of psychotropic drugs, especially antidepressants. Commercially available genetic assays are being ordered by providers with increased frequency for this purpose. Evidence for genetic testing is limited to the initial stages of drug use, but they can still be useful in refractory older adults, who are at a higher risk for the adverse effects of drug-gene interactions, even in the absence of polypharmacy. The cost-benefit ratio of these genetic assays is also improving as costs decline in response to increased competition. It is worth mentioning here that the interpretation of the genetic assay reports can be difficult and may require psychopharmacological expertise for optimal clinical applications.

## Pharmacokinetic Drug-Gene Interactions/ Pharmacokinetic Biomarkers:

Genetic variance in drug-metabolizing enzymes, such as phase 1 CYP enzymes, is responsible for most PK biomarkers and has produced one of the most frequently replicated and clinically relevant findings in patients who develop adverse effects from routinely administered drugs, including psychotropics. In this context, CYP2D6 is one of the most clinically relevant enzymes, given that it participates in the metabolism of approximately 25% of commonly used psychotropic agents, including antidepressants and antipsychotics.<sup>57,58</sup> Patients who are homozygous for wild-type alleles are known as *extensive (or normal) metabolizers* (EMs), those who are homozygous for loss-of-function alleles are called *poor metabolizers* (PMs), and those who are heterozygous for dysfunctional alleles are called *intermediate metabolizers* (IMs). Additionally, approximately 1% to 2% of whites with multiple copies of functional alleles are referred to as *ultra-rapid metabolizers* (UMs).<sup>59</sup> Compared with EMs, UMs require relatively higher doses of substrates to compensate for a more rapid rate of elimination. By contrast, drugs may accumulate more in PMs compared with EMs, causing adverse effects.<sup>57,60</sup> Several important classes of drugs are substrates of CYP2D6, including antipsychotics (risperidone, perphenazine, haloperidol), antidepressants (desipramine, nortriptyline, venlafaxine, mirtazapine), opioids (codeine), and a  $\beta$ -blocker (metoprolol).<sup>61</sup> The functional impact of CYP2D6 on these agents varies. Because CYP2D6 almost exclusively metabolizes desipramine and nortriptyline, PMs have a much higher risk of QTc prolongation with these antidepressants than with any others. Similarly, there is a lower risk for bradycardia with the  $\beta$ -blockers carvedilol, propranolol, and timolol, which are less substantially metabolized by CYP2D6.<sup>61</sup> A deficiency in CYP2D6 activity can also result in a loss of efficacy for some commonly prescribed prodrugs, such as codeine, which loses its analgesic effects if it is not converted by CYP2D6 into its active metabolite, morphine. By contrast, CYP2D6 UMs rapidly convert codeine into morphine, thereby increasing the risk for respiratory depression, which is more problematic in older individuals than in younger populations.<sup>62</sup>

Genetic variance can increase the enzymatic activity of CYP1A2 through an inducible gain-of-function

allele. CYP1A2\*1F, for example, requires an inducer such as omeprazole<sup>31</sup> or smoking.<sup>63,64</sup> Thus, smoking can increase the rate at which CYP1A2 metabolizes some of its common substrates (including caffeine, theophylline, clozapine, and olanzapine) in patients with CYP1A2\*1F.<sup>65</sup> By contrast, patients who require diazepam—a common benzodiazepine metabolized by CYP2C19—may require much higher doses if they express the genetic variant CYP2C19\*17, which does not require an inducer.<sup>66,67</sup>

## Pharmacodynamic Drug-Gene Interactions/Pharmacodynamic Biomarkers:

Evidence of PD biomarkers is not consistent enough to be of clinical relevance. A few interesting findings suggest their clinical significance in older individuals, however. SLC6A4, which encodes for a serotonin transporter,<sup>68</sup> has two main variants: *short* (S) and *long* (L). The S allele is associated with a decrease in *serotonin transporter* (SERT) activity and, consequently, less activity at sites with which SSRIs interact. This may be the reason why patients with S/S homozygosity have shown a significantly lower response and remission rates with SSRIs.<sup>69,70,71</sup> These findings are consistent with those from a post-hoc analysis of older patients treated with citalopram in the *Sequenced Treatment Alternatives to Relieve Depression* (STAR\*D) study, in which a positive association was found between the L/L genotype and remission in patients who developed major depressive disorder after age 55 years.<sup>72</sup>

*Catechol-O-methyltransferase* (COMT) breaks down norepinephrine and dopamine. Any variance in COMT gene function may affect cognitive functioning<sup>73</sup> and, thus, may be of clinical relevance in older adults. *Methylene tetrahydrofolate reductase* (MTHFR) catalyzes the conversion of inactive folate into its active form. A C677T *single nucleotide polymorphism* (SNP) in the MTHFR gene reduces the activity of the reductase enzyme.<sup>1</sup> Multiple studies have confirmed that serum folate levels are lower, and homocysteine levels are higher in individuals with this T allele.<sup>74</sup> A genetic polymorphism in the *human leucocyte antigen* (HLA) antigen B\*1502 has been linked with *Stevens-Johnson syndrome* (SJS) and with *toxic epidermal necrolysis* (TEN). These are medical emergencies involving carbamazepine that are seen most commonly in the Han Chinese population. This finding resulted in a block box warning for carbamazepine regarding the risk



for SJS and TEN in Asian patients, along with an FDA recommendation for HLAB\*1502 screening.<sup>75</sup>

## Drug-Herb Interactions

### Pharmacokinetic Drug-Herb Interactions:

One of the most well-documented PK drug-herb interactions involves *St. John's Wort* (SJW; *Hypericum perforatum*), which is often used by patients experiencing depression,<sup>76</sup> often without their providers' awareness. SJW has demonstrated antidepressant effects.<sup>76</sup> Commercially available preparations of SJW are readily available in health stores, where, unfortunately, quality control may be lacking.<sup>77</sup> The risks associated with SJW are related to its ability to induce CYP3A4 and P-gp, which can significantly reduce plasma levels of CYP3A4 and P-gp substrates.<sup>78</sup> **The most clinically serious example of this interaction is seen in transplant recipients, in whom SJW can lower plasma levels of cyclosporine (a substrate for CYP3A4) significantly enough to cause transplant rejection.**<sup>77</sup> Concomitant use of SJW and other CYP3A4 substrates—as well as protease inhibitors, oral contraceptives, calcium channel blockers, and some antidepressants, antipsychotics, and AEDs—can also reduce or eliminate the efficacy of all of these agents.<sup>77,79</sup>

Ginkgo biloba is also frequently used by patients, especially by the elderly, for its potential for procognitive effects. It reportedly reduces mood stabilizer, carbamazepine, and VPA levels.<sup>80,81</sup> A review of studies of interactions between ginkgo biloba and several drugs—including alprazolam, dextromethorphan, and donepezil—failed to reveal any clinically significant PK interactions.<sup>82, 83</sup>

### Pharmacodynamic Drug-Herb Interactions:

SJW-involved PD interactions have been seen when this herb is taken with serotonergic drugs, such as SSRIs, triptans, MAOIs, and narcotic analgesics. These interactions can lead to serotonin syndrome.<sup>84</sup> Older adults are at higher risk for interactions with SJW due to polypharmacy and medical comorbidities.

## Drug-Food Interactions

### Pharmacokinetic Drug-Food Interactions:

Grapefruit juice significantly inhibits the metabolism of CYP3A4 substrates and P-gp in a dose-dependent manner.<sup>5</sup> Consequently, it is a common participant in PK drug-food interactions. CYP3A4 is involved in the first-pass metabolism of drugs in the intestinal epithelium; the inhibition of this enzyme greatly increases the bioavailability of drugs. Unfortunately, the magnitude of the effect of grapefruit juice on this enzyme is unpredictable and varies considerably among individuals.<sup>85</sup> As little as 200 mL of grapefruit juice can inhibit this enzyme. This effect can be clinically significant in patients taking affected drugs by the oral route, especially drugs with low to intermediate levels of oral bioavailability and which are mainly metabolized by CYP3A4. This PK interaction is most pronounced in patients older than 70 years.<sup>86</sup> Certain vegetables also influence CYP1A2 activity, with broccoli and Brussel sprouts causing its activity to increase and carrots and parsnips causing it to decrease. Compared with a vegetable-free diet, onions and leeks have no effect at all.<sup>87</sup> Regular consumption of charcoal-broiled food induces CYP1A2 activity in the intestinal epithelium and liver.<sup>85</sup> This usually does not have a clinically significant effect on psychotropic drugs, however, given that they are not metabolized primarily by this enzyme, except for clozapine and olanzapine.

### Pharmacodynamic Drug-Herb Interactions:

The most well-known example of PD drug-food interactions is the interaction between MAOIs and tyramine-containing foods (aged cheese, processed beer, fava beans, *monosodium glutamate* [MSG]), which results in a potentially lethal hypertensive crisis ("cheese reaction"), especially in older adults. The recent availability of the *selegiline transdermal system* (Emsam-TD) provides an attractive alternative to oral selegiline, given that it bypasses the first-pass metabolic effect. The lowest (6-mg) daily dose permitted by the FDA can be used without dietary precautions.<sup>88</sup> Interactions among aspirin, warfarin,<sup>89</sup> SSRIs,<sup>42</sup> and some *complementary and alternative medications* (CAMs)—which include garlic, ginkgo

biloba, ginseng, green tea, saw palmetto, SJW, and fish oil—can increase the risk of bleeding.<sup>90</sup>

## Drug-Disease Interactions

### Pharmacokinetic Drug-Disease Interactions

The impact of physical illness on psychopharmacology in older adults cannot be emphasized enough. Changes in circulating high-capacity albumin and low-capacity  $\alpha_1$ -acid glycoprotein (AGP) levels occur in older adults more as a function of physical disease than age.<sup>91</sup> Intravascular serum albumin levels can decrease in certain disease states as a result of a reduced intake of protein, reduced albumin synthesis, liver disease, extravascular shifts, or increased losses (nephrotic syndrome). AGP is an acute-phase reactant; its levels increase with physiological trauma (cancer, inflammatory disease, trauma, or surgery) or stress and decrease with conditions that reduce its production (liver disease) or increase its rate of loss (nephrotic syndrome). AGP binds with clozapine, among other drugs.<sup>92,93</sup> In one pharmacokinetic study, a significant relationship was observed between elevated AGP plasma concentrations and a lower unbound fraction of clozapine;<sup>93</sup> in another study, proinflammatory cytokine-induced downregulation of CYP 1A2 was observed.<sup>94</sup> A reduction in creatinine clearance due to renal disease strongly affects drugs that are excreted mainly unchanged by the kidneys without undergoing significant biotransformation, such as lithium.

### Pharmacodynamic Drug-Disease Interactions:

PD drug-disease interactions are rare and not well described. These interactions may occur in clinical settings if the target of a drug is altered by a medical or psychiatric disorder. For example, Parkinson's disease is more sensitive to high-potency antipsychotic medications than low-potency drugs.<sup>95</sup> Cognitive decline has been associated with the acute intake of older antipsychotic medications in patients with dementia<sup>96</sup> or traumatic brain injury.<sup>97</sup> Older adults may be more sensitive to these effects; therefore, if possible, antipsychotic medications should be avoided in this population.

## Drug-Substance Interactions

### Pharmacokinetic Drug-Substance Interactions:

In elderly patients, the non-drug involved in these interactions is usually nicotine, caffeine, cannabis, or alcohol. Drug-substance interactions are most commonly reported for smokers. The polycyclic aromatic hydrocarbons in cigarette smoke are well known for their ability to induce CYP1A2\*1F.<sup>98</sup> As a result, plasma levels of drugs metabolized by CYP1A2 (e.g., clozapine and olanzapine) tend to decrease in smokers, especially those who express the CYP1A2\*1F variant. When such smokers are treated with clozapine or olanzapine, they are at a higher risk for a psychotic relapse after being discharged from a hospital, where smoking is not allowed. Once they resume smoking, their clozapine or olanzapine levels decline, allowing a psychotic relapse to occur, along with a risk for re-hospitalization.<sup>99</sup>

*Tetrahydrocannabinol* (THC) and *cannabidiol* (CBD) may be involved in significant PK drug-substance interactions. THC reportedly has inhibitory effects on CYP2C9,<sup>100,101</sup> whose substrates include drugs that are frequently used by the elderly (e.g., losartan, tolbutamide, or ibuprofen). The concurrent use of THC and CYP2C9 substrates can reduce the effectiveness of these drugs. CBD inhibits CYP2C19,<sup>100,101</sup> which mediates the metabolism of some benzodiazepines and, thus, can have clinical implications in the elderly. Both THC and CBD can inhibit CYP3A4,<sup>100,102,103</sup> which is the most abundant CYP enzyme and is responsible for approximately 60% of the bio-oxidative metabolism of a large number of drugs, including calcium channel blockers, protease inhibitors, antidepressants, antipsychotics, azole antifungals, and macrolide antibiotics. The inhibitory effect of both cannabinoids on CYP3A4 may be more clinically relevant than the inhibitory effect of other CYP enzymes.<sup>104</sup>

### Pharmacodynamic Drug-Herb Interactions:

PD interactions between drugs and herbs are not as common as PK interactions. One potentially dangerous interaction is seen when warfarin, which is prescribed for many older adults, is taken with marijuana, which can increase the anticoagulant effects of this drug.<sup>105</sup>

The most notable alcohol-drug interactions are PD and involve benzodiazepines; these can result in falls and dizzy spells. Depending on the frequency and magnitude of alcohol consumption and the benzodiazepine dose, this combination can result in respiratory depression, which can be fatal.<sup>106</sup> The most reliable estimates for the concurrent use of psychotropic drugs and alcohol place it at approximately 7.5% in older adults, and falls appear to be the most common adverse effect.<sup>107</sup>

## Conclusion

Age-related changes affecting a drug's response and tolerability, as well as medical and psychiatric comorbidities resulting in polypharmacy, are some of the most

significant factors that make older adults more vulnerable to experience serious adverse effects from drug interactions than younger people. Although drug interactions can occur between a drug and a substance, herb, or a dietary factor, the most clinically relevant interactions are those that occur between two or more concomitantly used drugs due to a higher incidence of polypharmacy in the geriatric than younger population. However, it is essential to note that a drug can also interact with genes, through genetic polymorphisms in metabolic enzymes or drug transporter(s), even in the absence of any polypharmacy. A basic understanding of psychopharmacological principles underlying drug interactions is crucial to prevent clinically serious drug interactions in an extremely vulnerable population.

**Table 1:**  
**Abbreviations Within This Lesson**

| Abbreviation | Meaning                                    | Abbreviation | Meaning                                   |
|--------------|--|--------------|---|
| PK           | Pharmacokinetic                            | IM           | Intermediate metabolizer                  |
| PD           | Pharmacodynamic                            | UM           | Ultra-rapid metabolizer                   |
| ADR          | Adverse drug reaction                      | SERT         | Serotonin transporter                     |
| DDI          | Drug-drug interaction                      | COMT         | Catechol-O-methyltransferase              |
| P-gp         | P-glycoprotein                             | MTHFR        | Methylene tetrahydrofolate reductase      |
| CYP          | Cytochrome P450                            | SNP          | Single nucleotide polymorphism            |
| SSRI         | Selective-serotonin reuptake inhibitor     | HLA          | Human leucocyte antigen                   |
| SNRI         | Selective-norpinephrine reuptake inhibitor | SJS          | Stevens-Johnsons syndrome                 |
| UDPGT        | Uridine diphosphate glucuronyl transferase | TEN          | Toxic epidermal necrolysis                |
| OTC          | Over-the-counter                           | SJW          | St. John's Wort                           |
| TCA          | Tricyclic antidepressants                  | MSG          | Monosodium glutamate                      |
| MAOI         | Monoamine oxidase inhibitor                | CAM          | Complementary and alternative medications |
| FDA          | US Food and Drug Administration            | AGP          | A1-acid glycoprotein                      |
| AED          | Antiepileptic drugs                        | THC          | Tetrahydrocannabinol                      |
| NMDA         | N-methyl-D-aspartate                       | CBD          | Cannabidiol                               |
| EM           | Extensive metabolizers                     |              |   |



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## Multiple-Choice Questions

**29. Which of the following statements is true regarding drug interactions?**

- A. Pharmacodynamic interactions are not as clinically relevant in older populations as they are in younger populations.
- B. Clinical response depends entirely on a drug's pharmacokinetics and pharmacodynamics.
- C. There are no age-related changes in pharmacodynamics in older adults.
- D. Metabolic drug interactions are the most frequently researched and clinically relevant interactions in elderly individuals.

**30. Which of the following statements is true for CYP1A2?**

- A. This enzyme provides the primary metabolic pathway for clozapine and olanzapine.
- B. This enzyme cannot be induced by omeprazole.
- C. This enzyme does not function in individuals with an ultra-rapid metabolizer genotype.
- D. Haloperidol is primarily metabolized by CYP1A2.

**31. All of the following statements are true, *except*:**

- A. Inhibition of P-glycoprotein increases plasma concentrations of its substrates.
- B. St. John's Wort can lower the plasma levels of cyclosporine to result in transplant rejection.
- C. Over-the-counter drugs do not participate in significant drug interactions in older adults.
- D. Antipsychotics are not indicated for dementia-related psychosis.

**32. Which one of the following statements about metabolic drug interactions is true?**

- A. Metabolic interactions are not relevant in geriatric populations.
- B. Metabolic drug interactions involve a change in the absorption rate of drugs.
- C. Herbal agents do not participate in metabolic interactions.
- D. Metabolic drug interactions are more commonly reported with SSRIs compared with pharmacodynamic interactions.

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# Best Practices in Continuing Medical Education

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## Clinically Relevant Psychotropic Drug Interactions in the Geriatric Population

By Mujeeb U. Shad, MD, MSCS; Vimal M. Aga, MD

ID#: L003450

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

Geriatric populations are at a significantly increased risk for drug interactions due to *pharmacokinetic* (PK) and *pharmacodynamic* (PD) factors that are complicated by age-related changes, an increased number of psychiatric and medical comorbidities, substance use, and polypharmacy. With regards to PK, metabolic factors are most clinically relevant, especially in geriatric population, primarily due to a high prevalence of polypharmacy. In this context, the metabolism of a drug is altered by the concomitant use of drug(s) with similar metabolic pathways. The metabolism of a drug can also be altered, even in the absence of polypharmacy, through genetic polymorphisms in metabolic enzymes or drug transporters. A better understanding of these basic psychopharmacological principles may facilitate a better understanding of the complexities of drug interactions in this extremely vulnerable population.

#### Key Point 1: Basic Concepts in Pharmacology

Learning basic concepts in pharmacology may be vital in understanding the mechanisms underlying drug interactions in geriatric populations.

#### Key Point 2: Review Different Types of Drug Interactions in Older Subjects

Clinicians should study different types of drug interactions to enhance their awareness and ability to identify clinically relevant drug interactions in geriatric populations.

#### Key Point 3: Discuss Commonly Reported Drug Interactions in the Geriatric Population

Clinicians should attempt to understand interactions within different classes of psychotropic drugs and between psychotropic drugs and other drugs commonly prescribed in older adults.

#### Key Point 4: Present Clinically Relevant Information on Drug Interactions in Older Adults

The clinical relevance of drug interactions in geriatric populations is reinforced by using clinical examples.

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# Prevention of Mental Health Disorders Using Internet- and Mobile-Based Interventions: A Narrative Review and Recommendations for Future Research, Part 2

David Daniel Ebert, PhD; Pim Cuijpers, PhD;  
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*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Mental health • Self-help • E-health • M-Health • Internet interventions • Depression • Anxiety • Prevention

**LEARNING OBJECTIVES:** Upon reading this lesson, readers will be introduced to the subject, narrative reviews and available evidence for the effectiveness of *internet- and mobile-based interventions* (IMIs); review how they may aid in the prevention of mental health disorders, and recognize the challenges and need for future research using this modality in the field.

**LESSON ABSTRACT:** Although psychological interventions might have a tremendous potential for the prevention of *mental health disorders* (MHD), their current impact on the reduction of disease burden is questionable. Possible reasons include that it is not practical to deliver those interventions to the community *en masse* due to limited health care resources and the limited availability of evidence-based interventions and clinicians in routine practice, especially in rural areas. Therefore, new approaches are needed to maximize the impact of psychological preventive interventions. Limitations of traditional prevention programs could potentially be overcome by providing *Internet- and mobile-based interventions* (IMIs). This relatively new medium for promoting mental health and preventing MHD introduces a fresh array of possibilities, including the provision of evidence-based psychological interventions that are free from the restraints of travel and time and allow reaching participants for whom traditional opportunities are not an option. This article provides an introduction to the subject and narratively reviews the available evidence for the effectiveness of IMIs with regard to the prevention of MHD onsets. The number of randomized controlled trials that have been conducted to date is very limited and so far it is not possible to draw definite conclusions about the potential of IMIs for the prevention of MHD for specific disorders. Only for the indicated prevention of depression there is consistent evidence across four different randomized trial trials. The only trial on the prevention of general anxiety did not result in positive findings in terms of *eating disorders* (EDs), effects were only found in *post hoc* subgroup analyses, indicating that it might be possible to prevent ED onset for subpopulations of people at risk of developing EDs. Future studies need to identify those subpopulations likely to profit from preventive. Disorders not examined so far include substance use disorders, bipolar disorders, stress-related disorders, phobic disorders and panic disorder, obsessive-compulsive disorder, impulse-control disorders, somatic symptom disorder, and insomnia. In summary, there is a need for more rigorously conducted large scale randomized controlled trials using standard

clinical diagnostic instruments for the selection of participants without MHD at baseline and the assessment of MHD onset. Subsequently, we discuss future directions for the field in order to fully exploit the potential of IMI for the prevention of MHD.

**COMPETENCY AREAS:** This lesson provides knowledge as it reviews the evidence and potential for utilizing internet- and mobile-based interventions in the prevention of mental health disorders. The lesson applies quality improvement as it explores treatment strategies concerning the patient and community needs and how the implantation of IMIs shows promise to prevent the onset of mental health disorders. Lastly, the lesson covers the need for further research in this field to address various populations, mental health disorders that have not been tested, among other barriers to implementation of this modality.

## Introduction

Part 1 of this lesson introduced the subject and reviewed the available evidence for the effectiveness of *internet- and mobile-based interventions* (IMIs) with regard to the prevention of *mental health disorders* (MHD) onsets.

Although significant strides have been made in recent years regarding the development of effective IMIs for the prevention of MHDs, there are several important directions for the future. Part 2 of this lesson continues the discussion of the need for more research.

## The Need For More Rigorously Conducted Large-Scale Randomized Controlled Trials

First, the number of randomized controlled trials that have been conducted to date is very limited and so far it is not possible to draw definite conclusions about the potential of IMIs for the prevention of MHD for specific disorders. Only for the indicated prevention of depression there is consistent evidence across four different trials (three primary prevention trials aiming to reduce first incidence, one relapse prevention trial). However, only one primary prevention trial<sup>48</sup> and the relapse prevention trial<sup>56</sup> used standard diagnostic procedures, while the other two trials relied only on self-report questionnaires for onset identification. The only trial on the prevention of general anxiety did not result in positive findings. In terms of EDs, effects were only found in *post hoc* subgroup analyses, indicating that it might be possible to prevent ED onset for subpopulations of people at risk of developing EDs. Future studies need to identify those subpopulations likely to profit from preventive IMIs. It should be noted that two of the five successful prevention trials with positive findings<sup>54,56</sup> were based on very small sample sizes, whereas several much larger trials did not

find positive results. Disorders not examined so far include substance use disorders, bipolar disorders, stress-related disorders, phobic disorders and panic disorder, obsessive-compulsive disorder, impulse-control disorders, somatic symptom disorder and insomnia. However, it is of note that there is quite substantial evidence for the effectiveness of health behavior change IMIs regarding the reduction of problematic alcohol consumption,<sup>24</sup> improving sleep,<sup>66,67,68</sup> reducing work-related stress,<sup>36,69,70,71</sup> all of which might be useful as MHD prevention IMIs as well. In summary, there is a need for more rigorously conducted large-scale randomized controlled trials using standard clinical diagnostic instruments for the selection of participants without MHD at baseline and the assessment of MHD onset.

## Assessing Diagnostic Status at Baseline and Follow-Up

Second, one general problem of prevention trials is that one needs very large sample sizes in order to be able to detect existing differences between groups, as transition rates to full blown disorders tend to be low during follow-ups of typical length of controlled studies even in high-risk groups. This problem is (could be) true of many of the studies reviewed above.<sup>49-51,53,54,58</sup> Given the low chance of positive findings in a trial that is not primarily designed nor powered to detect such findings, it is understandable that many prevention researchers abstain from assessing diagnostic status. However, even without positive findings such information would be very valuable for the field and we would like to encourage researchers to assess these data. Diagnostic status data could help to obtain the necessary information on the transition rates of the target population and generate hypotheses on the size of the effect on MHD onset, which are both necessary to design and power subsequent trials adequately.

Moreover, if several of such smaller trials would be conducted, the data of these trials could be combined using individual participant data meta-analytic techniques.<sup>72,73</sup> By collecting and pooling the primary data of individual trials, multiple underpowered trials can contribute to a large enough pooled sample size with sufficient power to examine effects on the incidence of MHD as well as analyzing patient subgroups and other effect modifying variables.<sup>74</sup> If conducting observer-based clinical interviews is too expensive, web-based self-administered version of instruments such as the WHO-CIDI could be a low-cost alternative.<sup>75</sup>

## Examining Different Prevention Settings and Approaches

Provided that preventive IMIs are transferable to clinical praxis, we further need to establish the best way to implement preventive IMIs into our health care systems. Integrating IMIs as a first step of stepped-care approaches might be one promising way. Prevention IMIs for MHDs might also easily be integrated in already existing prevention programs (blended MHD prevention). That this would be worthwhile is supported by recent meta-analytic findings, indicating that traditional FTF interventions profit from providing additional IMI-components.<sup>76</sup> Lindhiem and colleagues showed in their systematic review on 10 RCTs that a mobile component as a supplemental element in psychological interventions (e.g., SMS to support behavior changes between therapy sessions) considerably increase the effectiveness of these interventions compared to the respective strictly on-site interventions ( $SMD = 0.27$ ).<sup>76</sup> **IMIs also offer the unique potential of reaching people who would not access preventive mental health care via the established channels delivery, either because they do not utilize the available offers or because they do not feel comfortable discussing their mental health issues with their general practitioners and mental health specialists.** Thus, we should also think about implementing preventive MHD-IMIs in a way that allows people to self-refer to IMIs.<sup>10</sup> This might, for example, be achievable by providing preventive IMIs via websites of established associations or as a direct prevention offer from health insurance companies, which would probably make it necessary for several countries to think about alternative financing health care models

to integrate preventive IMIs in the best possible way. However, an approach just aimed at the GP and health insurance companies might be too narrow to exploit the potential of preventive services, as the majority of the target population might not use them. **Preventive IMIs should be, therefore, I think that preventive interventions should be delivered through multiple channels that have “natural” possibilities to engage people, such as schools (they can reach all students), universities and colleges, pregnant women (because they all receive prenatal care), patients with general medical disorders, but also, for example, companies.**

## Studies in Children, Adolescents, and Young Adults

Most of the trials that have been conducted up to this point have included only adults as participants. Although the general potential of IMIs to foster mental health in children and adolescents has been documented,<sup>20</sup> only one study has investigated the effects of a prevention IMI, delivered as a universal preventive approach, on MHD onset.<sup>52</sup> **Given that ~75% of all MHD have their onset before the age of 25,<sup>77</sup> future studies should explore the potential of IMIs for preventing the first incidence in children, adolescents and young adults.** That this is possible using a psychological intervention has been shown, for example, for depression.<sup>78</sup> An interesting development in this field is a shift away from traditional computerized and browser-based interventions to mobile-based smart phones interventions. Using the most up-to-date technology and/or access paths for providing mental health prevention might increase the interventions attractiveness and user-friendliness in this modern technology oriented age group. However, evidence from mobile-based interventions and other mode of deliveries is yet scarce and future studies are needed to explore their potential. **One of these other possibilities are serious games or even augmented reality interventions, that go beyond what can be done in typically “talking” interventions likely to attract children and adolescents. The potential of serious games to foster mental health has been shown, for example, in the field of depression,<sup>29,79</sup> but yet there is no evidence regarding the prevention of MHD onset, with one trial currently being conducted.<sup>80</sup> The use of augmented reality has to the best of our knowledge not yet**

been explored. One general problem with psychological interventions for the prevention of MHD in children and adolescents is that one needs parental consent, which is difficult to obtain online in a reliable manner, and which can be seen as barrier to reach these high-risk groups.

Although many MHD already have their initial incidence before college matriculation,<sup>81</sup> college entry might nevertheless be a very promising point in time to deliver preventive psychological interventions. **College entry allows screening of the whole college student population, identification of those at risk for development of mental health problems, and subsequent offers of targeted preventive interventions.** These might be disorder-specific prevention IMIs or trainings focusing on missing skills and competencies (e.g., procrastination, limited social competencies, and low self-efficacy) as well as other known risk factors for developing mental disorders. Similarly, entering vocational schools and the working environment might be a possibility to establish mental health screening and subsequent mental health trainings. In this context, where freshmen might be anxious about disclosing mental health issues, the possibility of IMIs being provided anonymously can be regarded as one substantial advantage over other occupational and college mental health management programs.

## Evaluating the Role of Human Support in Preventive Interventions

After development of an IMI, ongoing costs are directly related to guidance time. Hence, evaluating and comparing the effectiveness of interventions with different guidance formats is of particular importance. In the present review, only three of ten trials examined an unguided intervention, of which only one found significant, but very small effects on disorder onset. This is in line with previous findings from the clinical field that indicate that IMIs with human support have a significantly greater success than IMIs without therapeutic support.<sup>82-84</sup> However, unguided IMIs might still produce larger effects at population level with regard to the reduction of disease burden, as more individuals could be reached at a given budget.<sup>85</sup> A recent review on the cost-effectiveness of IMIs for improving mental health problems suggested that guided IMIs might be more cost-effective

than unguided IMIs despite their higher intervention costs per participants.<sup>86</sup> Hence, there is a need for studies that compare not only the cost-effectiveness of guidance vs. no guidance in randomized trials but also different intensities and forms of guidance [e.g., guidance concept with individual feedback on the completed exercises, i.e., content feedback, vs. feedback aiming only to increase the adherence to the intervention].<sup>37</sup> Moreover, the type of human support might not only have an impact on the effectiveness of interventions but also on the willingness to use such interventions. Given that the effects of interventions on a population level also depend on the acceptance and the reach of the target population, studies should address both effectiveness and reach of IMIs with different forms of guidance.

## Cost-Effectiveness Studies

Implementing preventive IMIs into our health care system might be a promising strategy regarding the cost-effectiveness of the health care system as has been recently estimated on the basis of a Markov-model study.<sup>87</sup> However, evidence from randomized controlled trials is still scarce when it comes to IMIs for the prevention of MHD. Studies indicated that guided Internet interventions for depression, anxiety, sleeping problems, smoking cessation, and alcohol consumption have favorable probabilities of being more cost-effective when compared to controls.<sup>86,88</sup> However, these studies were mainly directed at the treatment of mental health problems, and only one study has to the best of our knowledge been published so far, that investigated the cost-effectiveness of an IMI with regard to the prevention of MHD onset.<sup>59</sup> Two ongoing studies might provide first results in the near future.<sup>41,46</sup>

## Possible Adverse Effects of MHD Prevention IMIs

As with any other method, it is important to take into account the limitations and risks are involved with IMIs alongside all of the potential benefits of the procedure. At this stage, however, reliable empirical information showing negative effects of preventive IMIs has been very limited<sup>89</sup> and, also in the present review, none of the identified studies reported results on potential negative effects.



Potential risks and negative effects include, depending on the concept, the following points, among others: (1) limited ability to timely identify patients prone to self-injury, for example, in relapse prevention interventions; (2) the development of reduced health-related self-efficacy if participants are not successful with a stand-alone IMI; and (3) the development of negative attitudes of non-responders toward psychological interventions in general and as a result a reduced willingness to utilize mental health care in case of MHD onset. Possible negative effects of such interventions cannot be ruled out at present, which counts to a similar degree also to classical FTF psychological interventions. There is an urgent need for further research.

One “cautionary tale” that has been published involves a secondary analysis of the impact of a mood management intervention embedded in an online smoking cessation randomized control trial. Participants came to the online site in order to stop smoking. Half of the sample was randomly assigned to a cognitive behavioral mood management intervention. The authors wondered if smokers at risk for major depressive episodes (defined as having subthreshold levels of major depression symptoms at baseline) who had been randomly assigned to receive the mood management intervention had lower incidence of major depressive episodes at follow up, thus showing a preventive effect.

The results showed that the incidence was actually significantly greater for the group assigned to the mood management condition.<sup>90</sup> The authors speculate that being assigned to a mood management intervention when one is not looking for such might make a participant more aware of depressive symptoms, thus increasing their self-report scores at follow-up assessments. They then examined a subsequent study in which participants in a similar online smoking cessation trial could freely choose (rather than being randomly assigned to) the elements of the interventions provided, including the same mood management intervention. In this study, participants screening positive for major depression were more likely to choose the mood management intervention, and, if they did so, were more likely to quit smoking.<sup>91</sup>

These studies suggest that providing participants with a choice of interventions may be preferable to assigning them interventions that they did not choose and that

participants are likely to choose appropriate interventions for themselves.

## **Make Use of the Technological Potential of IMIs**

All of investigated interventions were delivered over the Internet, only one study additionally used the mobile phone to facilitate the transfer of learned skills in daily life routine.<sup>48</sup> None of the studies were delivered mobile only and none of the interventions’ used smartphone sensors, wearables, or artificial intelligence algorithms. It seems that the field so far focused mainly on delivering psychological intervention as a (guided) self-help format through the Internet, without making full use of the technological potential of such approaches. Artificial intelligence algorithms based on user behavior might bare a great potential for supporting participants to change behavior, for example, inform of just-in-time adaptive intervention.<sup>92</sup> However, their potential with regard to preventing MHD onset still needs to be proven and should be investigated in future studies.

## **Development of Multivariate Prediction Algorithms to Identify People at Risk and Match Participants to Interventions**

One general problem in the field of prevention is identifying the right people to target with specific preventive interventions. Many, if not most, individuals displaying single risk factors stay disease free without intervening, which has also occurred in most of the trials reviewed above. The combination of several specific risk factors might be a promising strategy toward overcoming this problem,<sup>93</sup> and has been utilized in some first trials.<sup>58</sup> Recent advantages in the field of precision medicine and machine-learning techniques might further help to identify the people at highest risk who might profit from a preventive intervention. There have been first studies in the mental health field predicting MDD onset<sup>94,95</sup> in the general population, general anxiety and panic onset in general practice attendees<sup>96</sup> panic recurrence,<sup>97</sup> or recurrence of suicidal ideation.<sup>97</sup> A next necessary step in the field is to develop and validate such algorithms further for different populations and then, subsequently,



test whether applying these risk prediction algorithms with subsequent preventive interventions is effective in reducing incidence of MHD in these high-risk groups.

The use of supervised machine-learning methods could also be used to explain the heterogeneity in intervention response<sup>98,99</sup> in order to finally match individual to specific interventions. The necessary large sample sizes to develop such prediction equations are feasible to obtain with scalable IMIs.

A high-risk group that has been noticeably absent from preventive IMI trials is the group of individuals with genetic markers associated with mental disorders. A recent study<sup>100</sup> suggests a method that could combine genetic research with IMI depression prevention research. A massive sample collected by the genetic screening company was used to identify 15 genetic loci associated with risk of major depression: 75,607 individuals reporting clinical diagnosis of depression were compared to 231,747 individuals reporting no history of depression. A replication data set (45,773 cases and 106,354 controls) was then used to confirm the findings.

This very large sample could be the basis for an interesting set of depression prevention studies. Subgroups of individuals who have no history of depression but have the genetic markers associated with risk could be recruited for randomized trials testing promising IMIs. Such studies could contribute to prevention science in several ways by helping to confirm whether individuals with the markers actually have higher risk for developing major depressive episodes, particularly when confronted with stressful life events. They could also determine prospectively which of the 15 loci yield the greatest risk and help determine whether interventions that can be conducted online can reduce incidence in individuals with genetic loading for depression.

## Targeting Underlying Risk and Protective Factors in Individually Tailored Interventions

**The use of IMIs allows the provision of tailored interventions on large scale to a degree unlikely ever to be implementable using traditional FTF approaches.** So far, most studies evaluated standardized interventions based on CBT, including standard packages (e.g., cognitive restructuring, behavioral activation, relaxation

in a depression prevention intervention, etc.) for all participants regardless of the individual specific risk or protective factors, as well as intervention preferences. One potential next step for the field would be to develop and provide intervention modules that target specific underlying risk or protective factors (e.g., rumination, emotion regulation, social skills, experiential avoidance, compensatory behavior anxiety sensitivity, and physical activity) and tailor the combination of these modules based on the individual risk and need profiles of the participant. However, whether such an approach is superior to far more simple to develop and maintain standardized interventions that provide non-tailored to all participants is an empirical question that has yet to be adequately addressed.

## Strategies to Increase Reach and Utilization of Available Interventions

The impact of evidence-based preventive intervention on population level incidence heavily depends on the acceptance and use of such interventions in the target population.<sup>101</sup> As the field of MHD prevention continues to make progress in identifying programs that yield positive effects, it will be important to develop and evaluate effective and cost-effective strategies to disseminate evidence-based programs. Hence, there is a need for studies that investigate potential obstacles in order to subsequently develop and evaluate strategies for overcoming them. For example, Ebert, Baumeister, and colleagues evaluated acceptance—facilitating interventions that address potential barriers for acceptance of IMIs in different target populations in a series of randomized controlled trials.<sup>102-104</sup> Moessner and colleagues evaluated the effectiveness and cost-effectiveness of different school-based dissemination strategies for the prevention and early intervention in EDs.<sup>105</sup> However, such experimentally examined strategies to increase the reach of preventive interventions are scarce and need to be conducted more often in order to fully exploit the potential of preventive interventions on the population level.

## Conclusion

Internet- and mobile-based interventions are flexible, technically diverse methods which lend themselves to a variety of application areas. Such approaches have an ability to reach target groups in a way not yet achieved by classical FTF activities. A number of studies have shown

that such interventions can be effective in preventing mental disorders. But clearly much more research is needed in order to fully determine the potential of IMIs for substantially reducing the immense disease burden of MHD at the population level. ■

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L003451

## Multiple-Choice Questions

33. Given that ~75% of all *mental health disorders* (MHDs) have their onset before the age of \_\_\_\_\_, future studies should explore the potential of *internet- and mobile-based interventions* (IMIs) for preventing the first incidence in children, adolescents and young adults.
- A. 10
  - B. 15
  - C. 20
  - D. 25
34. IMIs offer the unique potential of reaching people who would not access preventive mental health care *via* the established channels delivery, either because they do not utilize the available offers or because they do not feel comfortable discussing their mental health issues with their general practitioners and mental health specialists. This statement is:
- A. True.
  - B. False.
35. According to the lesson, preventive interventions such as \_\_\_\_\_ should be delivered through multiple channels that have “natural” possibilities to engage people, such as:
- A. Schools, universities and colleges (they can reach all students).
  - B. Pregnant women (because they receive prenatal care).
  - C. Patients with general medical disorders.
  - D. All of the above
36. According to the lesson, the potential of serious games or even augmented reality interventions to foster mental health has been shown, for example, in the field of:
- A. Depression.
  - B. ADHD.
  - C. Schizophrenia.
  - D. PTSD.



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# Best Practices in Continuing Medical Education

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## Prevention of Mental Health Disorders Using Internet- and Mobile-Based interventions: A Narrative Review and Recommendations for Future Research

David Daniel Ebert, PhD; Pim Cuijpers, PhD; Ricardo F. Muñoz, PhD; Harald Baumeister, PhD

ID#: L003451

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

Although psychological interventions might have a tremendous potential for the prevention of *mental health disorders* (MHD), their current impact on the reduction of disease burden is questionable. This article introduces the subject and narratively reviews the available evidence for the effectiveness of *internet- and mobile-based interventions* (IMIs) with regard to the prevention of MHD onsets. Disorders not examined so far include substance use disorders, bipolar disorders, stress-related disorders, phobic disorders and panic disorder, obsessive-compulsive disorder, impulse-control disorders, somatic symptom disorder, and insomnia. In summary, there is a need for more rigorously conducted large scale randomized controlled trials using standard clinical diagnostic instruments for the selection of participants without MHD at baseline and the assessment of MHD onset.

#### Key Point 1: Background

**Less than half of the individuals with a MHD are recognized and treated. Therefore, attention has increasingly been focused on the prevention of MHD. Preventive interventions can be classified as universal interventions, directed at the whole population; selective interventions, directed at individuals with specific risk factors for the development of a MHD; or as indicated preventive interventions, directed at individuals in the prodromal stage of a disorder, who do not yet fulfill the criteria for a full blown disorder but experience subclinical symptoms.**

#### Key Point 2: Current Use of IMIs

**Although internet- and mobile-based interventions have been shown to be effective in clinical populations, including the treatment of depression anxiety, alcohol use, and sleep disorders, evidence for their effectiveness in preventing the incidence of MHD is much less documented.**

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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### **Key Point 3: Technical Implementation**

For the implementation of IMIs, numerous technical possibilities are applicable. These range from (1) the provision of evidence-based strategies as interactive self-help lessons; (2) e-mail, chat, or video-based sessions;<sup>27</sup> (3) virtual reality for exposure interventions;<sup>28</sup> (4) serious-games, in which psychological strategies are trained in the context of a computer game;<sup>29</sup> (5) the use of automated memory, feedback, and reinforcement interventions, for example, through apps, e-mails, text messages, or short prompts, which support the participant in incorporating intervention content into everyday life; to (6) sensors and apps for monitoring health behavior such as physical activity.

### **Key Point 4: Need for More Rigorously Conducted Large-Scale Randomized-Controlled Trials**

Future studies need to identify those subpopulations likely to profit from preventive IMIs. Given that ~75% of all MHD have their onset before the age of 25, future studies should explore the potential of IMIs for preventing the first incidence in children, adolescents, and young adults. There is a need also for more large-scale randomized controlled trials using standard clinical diagnostic instruments for the selection of participants without MHD at baseline and the assessment of MHD onset.

# Psychological Impact of Hurricane Harvey on Patients With Cancer

Anis Rashid, MD; Richard De La Garza, II, PhD; Tamara Emmy Lacourt, PhD;  
Smita Saraykar, MD, MPH; Asim A. Shah, MD

*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Natural disaster • Psycho-oncology • Distress • Hurricane Harvey

**LEARNING OBJECTIVES:** Upon completing this lesson, the reader will be able to (1) describe the impact of direct versus indirect exposure to a natural disaster (Hurricane Harvey) on the mental health of patients with cancer, and (2) identify factors that may influence the severity of psychological symptoms that arise in such persons as a result of a natural disaster.

**ABSTRACT:** This study was carried out to evaluate the psychological impact of Hurricane Harvey, a category 4 storm that devastated a Houston, Texas, and surrounding areas in August 2017, on mood symptoms in patients with cancer. The primary cohort (n=22) consisted of individuals who were diagnosed with hurricane-related stress at a psychiatric oncology clinic. An additional 73 patients were recruited by phone, of whom 22 (30%) had been directly affected by the hurricane. Of those who had direct exposure to the hurricane, 15 (68%) reported experiencing hurricane-related stress; of those who had not been directly exposed to the hurricane, 26 (51%) reported experiencing hurricane-related stress. Stress was measured in terms of depression, anxiety, and distress, which were assessed using standard clinical instruments. Patients with direct hurricane exposure who reported experiencing hurricane-related stress scored higher on all three instruments than those without direct exposure who did not report hurricane-related stress ( $P < .05$ ). The fact that stress levels were not significantly elevated in a large portion of these patients may point to personal resiliency in the face of disaster, as well as psychological and cultural traits that allowed these patients to develop improved coping skills.

**CONCLUSION:** As proposed by our hypothesis, patients with cancer who had direct exposure to Hurricane Harvey and experienced hurricane-related distress exhibited significantly higher levels of depression, anxiety, and distress than those who had not developed hurricane-related stress. These findings must be confirmed in light of certain study-related limitations.

**COMPETENCY AREAS:** This lesson addresses the gap in learning in the area of knowledge, patient care, and practice-based learning related to issues in psycho-oncology. It also highlights the uniqueness of patients with cancer and their symptoms. Many clinicians lack an understanding of the effect a diagnosis of cancer can have on the patient's mental health. On concluding this lesson, readers will have a better understanding of (1) the presentation of patients with cancer when they are under stress; (2) the usefulness of this knowledge in different clinical settings and various age groups; and (3) the limitations of studies and challenges faced by researchers attempting to discern differences in the effects of disaster exposure on the mental health of patients with cancer versus patients with cancer who have not been exposed to disaster.

## Introduction

Psychological stress after any natural disaster can be intense and may result in an increased prevalence of emotional distress in any population.<sup>1</sup> **Indeed, studies have shown that the prevalence of mental health disorders is increased two- to three-fold in disaster-affected populations.**<sup>2</sup> Common mental health disorders that are likely to arise in populations affected by a disaster include adjustment disorders such as anxiety, depression, and posttraumatic stress; somatic symptoms; and substance use.<sup>3</sup> The initial response to a disaster is often shock; if the impact of the disaster is severe, the symptoms it induces may persist for long periods of time and result in depression and anxiety.<sup>4</sup> Emotional challenges may lead to irritability, anger, guilt, and low self-esteem.<sup>5</sup> It has also been reported that adult patients not only develop short-term anxiety but may also develop long-term conditions such as *posttraumatic stress disorder* (PTSD).<sup>3</sup> Substance use may increase when used to varying degrees as a coping tool.<sup>6</sup> For example, a steep rise in alcohol use was documented in more than a third of a population that was affected by floods.<sup>7</sup> Anger, aggression, and incidents of domestic violence have been reported to increase after a natural disaster,<sup>8</sup> along with the need for mental health services, as indicated by an increase in emergency room visits and hospital admissions following such events.<sup>9</sup>

Hurricane Harvey was a category 4 hurricane that devastated Houston, Texas, and the surrounding area in August 2017 and caused an estimated \$125 billion in damage. According to the National Hurricane Center Tropical Cyclone Report website, Hurricane Harvey resulted in 103 storm-related deaths, and more than 30,000 people were forced to leave their homes. The hurricane was followed by 50 inches of rainfall, which created major hurdles in rescue and evacuation efforts.<sup>10</sup> According to the US Department of Energy, power outages from the storm affected more than 291,000 customers across the State of Texas.<sup>11</sup> The overall effect on physical health due to contaminated water, exposure to toxins, and improperly stored food has not yet been estimated.

**The main concern in areas affected by natural disasters like Harvey include a disruption in access to housing and social support systems. The psychological impact of a natural disaster on patients with cancer can**

**be even higher than in populations without cancer, because cancer patients are more likely to develop anxiety and distress, particularly because of fear the disruptions in the continuity of medical care, loss of social support systems, and an increased financial burden.** To the best of our knowledge, no data are available regarding hurricane-related mental health issues in patients with cancer.

## Procedures:

### Study Design

We carried out a retrospective study of patients seen in an outpatient psychiatric oncology clinic at a comprehensive cancer care center (University of Texas M. D. Anderson) between September 5, 2017, and January 5, 2018. These individuals were screened for hurricane exposure and self-reported distress. Only patients who had already given consent to be included in an ongoing psychiatry database (*Psych Care* developed at the Department of Psychiatry at MD Anderson Cancer Center) were included in this study. The protocol (PA17-1031) was approved by the local internal review board. Hurricane exposure was first assessed by chart review using the ICD-10 code X37.0XXA as an indicator of hurricane exposure. Patients for whom this code was not recorded were contacted by phone. Patients who granted consent over the phone were asked two questions: (a) “*Were you directly impacted by Hurricane Harvey?*”, and (b) “*Did you experience stress during the time the hurricane occurred?*”

### Patient Selection

A total of 60 patients were identified as having had hurricane exposure using an ICD-10 code (X37.0XXA). Of these, 22 had given prior consent to be included in the psychiatric database and were included in this study. An additional 138 clinic patients were contacted by phone: Of these, 40 did not return the call, 8 did not give consent, and 17 did not qualify for the study. Of the remaining 73 patients, 22 of those who were contacted by phone had been affected by the hurricane: 15 (68%) reported hurricane-related distress, and 7 (31.8%) reported having no hurricane-related distress. A total of 51 patients reported they did not experience direct hurricane exposure; of these, 25 (49%) reported experiencing hurricane-related distress and 26 (51%) reported

not experiencing hurricane-related distress. Because the number of individuals with hurricane exposure who did not experience stress was small ( $n=7$ ), this sample was excluded from all analyses.

## Measures

### Negative Mood and Distress Assessments:

Mood assessments, which are part of the clinic's standard assessment procedure, were completed for each patient during each clinic visit. Distress was measured using the *National Comprehensive Cancer Network (NCCN) Distress Thermometer (DT)* scale—a validated tool that focuses on several domains—including practical problems, (e.g. challenges in transportation, work/school, child care and housing) as well as family, emotional, religious, and physical problems<sup>12</sup> (e.g., bathing, dressing, eating, sleep, memory and concentration)—measures the overall level of distress during the past week on a scale of 0 to 10, where 0 represents the absence of distress and 10 represents the highest distress level possible. For the purpose of this study, the distress level alone was evaluated without considering the domain. Depression was measured using the *Patient Health Questionnaire (PHQ-9)*, which is valuable for screening, measuring, and monitoring depression. Its nine questions are based on criteria presented in *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*, with each criterion receiving a score of 0 (not at all) to 3 (every day). A score of 5, 10, 15 and 20 represents mild, moderate, moderately severe, and severe depression, respectively. A total score  $> 10$  has a sensitivity and specificity of 88% for major depression.<sup>13</sup> Anxiety was measured using the 7-item *Generalized Anxiety Disorder (GAD-7)* scale, which captures DSM-5 criteria for GAD, the most common anxiety disorder in general medical practice.<sup>14</sup> Each question was given a score of 0 (not at all) to 3 (nearly every day). Scores were graded as mild (5-9), moderate (10-14), or severe ( $> 15$ ).

### Data Analysis

Patients were grouped according to hurricane exposure (*yes* via ICD-code, *yes* via self-report, or *no* via self-report) and self-reported hurricane-related distress (*yes*, *no*, *unknown*). Group comparisons were performed using *univariate analyses of variance* (ANOVA) or a chi-square test with alpha set at 0.05. Homogeneity of variance was assessed using the Levene test. Significant results were followed with post-hoc comparisons. Considering the explorative nature of these analyses, no adjustment for multiple tests was done.

### Results:

Table 1 presents the demographics of our sample and test results. Groups did not differ in terms of gender or ethnicity, but significant differences were noted for age and race. Specifically, patients reporting hurricane-related stress without hurricane exposure were significantly younger ( $P = .03$ ) and more frequently black ( $P = .004$ ). Patients reporting both hurricane exposure and hurricane-related stress were more frequently of a race other than White or Black.

Table 2 and Figure 1 show the mood and distress scale results. ANOVA analyses revealed significant differences among groups for depression ( $F(3,84) = 2.875$ ;  $P = .041$ ), anxiety ( $F(3,84) = 109.63$ ;  $P = .009$ ), and distress ( $F(3,84) = 46.88$ ;  $P < .001$ ) (Table 2). The group with the lowest negative mood scores was the one reporting no hurricane exposure and no distress. Interestingly, no differences were observed between the group reporting no hurricane exposure with hurricane-related distress versus each of the other two groups (i.e., hurricane exposure/hurricane-related distress and hurricane exposure/no hurricane-related distress). These results remained unchanged when age was included as a covariate to the models (all models  $P < .05$  for group effects).



**Table 1:**  
**Sample Demographics**

| Variable               | Hurricane Dx<br>(Yes)<br>& Stress<br>(Unk)<br>N= 22 | SR Hurricane<br>(Yes)<br>& Stress<br>(Yes)<br>N=15 | SR Hurricane<br>(No)<br>& Stress<br>(No)<br>N=26 | SR Hurricane<br>(No)<br>& Stress<br>(Yes)<br>N=25 | SR* Hurricane<br>(Yes)<br>& Stress<br>(No)<br>N=7 | Test results              | P value |
|------------------------|---|--|--|---|---|---------------------------|---------|
| <sup>1</sup> Age       | 59.95 ±1.21 <sup>b</sup>                            | 57.67 ±2.59 <sup>ab</sup>                          | 59.88 ±2.41 <sup>b</sup>                         | 51.68 ±2.11 <sup>a</sup>                          | 58.43 ±3.21                                       | F(3,84)=3.13              | .30     |
| <sup>2</sup> Sex       | 73:27   | 60:40  | 58:42  | 72:28   | 57:43   | X <sup>2</sup> (3)=1.88,  | .59     |
| <sup>3</sup> Race      | 68 <sup>a</sup> :9 <sup>ab</sup> :23 <sup>ab</sup>  | 53 <sup>b</sup> :0 <sup>a</sup> :47 <sup>b</sup>   | 81 <sup>a</sup> :8 <sup>a</sup> :11 <sup>a</sup> | 60 <sup>a</sup> :32 <sup>b</sup> :8 <sup>a</sup>  | 86:0:14   | X <sup>2</sup> (6)=18.99, | .004    |
| <sup>4</sup> Ethnicity | 72:27   | 67:33  | 88:12  | 88:8  | 86:14   | X <sup>2</sup> (6)=8.67,  | .24     |

<sup>1</sup>Age (M±SE)<sup>2</sup>Sex (F:M) (%)<sup>3</sup>Race (white:black:other) (%)<sup>4</sup>Ethnicity (non-Hisp:Hisp) (%)

Dx= diagnosis

SR=Self report

Unk=Unknown

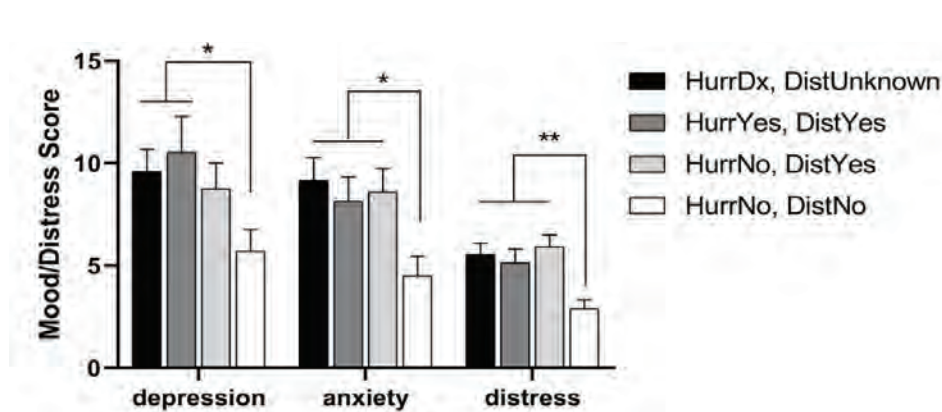
<sup>a,b</sup> denotes significant differences between groups.

\*The group reporting hurricane exposure but no stress was excluded from analyses due to its small sample size.

**Table 2:**  
**Negative Mood Symptoms Per Group (M ±SD)**

| Variable   | Hurricane Dx<br>(Yes)<br>& Stress<br>(Unk)<br>N= 22 | SR Hurricane<br>(Yes)<br>& Stress<br>(Yes)<br>N=15 | SR Hurricane<br>(No)<br>& Stress<br>(Yes)<br>N=25 | SR Hurricane<br>(No)<br>& Stress<br>(No)<br>(N=26 ) | Test results   | P value |
|------------|---|--|---|---|----------------|---------|
| Depression | 9.59 ±1.08 <sup>a</sup>                             | 10.53 ±1.75 <sup>a</sup>                           | 8.76 ±1.24 <sup>ab</sup>                          | 5.69 ±1.07 <sup>b</sup>                             | F(3,84)=2.875  | .041    |
| Anxiety    | 9.14 ±1.13 <sup>a</sup>                             | 8.13 ±1.20 <sup>a</sup>                            | 8.60 ±1.14 <sup>a</sup>                           | 4.50 ±0.95 <sup>b</sup>                             | F(3,84)=109.63 | .009    |
| Distress   | 5.55 ±0.55 <sup>a</sup>                             | 5.13 ±0.68 <sup>a</sup>                            | 5.92 ±0.57 <sup>a</sup>                           | 2.88 ±0.45 <sup>b</sup>                             | F(3,84)=46.88  | <.001   |

SR: self-reported

<sup>a,b</sup> denotes significant differences between groups**Figure 1:**

## Discussion

The frequency of natural disasters and their impact on populations are increasing due to global climate changes and increased population density.<sup>15</sup> In 2005, natural disasters affected 162 million people globally; almost twice as many people were affected by such disasters in 2010.<sup>15</sup> Natural disasters can affect the population exposed to them in many ways. The initial impact is the threat to safety—this results in a period of shock and fear, as well as displacement to search for safety.<sup>5</sup> The need for immediate psychosocial support under these circumstances is recognized, but it has to be appropriate and culturally sensitive to help promote long-term and sustainable mental health services.

After any natural disaster, the community and individuals respond in a predictable fashion, and that response usually occurs in four phases:

**Phase 1: *The rescue phase.*** Survivors and victims join hands and work long hours to save life and property. Hence, this is also known as the heroic phase.

**Phase 2: *The relief phase.*** Over a 2 to 4 week period, agencies and relief organizations provide food, medicine, supplies, and shelter to storm victims. Visits from higher authorities and the media are common. This phase is also known as the honeymoon phase.

**Phase 3: *The rehabilitation phase.*** Sometimes referred to as the disillusionment phase, this is a 1- to 2-year period during which the affected population experiences disappointment and frustration with legal barriers and bureaucratic delays.

**Phase 4: *The rebuilding phase.*** This phase may occur over several years, during which community organizations and individuals work closely together to restore a semblance of normalcy.<sup>5</sup>

Disease outbreaks are common among the displaced following a natural disaster, which affects the general physical health of this vulnerable population. Outbreaks of infectious disease occur because of water contamination,

poor sanitation, and overcrowding, which are major issues that result from natural disasters.<sup>16</sup> A recently published Hurricane Harvey registry indicates that approximately 25% of the population that was exposed to Hurricane Harvey developed migraine and difficulty concentrating, 20% suffered shortness of breath, and 10% had a skin rash.<sup>17</sup> The psychological impact of any natural disaster is not limited to the short-term anxiety or stress experienced during the initial phases of recovery but may lead to long-lasting depression or PTSD. Research has also shown that women are more likely than men to develop post-disaster mental health problems.<sup>18</sup> In this study, however, gender differences did not appear across groups.

As expected, the results from this study indicated that patients with cancer who experienced hurricane-related stress had higher scores on the depression, anxiety, and distress scales compared with the group with no hurricane exposure and no hurricane-related stress. It is important to note that there was no difference between patients who were diagnosed using an ICD-10 code or by self-reports of hurricane-related stress when contacted by phone.

**Researchers agree that natural disasters influence mood symptoms and that the severity of symptoms depends on the magnitude of the impact of the disaster and the losses individuals sustain.**<sup>19</sup> Other risk factors that aggravate this psychopathology include previous mental health history and the patient's own ability to adapt and respond to trauma. A subset of patients may be categorized as a "resilience" group. They may experience stress for a brief time following the disaster and recover much faster than patients in other groups. They have the ability to quickly adapt to and accommodate their current situation while continuing to function at a baseline level. This group is smaller in number among patients with chronic illnesses and cancer.<sup>15</sup>

In line with this, it is important to note that not all of the patients in this study with direct exposure to Hurricane Harvey scored higher on the mood scales. This may reflect an inherently superior ability to adapt and respond to disaster. This is important to bear in mind while working with disaster-stricken populations. Mental health clinicians evaluating patients with cancer who have been exposed to any natural disaster need to be diligent while taking a mental health history from these patients and should ask specifically about new physical symptoms.

The development of unexplained physical symptoms or somatization is not uncommon in populations exposed to any natural disaster; such symptoms may include headache, fatigue, and gastrointestinal distress.<sup>20</sup> A history of mental health issues or trauma, a lack of social support, or ongoing psychosocial stressors may make this patient population vulnerable to the development of somatic symptoms. This is particularly important in patients with cancer, who are not only likely to experience increased anxiety and distress compared with the general population but are also likely to have comorbid conditions that could confound the intensity of current symptoms. In this study, patients with cancer who had experienced a hurricane or self-reported hurricane-related stress exhibited significantly higher scores on the mood scales compared with the rest of the study population. **The single most important factor contributing to this finding was a fear of interruption of their cancer treatment. Patients with cancer must make frequent visits to the hospital to have their blood counts monitored, their performance status assessed, and, ultimately, to receive anti-cancer treatments. A natural disaster can easily compromise the functioning of the hospital facilities, which can lead to an interruption or delay in cancer treatments.** While it is unknown whether such interruptions can result in cancer progression, it seems reasonable to expect patients with cancer to exhibit significantly higher levels of anxiety and depression than those without cancer.

Another factor to take into consideration is the patient's cultural background. Certain aspects of behavior and responses to disasters vary from one culture to another. What may seem like a normal response in one culture may be characterized as a demonstration of psychopathology in another.<sup>21</sup> The key to an effective response to a disaster-affected population is a thoughtful organization and collaboration among local and national agencies. The psychosocial consequences of any disaster can be overwhelming; psychiatrists play an important role in improving the overall effectiveness of the disaster response by working closely with public health agencies. The importance of this collaboration has been recognized by the *World Psychiatry Association* (WPA) and *World*

*Health Organization* (WHO), which made a joint statement on the role of psychiatrists in the disaster response.<sup>22</sup> Additionally, the WPA has developed a Scientific Section on Disaster and Mental Health and disaster-specific task forces to help during the acute phase of disaster recovery and to help rebuild community mental health services after the acute phase is over.

It is important to note that although a substantial number of patients expressed high levels of stress due to a disruption in housing and transportation, clinic attendance was not notably affected. Indeed, the difference between pre- and post-disaster attendance was marginal. This suggests that the motivation to receive health care was high enough to overcome the temporary inconvenience of a hurricane.

By contrast, the COVID-19 pandemic has resulted in patients with serious health conditions (e.g., a heart condition) or with a medical emergency (e.g., chest pain or signs of symptoms of stroke) avoiding healthcare facilities. Hospitals and emergency rooms across the country are reporting a substantial drop in the number of patients with non-covid conditions; in some centers, the attendance rate has dropped by as much as 40%.<sup>23,24</sup> The explanation for this appears to be the extreme fear of becoming infected with the coronavirus. This could be highly dangerous in a high-risk population, such as elderly patients with a heart condition, diabetes, cancer, or a respiratory disease. This reluctance to seek medical care may change with the passage of time. WHO and the US Centers for Disease Control and Prevention are determined to find ways to control the spread of COVID-19 through preventive measures, education, and assurance.

The findings of this study must be viewed in light of its limitations. The fact that this was a single-center retrospective study with a small sample whose participants were recruited from a specialized psychiatric oncology clinic embedded within a comprehensive cancer center limits the generalizability of its findings. Selection bias and its cross-sectional design also limit its applicability to other populations. We therefore suggest that a similar study should be carried out in other cancer settings, preferably longitudinal analyses with larger sample sizes. ■

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## Multiple-Choice Questions

- 37. According to the lesson, patients with cancer experience more stress after a natural disaster because they:**
- A. Are more likely to be affected by a natural disaster.
  - B. Are unable to handle stress.
  - C. Are afraid of the loss of continuity of treatment.
  - D. None of the above.
- 38. Studies have shown that the prevalence of mental health disorders in disaster-affected populations is:**
- A. Lower than in non-affected populations.
  - B. Same as in non-affected populations.
  - C. Two to three times higher than in non-affected populations.
  - D. Ten times higher than in non-affected populations.
- 39. After any natural disaster, the community and individuals respond to the needs of survivors in a predictable fashion, usually in four phases listed in the following order:**
- A. Rescue phase, honeymoon phase, relief phase, rehabilitation phase.
  - B. Rebuilding phase, survivor phase, shelter phase, disappointment phase.
  - C. Rescue phase, relief phase, rehabilitation phase, rebuilding phase.
  - D. Anger phase, acceptance phase, rebuilding phase, honeymoon phase.
- 40. Mental health disorders commonly seen in disaster-affected populations include all of the following, *except*:**
- A. Adjustment disorders with anxiety and depression.
  - B. Posttraumatic stress disorder.
  - C. Substance use.
  - D. Attention-deficit hyperactivity disorder.

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# Best Practices in CME

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## Psychological Impact of Hurricane Harvey on Patients With Cancer

By Anis Rashid, MD; Richard De La Garza, II, PhD; Tamara Emmy Lacourt, PhD;

Smita Saraykar, MD,MPH; Asim A. Shah, MD

ID#: L003452

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

The information in this lesson is meant to educate mental health professionals—primarily psychiatrists but also psychologists, social workers, mental health counselors, and anyone who works with patients with cancer—about the increased stress these patients experience after a natural disaster as a result of their fear of the uncertainty of continuation of treatment.

#### Key Point 1: Natural Disaster

Natural disasters are major adverse events resulting from natural processes, e.g., floods, tornadoes, hurricanes, earthquakes, and storms.

#### Key Point 2: Psycho-Oncology

Psycho-oncology embraces psychological reactions to cancer and the behavioral component of coping with it. It is a less well-known area of study but very important to keep in mind when treating patients with cancer, given that behavior is a major component of their will to recover.

#### Key Point 3: Distress

Distress is defined as extreme anxiety. It can be seen in anyone with any severe medical condition. Patients with cancer are noted to have extreme anxiety or distress because of the uncertainty of their prognosis treatment outcomes.

#### Key Point 4: Comorbidity

Patients with cancer are not only likely to experience increased anxiety and distress compared to the general population during a natural disaster, but are likely to have intensified symptoms of comorbid conditions. Further, vulnerability to develop somatic symptoms is common in patients who lack social support, or have ongoing psychosocial stressors.

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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This image shows a full page of blank, lined paper. It features approximately 20 horizontal blue or grey lines spaced evenly apart, typical of notebook paper. The lines extend across the entire width of the page, leaving small margins at the top and bottom. There are no vertical lines, text, or other markings on the page.

# Review of Suicide Risk in the United States During the COVID-19 Pandemic

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**KEY WORDS:** Suicide • COVID-19 • Pandemic

**LEARNING OBJECTIVES:** Upon completion of this lesson, the clinician will be able to (1) identify risk factors for suicide; (2) explain the origin of COVID-19 and how the current pandemic unfolded; (3) explain the impact of the COVID-19 pandemic on economic, psychological, and social issues affecting individuals in the United States; (4) identify risks for suicide that are related specifically to the COVID-19 pandemic, and (5) find citations to references with information relevant to the risk for suicide during the COVID-19 pandemic.

**LESSON ABSTRACT:** The current COVID-19 pandemic presents many challenges, including the possibility of a significant increase in the risk of suicide. Many areas around the globe have already limited the spread of the virus. However, the United States is still struggling to implement relevant strategies—including stay-at-home orders, closure of indoor dining and entertainment spaces, and limited close contact among individuals from different households—in a consistent manner across the nation. The result has been a prolongation and expansion of infection, which increases risk factors for suicide, including distress, insomnia, unemployment, isolation, and an increase in the availability of firearms in the home. These factors can place a mental toll on the public, which can increase the incidence of suicidal ideation and attempts. The contraction of the virus has proven to be just as troublesome for the mental health of individuals. Earlier literature indicates that vigilance and care are needed for mental well-being to limit the spread of suicide that may accompany the COVID-19 pandemic.

**COMPETENCY AREAS:** This lesson addresses the evolving COVID-19 pandemic and lesser-known mental health issues that may affect those infected with the virus and those who are not. After reading this lesson, readers will gain comprehensive knowledge of factors associated with the increase in suicide risk that has been exacerbated by the current pandemic.



## Introduction

### Suicide:

Suicide, the deliberate act of killing oneself, is committed worldwide. According to the *World Health Organization* (WHO) approximately 800,000 people die by suicide annually.<sup>1</sup> In 2018, suicide was the 10th leading cause of death in the United States.<sup>2</sup> **Between 60% and 98% of all reported suicides are associated with mental illness; the remainder are associated with stressors—including financial strain, disasters, and interpersonal issues in the absence of an identifiable mental illness.**<sup>3</sup> Thus, it can be predicted that a crisis like the COVID-19 pandemic will contribute to an increase in suicide rates.

The risk of suicide has been attributed to various personal factors. Suicide rates are more pronounced in young adults from lesser developed countries compared with more developed countries, including the United States, where the rate is higher among middle-aged and elderly individuals.<sup>3</sup> Socioeconomic status also plays a role, with low-income and unemployed individuals being more inclined toward suicide because of the stress associated with their economic status.<sup>4</sup> In 2016, global suicide rates were higher for males than for females (1.8:1.0).<sup>5</sup> Depression and substance abuse (mainly alcohol use) were most strongly associated with suicide across the globe. Depression has been associated with the greatest number of suicides, with rates highest among the elderly, demonstrating the significant contribution of mental illness to suicide.<sup>3</sup> Poor physical health may also contribute to suicide. For example, patients with cancer are twice as likely to commit suicide than the United States general population.<sup>6</sup> Finally, the risk of suicide varies with the position of the individual in society. The risk is higher, for example, among young sexual minorities (i.e., lesbian, gay, bisexual, and transgender individuals) compared with young heterosexuals;<sup>7</sup> similarly, risk is higher for those who work in frontline jobs (including healthcare personnel, police officers, and members of the armed forces), who are more likely to witness the most traumatic events that can occur. This is especially relevant today for healthcare personnel, who carry the burden of spending extraordinarily long hours each day treating patients with COVID-19 while facing an increased risk infection themselves.<sup>8</sup>

**Methods of suicide vary across the globe. In 2017, the use of firearms was responsible for the most deaths from suicide in the United States, accounting for 23,854 out of a total of 47,173 suicides in the country.**<sup>9</sup> In most Asian countries (e.g., Hong Kong, Japan, and Kuwait), hanging is the most common method for suicide; this is also true for Australia and New Zealand and males in most European countries.<sup>3</sup> Suicide by burning (self-immolation) is seen most often in Middle Eastern countries, such as Iran.<sup>10</sup> The frequency of suicide attempts and ideation are significant to the act of suicide. The 2018 National Survey of Drug Use and Mental Health revealed that 0.5% of individuals aged 18 years or older had attempted suicide at least once in the United States. The rate of suicidal ideation in this age group has also increased, rising notably in 2018 compared with the period of 2008 to 2014.<sup>11</sup>

### COVID-19:

**The first cases of infection with coronavirus in humans were reported in China in late 2019.** In December 2019, these reports consisted primarily of several cases of pneumonia caused by a new strain of coronavirus that was identified in Wuhan, China. The virus was initially named the 2019-novel coronavirus (2019-nCoV) by WHO, which later renamed it COVID-19 (*Co* for corona, *vi* for virus, and *d* for disease). The virus spread quickly across the world in just a few months. On March 11, 2020, WHO declared COVID-19 a pandemic. The United States currently has more cases of COVID-19 than any other country in the world.

COVID-19 is an infection with a  $\beta$ -coronavirus. An  $\alpha$ -genre of this virus is known to infect mammals, whereas other genre ( $\gamma$  and  $\delta$ ) generally infect birds. Prior to the appearance of COVID-19, six CoVs had been identified as being capable of infecting humans. The  $\alpha$ -CoVs HCoV-229E and HCoV-NL63, as well as  $\beta$ -CoVs HCoV-HKU1 and HCoV-OC43, are of limited pathogenicity, in most cases causing only mild respiratory symptoms similar to those of the common cold. **Two other known  $\beta$ -CoVs, SARS-CoV and MERS-CoV, can cause severe respiratory symptoms and fatal respiratory tract infections.**<sup>12</sup> It had been suspected that bats are the natural hosts of COVID-19. It was initially believed that the virus spread through transitional hosts that were later used as food before spreading from human

to human. COVID-19 has almost 90% genomic identity with the bat-derived coronavirus that causes *severe acute respiratory syndrome* (SARS); this demonstrates that bats are likely the agents of its transmission to humans. It has been well established that human-to-human transmission occurs mainly through direct contact with an infected person or through droplets emitted by that person; the means of transmission from bats to humans remains unclear.<sup>13</sup>

Within just a few months following the first reported cases in China, COVID-19 had spread to more than 200 countries and territories worldwide. By May 2020, countries in Europe and the western hemisphere had the greatest number of cases. Those most greatly affected were the United States, Spain, Russia, the United Kingdom, Italy, Brazil, France, Germany, Iran, and Turkey. Together, these countries had approximately 70% of the total number of cases, 80% of the total number of deaths, and more than half of the total number of new cases of COVID-19 in the world. As of October 2020, the United States had reported more than 7.7 million total cases of COVID-19 and more than 214,108 COVID-19–related deaths.<sup>14</sup>

What makes COVID-19 more dangerous than any other SARS virus is that infected people can be contagious before the onset of symptoms, which makes the task of tracing contacts with presymptomatic and asymptomatic patients extremely challenging. COVID-19 also has a significantly long viral shedding period, with a median of 20 days and as many as 37 days, based on observations of survivors. COVID-19 affects patients in all age groups. Disease severity can range from a lack of symptoms to mild symptoms of an acute upper respiratory tract infection to moderate symptoms of pneumonia (fever, cough, wheezing, but no obvious hypoxemia) to severe symptoms of dyspnea and hypoxemia to the critical stage of acute respiratory distress syndrome, respiratory failure, shock, and organ dysfunction. The majority (approximately 80%) of adult COVID-19 patients have mild to moderate symptoms, and most children with COVID-19 develop only mild symptoms. However, the mortality associated with this virus is high, especially among elderly patients and patients with comorbid autoimmune conditions such as diabetes and hypertension. **Despite the remarkable differences in mortality among countries, one common finding is that the majority (70%-80%)**

**of COVID-19–related deaths have occurred in individuals aged 70 years or older.**<sup>15</sup>

## Risk Factors for Suicide During the COVID-19 Pandemic

### Distress and Insomnia:

The rapid spread of COVID-19 in early 2020 has caused a considerable amount of anxiety and distress throughout the world, especially in the hardest-hit countries, such as the United States. Anxiety and distress are natural psychological responses to a pandemic, according to the WHO. However, they can be exacerbated by related factors that arise as the pandemic continues, including prolonged social isolation and disruption in routines that accompany mass lockdown programs, as well as a sense of loss of control, financial loss, hopelessness, and helplessness. The perception of risk is magnified and distorted because of mixed messages and vague communication from governmental entities. Excessive media coverage, combined with the overconsumption of daily news reports of the number of deaths and the accelerating number of new cases, has contributed to an increase in fear, anxiety, and sense of loss of control, helplessness, and frustration. In one study of 1200 subjects in China, almost one-third of respondents reported moderate to severe anxiety levels.<sup>16</sup>

Excessive anxiety over health status, which is expected during the early stages of any pandemic, is particularly widespread in hard-hit areas following exposure to the disease. Such anxiety can be detrimental to one's mental health. Individuals with high levels of health-related anxiety are more likely to misinterpret benign bodily sensations such as muscle aches as signs of COVID-19 infection; this, in turn, can increase the level of anxiety even further.<sup>17</sup>

Past epidemiological studies have shown that individuals with distress or anxiety disorders are at increased risk for sleep disturbances. **They also demonstrated that sleep disturbance is the second most common symptom of mental distress.**<sup>18</sup>

Killgore and colleagues assessed the link among anxiety, insomnia, and suicidal ideation in 1023 U.S. adults during the first few weeks of the COVID-19 lockdown and found that 56% reported at least some evidence of insomnia, with 30.9% in the subthreshold range,

19.8% in the moderate range, and 5.2% in the severe range. These levels are much higher than have been seen historically in the general population. A greater level of worry over COVID-19 correlated with both self-reported insomnia ( $r = .37$ ,  $P < .000001$ ) and increased suicidal ideation ( $r = .11$ ,  $P = .001$ ). The severity of insomnia also correlated with an increased rate of suicidal ideation ( $r = .31$ ,  $P < .000001$ ). Although longer-term effects of the pandemic on mental health have just begun to emerge, this study established a clear relationship between COVID-19–related anxiety and an increase in suicidal ideation. The study also suggests that the effect of worry over COVID-19 on suicidal ideation is transmitted completely through its effect on sleep. It has long been established that sleep problems contribute to a host of mental health issues, including an increased risk of suicidal ideation. Distress related to the COVID-19 pandemic—such as social isolation, fear, economic uncertainty, and routine disruption—has resulted in heightened anxiety levels, which, in turn, cause sleep problems that can lead to increased suicidal ideation.<sup>19</sup>

### Unemployment:

It is well known that natural disasters can have a profound effect on mental health. A larger percentage of people who experience a natural disaster will be at increased risk of exhibiting mental health disorders and psychological stress. Thousands of suicides are seen each year as a result of unemployment alone. For instance, when the 2008 economic crisis occurred, the relative risk of suicide associated with unemployment was approximately 20% to 30% in 53 European countries and the United States.<sup>20</sup>

Nationwide lockdowns in March and April 2020—which involved travel restriction, social distancing, and closure of schools and nonessential businesses—caused the U.S. economy to contract at an annualized rate of 5% during the first quarter of the year. Among the industries worst hit by the lockdown are travel, indoor entertaining, restaurants, and bars. In just a few months, more than 14 million Americans had lost their jobs. The number of unemployed Americans skyrocketed from just over 6 million in January 2020 to 20.5 million in May 2020, thereby greatly exceeding the 8.8 million unemployed individuals during the first 2 years of the Great Recession (2008 and 2009). The unemployment rate quickly rose to 14.4% in April, subsiding only slightly in May to 13.3%.<sup>21</sup> It may

still be too early to estimate the total economic cost of this pandemic accurately, although dramatic changes in certain metrics (e.g., the quarterly Gross Domestic Product and unemployment rate) already reflect obvious changes in the economy. Unemployment rates among the most vulnerable populations were substantially higher than among those with more advantages in life. For example, in terms of education, **almost 19% of workers without a high school diploma were unemployed compared with 7.2% of workers with a bachelor's degree or higher.** Recent studies support the long-held hypothesis that mass layoffs and prolonged unemployment (15 to 26 weeks) increase the risk of suicide.<sup>22</sup>

In an attempt to soften the economic blow to businesses and individuals, the federal government created the multitrillion-dollar Coronavirus Aid, Relief, and Economic Security (CARES) Act on March 27, 2020. Additionally, unemployment benefits were expanded temporarily beginning in March, with the increased payout to last until the end of July and possibly beyond. However, the economic uncertainty established by the pandemic is expected to remain at least into the near future.<sup>23,24</sup>

As the COVID-19 pandemic unfolds, Americans continue to experience multiple stressors in addition to the stressors associated directly with the virus itself. Approximately 80% to 88% of the individuals who responded to an April 2020 survey named uncertainty and changes in routine as the most prevalent stressors in their lives. **Financial concerns, even though less frequently named, stood out as the most stressful issue.**<sup>25</sup> In April 2020, more than 22 million Americans applied for unemployment insurance within just 4 weeks. That stressor, coupled with social isolation, could not only increase the risk for psychological disorders (e.g., depression and suicide), it would also increase the risk for various health problems, including heart disease, depression, and dementia, each of which could also trigger suicidal behavior.

According to the Pew Research Center, more than 40% of adult Americans reported that they or someone in their family lost a job or had to take a pay cut during the outbreak. Financial stress was even more notable in vulnerable populations, with about half of lower-income Americans reporting a household job

loss or wage reduction because of COVID-19. As in previous financial crises, lower-income Americans are less prepared to weather the storm. Only a quarter of low-income Americans have enough emergency funds to pay for essentials for at least 3 months compared with almost 50% of middle-income and 75% of higher-income families. Additionally, low-income adults had more difficulty paying bills in April 2020 compared with 25% of middle-income and 11% of higher-income families. More than half of low-income American adults frequently expressed concern over their basic financial needs. Minority groups are often the most vulnerable: Only one-third of African-American and Latino adults younger than 30 years and without college experience had a 3-month “rainy-day” fund.<sup>26</sup>

### Isolation:

Currently, a large portion of the world’s population is confined to their homes because of lockdown orders issued to prevent further transmission of the disease.<sup>27,28</sup> This prolonged confinement has caused universal anxiety and distress, which WHO has identified as natural responses to stress.<sup>28</sup> Previous studies indicated that mental well-being is heavily affected during a global pandemic.<sup>29,30</sup> Quarantine, when imposed nationwide, can induce anxiety and distress, as well as mass hysteria, resulting from a sense of feeling cornered and sensing a loss of control over one’s life. These feelings may be intensified by familial separation, financial loss, insufficient amounts of basic essentials, and an increased perception of risk due to inefficient and incorrect communication from government sources and the media.<sup>31</sup> In the past, similar outbreaks were accompanied by an increased number of reports of irritability, anger, confusion, loneliness, depression, and, in some cases, suicide.<sup>32</sup>

The fact that the elderly population is particularly vulnerable to the effects of COVID-19 has created a substantial amount of fear in this age group, possibly accompanied by anxiety, stress, anger, and irritability.<sup>33,34</sup>

**Older adults with cognitive decline are at particular risk of becoming anxious, agitated, and socially withdrawn. This heightened sense of social isolation may increase the risk of anxiety and depression, which, in turn, may put these individuals at increased risk for suicide.** These feelings may be intensified if the elder already feels like a burden on society and feels devalued,

particularly if s/he believes older people might not receive adequate healthcare when resource rationing is enforced.<sup>35</sup>

Stressors and other factors that correlate with poor mental health and isolation include a prolonged quarantine, coupled with the sense of frustration, boredom, and social isolation that accompanies it.<sup>32</sup> Other risk factors include the existence of psychiatric illness, especially an affective disorder.<sup>36</sup> This pandemic has resulted in new cases of affective disorder while creating barriers to treatment. During the SARS epidemic, a high rate of psychological distress, including depression and *posttraumatic stress disorder* (PTSD), was associated with quarantine; the frequency with which these stressors were reported increased with the duration of the lockdown.<sup>37</sup> This distress has been amplified during the current pandemic, thereby amplifying the risk of suicide and the exhibition of mental illness.<sup>38,39</sup>

**Those who are most vulnerable to suicide include individuals with a preexisting mental health disorder and older adults living in isolation.** Prolonged isolation may cause these individuals to become very self-judgmental and, thus, may severely increase the risk of suicidality. The forced isolation imposed by the pandemic may result in fear of being trapped for an indefinite period of time.

We saw the first suicide in South India on February 12, 2020. The victim was a 50-year-old man who wrongly believed that his normal viral count was an indication of infection with COVID-19.<sup>40</sup> Out of fear and consideration for his family, he placed himself in isolation, but later committed suicide after being disturbed by reports of COVID-19–related deaths in the newspaper.

Thus, we can expect to see severe deterioration in some individuals’ mental health during this pandemic due to prolonged isolation and consequential depression. Along with this, we can expect an increasing number of suicides.

### Access to Lethal Weapons:

During February 2020, while public health officials focused on limiting the spread of COVID 2019, firearm sales spiked in the United States. During March alone, more than 2.5 million firearms were sold, including 1.5 million handguns.<sup>41</sup> Even under ideal circumstances, an increase in gun ownership correlates with an increased risk for suicide with firearms—and these are not the best



of circumstances.<sup>42</sup> A high portion of the population lives in isolation, making them more vulnerable to the deterioration of their mental health. These two factors together created a climate in which the risk for firearm-related suicide is increased. The firearm-related suicide crisis had been ongoing well before the COVID-19 pandemic began.<sup>43</sup> Between 2006 and 2018, the rate of firearm-related suicides increased by 25%. In 2018 alone, there were 24,432 firearm-related suicides in the United States.<sup>43</sup> The total number of firearm background checks increased by 40% from 10,036,933 in 2006 to 28,369,750 in 2019.<sup>44</sup> The highest ever recorded number of firearms sales was seen in March 2020, when the total number of sales rose by 85% compared with March 2019.<sup>41</sup>

There is a 22-fold increase in the rate of firearm-related suicide within the first year the individual purchases a handgun compared with those who do not purchase a handgun.<sup>45</sup> With every 10% increase in household firearm ownership, we see an increase in the firearm suicide rate of about 3.1 per 100,000 persons.<sup>45</sup> **The presence of a firearm in the home presents a 2- to 10-fold increased risk for suicide compared with the absence of firearms.**<sup>46</sup> The risks posed by guns are not new. What is new, however, is the economic and social impact of COVID-19, which, combined with the increased availability of firearms, could be responsible for the current wave of suicide.

When all of the possible mechanisms for committing suicide are considered, it is surprising that most suicide attempts are unsuccessful. One exception is firearm-related suicide (the most common method used), which is associated with a fatality rate that is 40 times greater than with drug poisoning.<sup>47</sup> Therefore, the number of suicides from firearms should be expected to increase, considering the extreme circumstances of this pandemic.

### Contracting COVID-19:

This pandemic has understandably brought uncertainty regarding the direction society should take to battle the COVID-19 virus. What is more troubling is the impact of anxiety on patients already infected with this virus. The *European Journal of Case Reports in Internal Medicine* contains a report of a male COVID-19 patient who jumped from the hospital building to which he had been admitted in an attempted suicide. One reason for this act

may have been a sense of guilt for possibly having exposed family members and friends to the virus. Alternatively, he may have endured prolonged loneliness while isolated in the hospital ward, or he may have wanted to protect surrounding individuals by ending his life.<sup>48</sup> Another case of suicide, which was reported in March 2020 in Wuhan, China, involved a patient who had exhibited symptoms of depression but had not expressed any suicidal ideation or behavior. Thus, it is worth noting the potential for untreated depression to progress to suicide.<sup>49</sup>

Patients showing symptoms for COVID-19 are required to stay in quarantine at home or in a hospital facility. These conditions can be quite burdensome, especially if the patient feels ashamed for possibly causing family members and other close associates who may have been exposed to the virus through him to have to go into quarantine. The psychological impact can be transferred to family members and close associates if they are experiencing depression or PTSD.<sup>50</sup> These cases illustrate the need to attend to the psychological needs of COVID-19 patients, as well as their physiological distress.

## Review of Papers

From the start of the COVID-19 pandemic, published articles have described a potential rise in suicide rates. Gunnell and colleagues provided a comprehensive overview of the predicted effects of the virus on suicide. They described how the increase in suicide rates might be due to the stigma of being infected with or testing positive for COVID-19, the existence of psychiatric issues, and being a frontline healthcare worker who interacts with infected patients daily. These individuals may require special attention, and mental health services must be vigilant for this. Other troubling factors include financial fears, isolation, and access to lethal means.<sup>51</sup>

Dr. Leo Sher provides more insight into the role of the virus in suicide, citing studies conducted in China and in the United States of the psychological impact the virus has had on society. Surveys conducted by both countries indicate that a significant proportion of individuals have reported some form of psychological distress due to COVID-19. Suicides associated with the pandemic are also discussed in this lesson, including suicides by individuals who were believed to have tested positive for the virus or who may have been in contact

with others who tested positive. What is alarming, yet expected, is the increase in the number of calls to suicide prevention hotlines in the United States since the start of the pandemic. Dr. Sher explains why it is imperative to boost the morale of individuals to improve their mental health through positive and reinforcing messages of hope, either by connecting with them virtually or by providing a means for them to seek and obtain the assistance of mental health professionals.<sup>52</sup>

Another consideration for suicide risk during the current pandemic may consist of living in a rural community. Approximately 23% of the U.S. population lives in areas that are classified as “rural.”<sup>53</sup> Monteith and colleagues point out that the less dense the population, the greater the risk for social isolation and more limited the availability of social support. Domestic violence with a spouse or intimate partner is more likely to occur in rural communities, and such psychosocial trauma can exacerbate suicidal ideation. Also, there are more likely to be firearms in a rural home. Finally, fewer mental health providers are available in such communities.<sup>54</sup> For these reasons, it is necessary to pay special attention to the suicidal effects of the pandemic in rural communities across the United States.

Gratz and colleagues associate the risk of suicide during this pandemic with the “Interpersonal Psychological Theory of Suicide.” According to this theory, suicidal ideation can arise from two elements: (1) perceived burdensomeness, in which there is a personal notion of being a burden to others; and (2) thwarted belongingness, in which the individual feels isolated from others. Perceived burdensomeness may be evident in individuals who contracted the virus and must stay away from family and friends; this adds to the perceived burden of not spreading the virus to family and friends and not participating in normal daily activities. Thwarted belongingness is similar, in that the infected individual may not be able to come in close proximity with loved ones and, consequently, develops a feeling of disconnectedness. Gratz and colleagues also conducted a study in the United States to determine whether this theory can be applied to the risk of suicide resulting from stay-at-home orders and unemployment. In the preliminary analysis, 58 of 467 participants who were either under stay-at-home orders or unemployed were at increased risk of suicide. Significantly, they

discovered a direct and indirect relationship through perceived burdensomeness and between job loss and suicide risk, as well as an indirect relationship through loneliness and thwarted belongingness between being under a stay-at-home order and suicide risk.<sup>55</sup> This study highlights the significance of the impact of changes brought by the COVID-19 pandemic on suicidal ideation.

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## Conclusion

In the past, pandemics created troubling times for many individuals, and the current COVID-19 pandemic is no different. As of October 2020, the United States continued to battle the omnipresent virus, with more 7.7 million cases of infection and more than 214,108 deaths.<sup>14</sup> Healthcare professionals continue to do their best to treat infected individuals, and government bodies are gradually becoming persistent about requiring individuals to wear masks and stay away from large gatherings. While this act of quarantine will prevent more people from being infected, hospitalized, and dying, the resulting social isolation may be detrimental to the mental health of the individual. This issue must continually be addressed so that individuals never feel socially rejected. We must continue to find ways to help isolated individuals maintain a sense of connectedness with loved ones who may also be in social isolation.<sup>56</sup> This would allow mental health workers to focus on other factors that can contribute to suicidal ideation, including distress, insomnia, unemployment, access to lethal weapons, and infection.

It is just as important now for mental health providers to assist those who are coping with mental distress. Online resources are available so that individuals do not have to put themselves at risk of direct contact with someone who may be infected. For example, Mental Health America’s website contains blogs and webinars that are readily accessible to members of the general public who need psychological support.<sup>57</sup> Such resources may prove beneficial for vulnerable members of the population who cannot afford physical and mental health support. Children, adolescents, and residents of rural communities must also be accounted for.<sup>58</sup> This would allow for suicide prevention and ensure that care is taken to avoid suicidal ideation.

While news media and online sources provide a plethora of information about COVID-19, this has been

shown to lead to anxiety, thereby increasing worry in the general public about the future. During this time, it is the responsibility of health professionals and journalists to make accurate assessments of incoming statistics to lessen anxiety to the public. Although CDC guidelines are subject to change daily, they continue to provide the latest on what is known about behaviors that are likely to keep the public safe.

Even before the COVID-19 pandemic began, suicide had been a pervasive public health issue, especially in the United States. Support for individuals is necessary now more than ever. As we continue to learn more about the physiological effects of the virus, it also becomes imperative to stay vigilant regarding the mental health issues individuals are facing because of COVID-19. ■

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L003453

## Multiple-Choice Questions

**41. In what country were COVID-19 cases first identified?**

- A. China
- B. Vietnam
- C. Korea
- D. Japan

**42. The rate of suicide cases in the United States that are linked to mental illnesses falls in the range of:**

- A. 20% to 30%.
- B. 30% to 40%.
- C. 60% to 80%.
- D. 60% to 98%.

**43. The most common method of committing suicide in the United States is:**

- A. Poison.
- B. Firearms.
- C. Cutting.
- D. Hanging.

**44. Two  $\beta$ -CoVs that can cause severe respiratory symptoms in humans are:**

- A. HCoV-229E and HCoV-NL63.
- B. HCoV-HKU1 and HCoV-OC43.
- C. SARS-CoV and MERS-CoV.
- D. SARS-CoV and HCoV-OC43.

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# Best Practices in Continuing Medical Education

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## Review of Suicide Risk in the United States During the COVID-19 Pandemic

By Saad Sidiq; Hai Le, MD; Burhan Ahmed Khan, MD; Asim A. Shah, MD

ID#: L003453

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

The information in this lesson is aimed to educate mental health professionals, primarily psychiatrists but also psychologists, social workers, and mental health counselors, and anyone who works with cancer patients, that they experience more stress after a natural disaster, as they fear the uncertainty of treatment.

#### Key Point 1: Suicide

**Suicide, the deliberate act of killing oneself, is an action committed by individuals worldwide. The most common method of suicide in the United States is firearms. Between 60% and 98% of all reported suicides are associated with mental illness.**

#### Key Point 2: What is COVID-19?

**COVID-19 is a  $\beta$ -coronavirus, along with  $\alpha$ -genre, which is known to infect mammals while other genre,  $\gamma$ - and  $\delta$ , generally infect birds. The virus was initially named the 2019-novel coronavirus (2019-nCoV) by the World Health Organization (WHO); later, WHO renamed it as COVID-19 (Co for corona, vi for virus and d for disease). COVID-19 has almost 90% genomic identity with the bat-derived coronavirus that causes severe acute respiratory syndrome (SARS). Disease severity can range from a lack of symptoms to mild symptoms of an acute upper respiratory tract infection to**

**moderate symptoms of pneumonia (fever, cough, wheezing, but no obvious hypoxemia) to severe symptoms of dyspnea and hypoxemia to the critical stage of acute respiratory distress syndrome, respiratory failure, shock, and organ dysfunction.**

#### Key Point 3: Pandemic

**A pandemic is a disease that spreads over multiple countries or continents. In other words, it is an epidemic that occurs worldwide or over a vast area. COVID-19 was declared a pandemic by WHO on March 11, 2020.**

#### Key Point 4: Risk Factors for Suicide During COVID-19

**Excessive anxiety, distress and insomnia, unemployment and financial concerns, isolation, access to lethal weapons, and contracting COVID-19 are among risk factors associated with suicide during this pandemic.**

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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This image shows a single sheet of white paper with horizontal ruling lines. The lines are evenly spaced and run across the width of the page. There are no margins, text, or other markings on the paper.



# Counseling Individuals Who Engage in Nonsuicidal Self-Injury

William A. Ramsey, PhD

*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Nonsuicidal self-injury • Assessment • Dialectical Behavior Therapy

**LEARNING OBJECTIVES:** Upon completing this lesson, clinicians with individuals who engage in *nonsuicidal self-injury* (NSSI) will be able to (1) describe the etiology of NSSI; (2) identify the contingencies necessary to maintain NSSI behaviors; (2) categorize various methods of assessing NSSI; and (3) describe evidence-based treatment for NSSI.

**LESSON ABSTRACT:** NSSI is a particularly effective, albeit maladaptive, strategy for regulating intense aversive emotions. It commonly occurs across clinical and community settings with similar rates of prevalence around the world. This lesson addresses NSSI and its etiology, focusing on why individuals engage in such pernicious behavior. It also explores evidence-based practices used to assess NSSI, including functional analysis, self-report measures, and structured interviews. Lastly, it will review dialectical behavior therapy—for which a considerable amount of evidence has been found in support of its efficacy in the treatment of individuals who engage in NSSI—and offer pragmatic strategies for intervention. The importance of treating patients who engage in NSSI cannot be overstated owing to its association with suicide. Therapists, counselors, and clinicians should consider using a functional approach in the assessment of NSSI to gain a thorough understanding of the antecedents, contingencies, and contextual influences that promote and maintain the behavior. This lesson is primarily for clinicians and therapists working with individuals who engage in NSSI and is intended to equip them with evidence-based assessment and counseling strategies, as well as provide practice-based learning.

**COMPETENCY AREAS:** This lesson addresses the gap in learning in the area of knowledge, patient and client care, and practice-based learning. Further, readers who do not understand how to adequately assess and treat patients who engage in NSSI, which is a potentially life-threatening behavior, will become equipped to provide better care to this population. Upon concluding this lesson, readers will have a better understanding of NSSI and how to assess and manage this pernicious class of behaviors.

## Introduction

***Nonsuicidal self-injury (NSSI) is the intentional self-mutilation of the body without suicidal intent. Classified as a “condition for further study” by the American Psychiatric Association,<sup>1</sup> it has gained increased attention from clinicians and researchers over the past decade.*** The purpose of this lesson is to inform practitioners of various essential aspects of NSSI, including methods of determining the etiology of NSSI behaviors in each patient, as well as assessment and counseling strategies, with a special emphasis on the role of *dialectical behavior therapy* (DBT) in helping the individual alter harmful behaviors. NSSI can be a life-threatening behavior; therefore, treatment professionals must consider the client’s motivation for change, the severity of the NSSI behaviors, and the overall functioning of the client, as well as the client’s suicidality to determine the appropriate level of care (e.g., outpatient, intensive outpatient, partial hospitalization, residential, or inpatient hospitalization).

## Etiology, Function, and Prevalence of NSSI

The onset of NSSI is typical during early adolescence (ages 12–14 years), with no reported difference in prevalence between males and females.<sup>2–4</sup> Prevalence rates of 38% to 21% have been reported for clinical and community adolescent populations, respectively, and these rates are relatively consistent across the globe.<sup>5–7</sup> **Importantly, NSSI is a robust predictor of attempted suicide,<sup>5,8–11</sup> which is the second leading cause of death between the ages of 10 and 34 years.<sup>12</sup>**

NSSI encompasses a heterogeneous group of behaviors that are seen along a continuum, with NSSI at one end and suicidal self-injury at the other. **To meet the criteria for NSSI, the injury must be an intentional self-inflicted mutilation of bodily tissue that was carried out with no suicidal intent but outside of socially sanctioned norms (e.g., tattooing and piercing).**<sup>8,13,14</sup> Although NSSI and suicidal self-injury are conceptually related, several factors can distinguish these two constructs, including form, frequency, function, and intensity of the injury. Common methods of NSSI include cutting, burning, and scratching with

an intensity ranging from superficial abrasions to severe scarring requiring medical treatment.<sup>2</sup> NSSI occurs much more frequently than suicidal self-injury. Nock and Prinstein<sup>3</sup> observed an average of 80 incidences of NSSI over a 12-month period in an adolescent inpatient unit compared with a 2.8 lifetime incidence of reported suicidal self-injury in a similar population.<sup>15</sup> Lastly, and perhaps most importantly, NSSI is distinguished from suicidal self-injury in that it is performed in the absence of suicidal intent.<sup>8</sup>

**NSSI is considered a particularly effective, albeit maladaptive strategy for coping with or regulating intense aversive emotions.<sup>13,16–18</sup> Individuals engage in NSSI while in a negative cognitive, emotional, or physiological state to gain a sense of relief. From an operant conditioning perspective, this reinforcing pain-offset feature makes it likely that NSSI will occur again under similar circumstances.** Haines and colleagues gathered convincing empirical support for this hypothesis through a novel, experimental investigation in which they exposed subjects to specific images and measured their physiological responses while viewing the images.<sup>19</sup> Their findings heavily influenced the development of theoretical models to explain why individuals engage in NSSI.<sup>20</sup>

### Four-function Model of NSSI:

Nock and Prinstein developed a *four-function model* (FFM) of NSSI to explain the contingencies that maintain NSSI behaviors.<sup>3</sup> They maintain that a functional approach to this inquiry (i.e., to understand the antecedents, contingencies, and contextual influences that promote and maintain a behavior) has led to innovations in the conceptualization, assessment, and treatment of a wide range of behavioral problems. Over a series of studies, they acquired strong empirical support for their FFM of NSSI.<sup>3,4</sup> The model is comprised of two dichotomous dimensions: (1) positive reinforcement vs negative reinforcement and (2) intrapersonal reinforcement vs interpersonal reinforcement. More specifically, **individuals who engage in NSSI commonly endorse the intrapersonal–negative reinforcement function more than any of the other three possible combinations.<sup>13</sup> Thus, most people report engaging in NSSI to regulate aversive affective, cognitive, and physiological states. Intrapersonal–positive**

**reinforcement is the second most commonly reported function, in that NSSI is commonly described as a form of self-punishment**, which is associated with the generation of desired feelings (e.g., a sense of relief and vindication). **Nonsuicidal self-injurers tend to be highly self-critical and engage in NSSI as a means of alleviating any cognitive dissonance with their perceived sense of self (i.e., deserving punishment).** The interpersonal functions of NSSI are exhibited at similar rates by nonsuicidal self-injurers and indicated by their engagement in NSSI to influence the behavior of others. **Counselors must recognize that NSSI is a multidetermined behavior with multiple functions—the two most common being emotion regulation and self-punishment—that address the contingencies that reinforce this class of behaviors.** Thus, an individual may engage in NSSI to regulate a distressing cognitive, emotional, or physiological state to inflict self-punishment and/or gain attention.

### **Assessment and Diagnosis of NSSI:**

The American Psychiatric Association<sup>1</sup> has proposed specific criteria for a diagnosis of NSSI, which include the following:

- **Engagement in self-injurious behavior on five or more days in the past year that causes minor to moderate damage of bodily tissue in the absence of suicidal intent.**
- **The individual engages in NSSI to generate a desired emotional or cognitive state or to “resolve an interpersonal difficulty.”**
- **The NSSI involves one or more of the following:**
  - **Aversive cognitive, emotional, or interpersonal difficulties leading up to the engagement of NSSI**
  - **Rumination concerning NSSI prior to engagement in the behavior**
  - **Frequent thinking about NSSI, whether or not the individual engages in the behavior**
- **The behavior is engaged in outside of socially sanctioned practices (e.g., piercing, tattooing, religious practices).**

- **The behavior or its sequela interfere with academic, occupational, social, or “other areas of important functioning.”**
- **The behavior is not better explained by another mental disorder or medical condition and does not exclusively occur during psychotic episodes or under the influence of or during withdrawal from substances.**

### **Differential Diagnosis:**

Individuals who engage in NSSI commonly exhibit characteristics that meet the criteria for a diagnosis of a depressive disorder, eating disorder, or substance use disorder.<sup>13</sup> Historically, NSSI was believed to occur exclusively within the context of borderline personality disorder. This notion has been dismissed, however, because of an accumulation of evidence supporting its occurrence across multiple disorders.<sup>21,22</sup> Individuals with borderline personality disorder tend to display patterns of unstable and intense relationships, identity disturbance, impulsivity, and affective instability, whereas those who engage in NSSI are more likely to exhibit symptoms of severe depression, anxiety, or suicidality. An example of self-injurious behavior that is not categorized as an NSSI is trichotillomania (hair-pulling disorder), which, though self-injurious, is distinguished from NSSI by the fact that hair-pulling is most likely to occur during a relaxed state.<sup>1</sup>

### **Measures of NSSI:**

**Standardized measures for assessing NSSI include both self-report inventories and structured interviews.** The instruments presented in Table 1 vary in purpose, aim, and conceptualization. Some conflate NSSI with suicidal self-injury;<sup>2,23</sup> whereas others provide an more inclusive assessment of life-threatening behaviors; and still others provide an even more comprehensive assessment of NSSI that includes age of onset, as well as the form, frequency, and function of the injury.<sup>24-29</sup> **Clinicians should consider the purpose of their assessment, the needs of their patients, and the context of their practice when seeking an appropriate assessment method.**

**Table 1:**  
**Standardized Assessments of NSSI**

| Name of Measure   | Type of Measure |                      |
|---|-----------------|----------------------|
|   | Self-Report     | Structured Interview |
| Alexian Brothers Urge to Self-Injure Scale <sup>28</sup>      | ✓               |                      |
| Deliberate Self-Harm Inventory <sup>2</sup>                   | ✓               |                      |
| Inventory of Statements About Self-injury <sup>25</sup>       | ✓               |                      |
| Lifetime Parasuicide History <sup>23</sup>                    |                 | ✓                    |
| Self-Injurious Thoughts and Behaviors Interview <sup>27</sup> |                 | ✓                    |
| The Nonsuicidal Self-Injury Assessment Tool <sup>29</sup>     | ✓               |                      |
| The Ottawa Self-Injury Inventory <sup>26</sup>                | ✓               |                      |
| The Self-Injury Questionnaire—Treatment Related <sup>24</sup> |                 | ✓                    |

## Functional Analysis:

Functional analysis<sup>30</sup> is an evidence-based process that leads to a testable hypothesis concerning motivating factors, antecedents that make the target behavior more likely to occur, and the function the behavior serves. We will begin our focus specifically on a type of functional analysis referred to as a chain analysis.<sup>31</sup>

## Chain Analysis

Chain analysis features prominently within *dialectical behavior therapy* (DBT),<sup>32</sup> which is described in detail in a subsequent section entitled, “Treatment of NSSI.” The chain analysis technique is considered an ideographic assessment,<sup>33</sup> given that it concerns the individualized assessment of variables and stimuli that have been selected based on their relevance to a given individual. **A chain analysis involves a thorough assessment of an instance**

**of the targeted behavior (e.g., NSSI) and is carried out to help the counselor and patient understand the antecedents and contingencies that promote and maintain the behavior.** The counselor may consider adopting a neutral stance throughout the analysis, because the process can provoke strong emotional reactions from individuals.

**A typical chain analysis begins with a thorough assessment of the problematic behavior.** It is not enough to know that the patient engaged in NSSI over the past week. Therapists need to know where the individual was when the NSSI occurred (e.g., in his/her bedroom), whether it occurred while the individual was alone or in a group, how the NSSI was enacted (e.g., razor blade, kitchen knife), the severity of the injury, how many times the patient engaged in NSSI, and over what period of time the behavior occurred. A sample of a complete description is as follows: “*The patient superficially cut the inside of his/her thigh with a razor blade five times over a 10-minute period in private in his/her bedroom on Saturday evening.*” For the purpose of illustration, a sample chain analysis will be described herein based on a fictitious patient (James) and his significant other (Lucy).

**An effective chain analysis involves identification of the prompting event (i.e., the antecedent).** The prompting event might be thought of as the event that occurs and leads up to the problematic behavior. For example, James had made plans for dinner and a movie with Lucy on Saturday night; he had been looking forward to it over the past week. Unfortunately, James and Lucy had a disagreement on Saturday afternoon that resulted in the cancellation of the plans at Lucy’s “request.” After the plans were cancelled, James experienced an aversive cognitive, emotional, and physiological state that he felt he had limited ability to regulate. James ruminates over the event, believing that he was responsible for the disagreement and, ultimately, for the cancellation of night out. James decided to engage in self-mutilation as a form of self-punishment, which he anticipated would decrease his distressing cognitive and emotional state. The counselor might identify the disagreement as the prompting event for James’s episode of NSSI on Saturday evening.

**Table 2:**  
**Chain Analysis: Key Assumptions**

1. A thorough assessment must be conducted to determine the antecedents, consequences, and motivating factors for a given problem behavior.
2. Vulnerability factors increase the likelihood of the behavior occurring.
3. Problematic behaviors are believed to develop in the absence of more skillful behaviors.
4. Patients and clients can learn new skills and behaviors to replace the problem behavior; they may include contingency management and/or making changes to one's environment.
5. It is imperative to thoroughly assess the problematic behavior to identify key points at which an intervention may be most successful.
6. Understanding the topography (i.e., form, function, frequency, intensity, duration, and context) of the problematic behavior is a requisite.
7. A thorough assessment must be conducted to determine the antecedents, consequences, and motivating factors for a given problem behavior.
8. Vulnerability factors increase the likelihood of the behavior occurring.
9. Problematic behaviors are believed to develop in the absence of more skillful behaviors.
10. Patients and clients can learn new skills and behaviors to replace the problem behavior; they may include contingency management and/or making changes to one's environment.
11. It is imperative to thoroughly assess the problematic behavior to identify key points at which an intervention may be most successful.
12. Understanding the topography (i.e., form, function, frequency, intensity, duration, and context) of the problematic behavior is a requisite.
  - a. What is/are the form(s) of the problematic behavior (e.g., cutting, hitting, scratching)?
  - b. What is/are the function(s) of the problematic behavior (i.e., what occurs during and after engagement in the problematic behavior)?
  - c. With what frequency does the problematic behavior occur?
  - d. Does the person engage in the problematic behavior once per episode or multiple times per episode?
  - e. How often do the episodes occur?
  - f. How intense is the problematic behavior? For example, does it cause superficial injury or is medical attention required?
  - g. What was the duration of the problematic behavior in this instance?
  - h. Where is the problematic behavior most likely to occur (e.g., in private, in a group)?

**An effective chain analysis requires the identification of vulnerability factors that may increase the risk of engaging in the problem behavior.** Vulnerability factors that increase the risk of engaging in NSSI may include intrapersonal variables (e.g., high levels of stress, lack of sleep, physical pain), contextual influences (distressing work environment, family system, or peer group), and other factors that may contribute to the individual's risk of carrying out the problem behavior (e.g., a heightened emotional state stemming from a history of emotional, physical, and/or sexual abuse). In this case, the therapist found that James had not slept well because he ran out of his sleeping medication two days earlier. Moreover, James noted that he had not eaten that Saturday because he planned to eat dinner with Lucy that evening. He also indicated that he often restricted his caloric intake because of concerns over

his body image. The counselor identified James' lack of sleep and lack of adequate nutrition as vulnerability factors.

**When conducting a chain analysis, the counselor must consider any links in the chain (e.g., the individual's thoughts, emotions, and behaviors, as well as environmental factors) that can lead to the problematic behavior.** These elements occur between the time the precipitating event occurs and the problem behavior is carried out, which may vary from seconds to hours. In this case, Lucy and James had gotten together on a Saturday afternoon to prepare their plans for their Saturday night date. James had been searching for employment over the last several months, and Lucy excitedly asked about his interview last week. James responded, "*Obviously it did not go well—otherwise, I would have been offered the job,*" feeling indignant because he thought Lucy was criticizing



him. Lucy responded, *"You always take what I say out of context! I can't stand it when you act like this. Our plans for tonight are CANCELLED!"* Lucy left. James was physically trembling, feeling overwhelmed with shame, guilt, and outrage. James locked himself in his bedroom, ruminating over the event. *"It was my fault. I always overreact. It's no wonder that Lucy never wants to spend time with me. I'm such an idiot!"* He then took a razor blade that he kept in his nightstand. The counselor identified the argument as the precipitating event, noting James' perception of Lucy's criticism as a potential cognitive distortion. Moreover, the counselor identified the strong aversive emotions of shame, guilt, outrage, and indignation, as well as his self-criticism and behavior (i.e., securing the readily accessible razor blade) as factors leading up to the problem behavior.

**The final component of a successful chain analysis is the assessment of contingencies that maintain or reinforce the problem behavior.** The behavior may be carried out to cope with or regulate intrapersonal factors, interpersonal factors, or both. For example, James noted a sense of relief after making the first incision with the razor blade and watching the blood run down his thigh. After cutting himself, James reported a sense of remuneration and expiation for his perceived sense of wrongdoing and responsibility for the argument and cancellation of their plans for the evening. After experiencing the relief associated with the NSSI, James contacted Lucy to tell her that he was so distressed by their disagreement that he hurt himself to feel better. Lucy remarked *"James, I'm so sorry! I didn't mean to make you hurt yourself. I feel terrible. Is it alright if I come over to talk? I'm on my way!"* Lucy implicitly learned to mind the statements she made toward James, often worrying about sending him down a path to self-injury. The alleviation of James's aversive cognitive, emotional, and physiological state is conceptualized as an intrapersonal factor (negative reinforcement), whereas the influence of Lucy's behavior is conceptualized as an interpersonal factor (positive reinforcement).

**Here we have described the five-part process of conducting a chain analysis: (1) assess the target behavior, (2) identify the prompting event, (3) consider vulnerability factors, (4) distinguish linking events on the chain, and (5) evaluate the function(s) of the target behavior.** Although presented sequentially

for didactic purposes, a counselor may carry out the chain analysis in a flexible manner appropriate for the needs of the individual and flow of the session. Moreover, conducting an effective chain analysis is only half of the equation. It should be integrated into a solution analysis so that the therapist and individual can identify alternative behaviors that may be utilized in the future to decrease the risk of engaging in the target behavior. The solution analysis is described later in this lesson in greater detail.

## Treatment of NSSI

**DBT is the therapeutic modality with the most evidence of appropriateness for those who engage in NSSI.**<sup>34</sup> The description of DBT provided herein reflects the process adapted for use with adolescents. Counseling strategies that may be utilized to reduce the incidence of NSSI are also described and include a brief cognitive intervention targeting self-critical thoughts and solution analysis.

### Dialectical Behavior Therapy:

DBT<sup>32</sup> was developed in response to the needs of chronically suicidal women with borderline personality disorder. **DBT is perhaps best conceptualized as a cognitive-behavioral approach with enhanced effectiveness across multiple clinically relevant outcomes, including a reduction in the frequency of self-injurious behaviors.** DBT is a highly flexible, multistage, multimodal treatment that has been shown to be more effective than treatment-as-usual (i.e., individual psychotherapy and ancillary non-manualized pharmacotherapy as needed) across multiple clinically relevant variables in two randomized clinical trials.<sup>35,36</sup>

**DBT is provided across four therapeutic modalities—individual therapy, group skills training, consultation group, and phone coaching—that serve five therapeutic functions: (1) enhancing patient motivation for treatment, (2) enhancing patient capability, (3) generalizing learned behavior to the patient's natural environment, (4) enhancing the ability and motivation of the therapist to treat patients effectively, and (5) structuring the environment for success.** DBT utilizes a stage model to dictate targets for treatment. For example, during the pretreatment stage, the patient is



oriented to treatment and to the collaborative development of agreed-upon treatment goals.

**The following five areas are targeted hierarchically within the first stage of treatment: (1) reduction of life-threatening behaviors; (2) reduction of behaviors that interfere with therapy; (3) reduction of behaviors that interfere with quality of life; (4) acquisition of the core DBT skills of mindfulness, interpersonal effectiveness, emotion regulation, and distress tolerance; and (5) progress toward the patient's goals.** The second stage of therapy typically involves helping the individual experience emotion more fully. The third stage focuses on helping the individual achieve a reasonable degree of happiness. The fourth and final stage is characterized by helping the individual develop and pursue psychological insight, spirituality, and an expanded sense of awareness.

### ***Dialectical Behavior Therapy for Adolescents***

Miller, Rathus, and Linehan adapted the original DBT protocol to meet the needs of suicidal adolescents.<sup>37</sup> **The primary features of *dialectical behavior therapy for adolescents* (DBT-A) that distinguish it from DBT include (a) shortened treatment duration; (b) inclusion of family members in a skills training group; (c) simplification of language in skills training materials; and (d) the addition of family meetings.** Preliminary support for the efficacy of this approach was gained through a quasi-experimental investigation in 111 participants.<sup>38</sup> The group that received DBT-A experienced fewer psychiatric hospitalizations; a greater number of completed treatments; and a decreased frequency of suicidal ideation, anxiety, depression, and emotional dysregulation compared with those who received treatment-as-usual.

Two recent randomized controlled trials produced similar findings for DBT-A in suicidal teens.<sup>39-41</sup> Mehlum and colleagues found that DBT-A was superior to enhanced usual care (i.e., at least one scheduled session of psychotherapy per week and ancillary non-manualized pharmacotherapy as needed) in reducing the frequency of self-harm behavior, suicidal ideation, and depressive symptoms over a 19-week treatment period.<sup>41</sup> In a one-year prospective follow-up study, they found

that the DBT-A group maintained a greater reduction in frequency of self-harm behavior compared with the group that received enhanced usual care.<sup>40</sup> In a multisite randomized clinical trial of the efficacy of DBT-A versus individual or supportive group therapy in reducing the frequency of suicide attempts and NSSI,<sup>39</sup> McCauley and colleagues had findings similar to those of Mehlum and colleagues, with the DBT-A group experiencing a greater reduction in frequency of both suicide attempts and NSSI behaviors compared with those who received individual or supportive group therapy.

### **The Role of Self-Criticism:**

**The majority of NSSI interventions target the regulation of emotions.<sup>14,16,42</sup> There is evidence, however, supporting the importance of targeting self-punishment,<sup>3,4,9,17</sup> particularly given the observation that nonsuicidal self-injurers tend to be highly self-critical.** Glassman and colleagues found that self-criticism fully mediated the relationship between childhood emotional abuse and NSSI during adolescence.<sup>43</sup> Gilbert and associates assessed the relationship between self-criticism and NSSI and determined that the self-persecutory form of self-criticism may be especially linked to self-harm.<sup>44</sup> Evidence from laboratory investigations suggests that self-criticism has a causal relationship to NSSI.<sup>45</sup> **Hooley and St. Germain<sup>45</sup> found that exposure to a brief cognitive intervention designed to decrease self-criticism also decreased the willingness to endure pain in nonsuicidal self-injurers. Moreover, Ramsey and colleagues found that direct targeting of self-critical thoughts resulted in both a reduction in instances of self-criticism and NSSI in adolescents undergoing DBT-A over the course of four to six 15-minute weekly sessions.<sup>46</sup> These findings, coupled with the experimental nature of these designs, underscore the need to address self-criticism in the treatment of NSSI.**

### **Counseling Strategies for NSSI:**

#### ***A Brief Cognitive Intervention Targeting Self-Criticism***

**The brief cognitive intervention developed by Ramsey and colleagues has resulted in decreased frequency of both self-criticism and NSSI in adolescents undergoing DBT-A.<sup>46</sup> At the beginning of each session, the practitioner states the rationale for the intervention: “We’ve**

*found that individuals who are better able to identify the positive aspects of themselves tend to feel better about themselves—and individuals who feel better about themselves tend to be less likely to hurt themselves.*” The practitioner then discusses the rationale with their patients to make sure they understand before proceeding with the intervention.

Next, the practitioner gives each patient a checklist of 20 common positive characteristics (e.g., caring, dependable, kind, loyal) and asks clients to select any characteristics they believe applies to them and list any additional positive attributes that may not be listed. Recognizing that clients are likely to be highly self-critical, they are asked to select items that a close friend or family member might say about them. After at least three positive characteristics have been identified, the client is asked to provide a brief narrative about a time when they behaved in a manner consistent with one of the positive characteristics they selected. The practitioner encourages clients to identify and describe a specific event, e.g., by offering such statements as: “*Tell me a story about a time you were kind or dependable.*” The practitioner is encouraged to utilize paraphrasing, reflection of feeling and meaning, and additional prompts to facilitate a therapeutic dialogue (e.g., “*Can you say more about that?*” “How do you think your friend felt when you listened to them?” “*What was it like for you to be kind and listen to your friend?*”).

After the client finishes recounting an instance in which he or she behaved in a manner consistent with one of the selected characteristics, he or she is asked to process what it was like to recall the event in detail and share it with the practitioner (e.g., “*What is it like for you now to share with me about being kind and listening to your friend?*”). In particular, the client is asked to identify cognitions, emotions, images, or physiological responses to share their narrative. The practitioner may model responses as appropriate to facilitate the intervention (e.g., “*It made me feel happy to hear about your being kind and supporting your friend.*”) Moreover, the practitioner provides positive feedback and encouragement in response to the client’s narrative (e.g., “*It sounds like you were kind and your friend appreciated your support.*”) A major aim of the intervention is to guide clients through the process of accentuating and integrating positive aspects of themselves to decrease self-criticism.

## Solution Analysis

**The solution analysis is complementary to the chain analysis, which is described in the preceding section.** Solution analysis is carried out after a thorough chain analysis has been conducted to help the client determine where s/he might have intervened earlier in the chain of events to prevent the problematic behavior. **The goal of solution analysis is to promote the adoption of an alternative behavior for future circumstances.** Strategies used in solution analysis include contingency management (e.g., rewarding alternative behaviors) and environmental manipulation (e.g., removing sharp objects from one’s area). **It is imperative to thoroughly assess the problematic behavior in order to identify key areas in which this intervention may be most successful.** Chain analysis and solution analysis are presented separately here for the purpose of conceptual clarity. As the counselor and client become more comfortable and fluid in the use of chain analysis, they may decide to integrate it concurrently with solution analysis.

**To aid in the conceptualization of the processes underlying effective solution analyses, we should consider strategies for interventions that occur before (i.e., antecedents) and after (i.e., contingencies) the problem behavior occurs.** Many of the potential solutions commonly implemented before the occurrence of the problem behavior involve the core skills (distress tolerance, emotion regulation, interpersonal effectiveness, and mindfulness) described for DBT.<sup>32</sup> Potential solutions that may be implemented after the problem behavior occurs primarily concern the use of contingency management.<sup>47</sup> Let us again consider our fictitious client, James, and his significant other (Lucy) for the purpose of illustration.

In conducting the chain analysis, James and his counselor identified a number of antecedent-focused solutions, e.g., the strong emotional reaction he had to Lucy’s question about his recent job interview. James stated that he felt incompetent and criticized, and this prompted his angry response. The counselor began to conceptualize the client’s difficulties related to distress tolerance, emotion regulation, and interpersonal effectiveness. James and his counselor opted to role play using the DEAR MAN approach (**d**escribing, **e**xpressing, **a**sserting, **r**einforcing, staying **m**indful, **a**ppearing confident, and **n**egotiating). The counselor modeled the response: “*Lucy, I feel*

*criticized when you bring up my job search. It's a sensitive subject for me. I know you care about me, and I appreciate you checking in with me. Would we be able to talk about this after dinner? I'm not feeling up to it at the moment.*" Similarly, James' counselor also discussed utilizing a "Check the Facts" approach (i.e., assessing for cognitive distortions) to better understand whether his reaction was appropriate to the situation. Lastly, James and his counselor discussed the need to increase the distance between himself and the razor blades he uses to injure himself. James agreed to give his box of sharp objects to his counselor to decrease his access to them. This brief solution analysis was not intended to be exhaustive, because there are many other potentially important areas that may have been addressed (e.g., James' use of food restriction). Moreover, it is important to assess the likelihood that the client perceives any barriers to the implementation of the agreed-upon interventions so they can be resolved during the session.

## Summary

DBT has garnered significant support for its efficacy in the treatment of patients who engage in NSSI. Therefore, counselors working with this population may consider being trained in this therapeutic modality. Its use of a stage model in which NSSI and suicidal behaviors are the first targets of treatment may make it

ideal for treating individuals with this pernicious class of behaviors. NSSI typically begins during early adolescence, is prevalent in both clinical and community-based individuals, and robustly predicts future suicide attempts. **The importance of treating individuals who inflict NSSI cannot be overstated, given its association with both attempted and completed suicides.** Individuals engage in NSSI to regulate negative cognitive, emotional, and physiological states; thus, it often has multiple functions. Effective treatment begins with a thorough assessment. Multiple assessments have been developed to comprehensively assess the forms, functions, and frequency of NSSI. **Clinicians should consider using a functional approach to assess NSSI in order to understand the antecedents, contingencies, and contextual influences that promote and maintain the behavior.** This approach dovetails with DBT in terms of its use of chain analysis and can be used to collaboratively set treatment targets with their patients. **Nonsuicidal self-injurers tend to be highly self-critical and engage in NSSI to alleviate any cognitive dissonance with their perceived sense of self (i.e., deserving of punishment).** Therapists and clinicians should help their clients who engage in NSSI accentuate and integrate the positive aspects of themselves, given that this population is particularly prone to perseverate and punish themselves for their perceived shortcomings. ▮

## About the Faculty

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## Multiple-Choice Questions

**45. According to the lesson, *nonsuicidal self-injury* (NSSI) is:**

- A. A disorder classified as a “condition for further study” by the American Psychiatric Association.
- B. The intentional self-inflicted mutilation of bodily tissue with no suicidal intent and outside of socially sanctioned practices (e.g., tattooing and piercing).
- C. A pernicious class of behaviors that are enacted in the presence of negative cognitive, emotional, and physiological states to experience a sense of relief.
- D. All the above.

**46. Which of the following is *not* true regarding NSSI?**

- A. The onset of nonsuicidal self-injury is typically during early adolescence between the ages of 12 and 14 years.
- B. NSSI is best classified as an attention-seeking behavior.
- C. NSSI is a robust predictor of suicide attempts.
- D. NSSI is often enacted in the service of multiple functions.

**47. The second most commonly endorsed reason given for engaging in NSSI is:**

- A. Relief from aversive affective, cognitive, and physiological states.
- B. Self-punishment due to high levels of self-criticism (i.e., generation of desired feelings).
- C. Manipulation of environment via recruitment of attention or relief from a social responsibility.
- D. The desire to end one's life.

**48. What form of psychotherapy has garnered the highest level of evidence in support of its efficacy in the treatment of individuals who practice NSSI?**

- A. Acceptance and commitment therapy
- B. Cognitive-behavioral therapy
- C. Dialectical behavior therapy
- D. Mindfulness-based cognitive therapy

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# Best Practices in Continuing Medical Education

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## Counseling Individuals Who Engage in Nonsuicidal Self-Injury

By William A. Ramsey, PhD

ID#: L003454

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

*Nonsuicidal self-injury* (NSSI) encompasses a heterogeneous group of behaviors that fall along a continuum, with NSSI at one end and suicidal self-injury at the other. NSSI commonly occurs in both clinical and community settings, with similar rates of prevalence across the globe. The importance of treating individuals who engage in NSSI cannot be overstated owing to its association with both attempted and completed suicides. This lesson will provide guidance to clinicians working with clients who engage in NSSI, thereby enabling the clinician to (1) examine the etiology and contingencies that maintain NSSI; (2) categorize and utilize different methods of assessing NSSI; and (3) review evidence-based treatment for patients who engage in NSSI.

#### Key Point 1: Conceptual and Etiological Considerations

The onset of NSSI is typically during early adolescence between the ages of 12 and 14 years, with males and females engaging in this pernicious behavior at similar rates. To meet the criteria for NSSI, the injury must be an intentional, self-inflicted mutilation of bodily tissue with no suicidal intent and outside of socially sanctioned practices (e.g., tattooing and piercing). NSSI and suicidal self-injury are conceptually related but can be distinguished by the form, frequency, function, and intensity of the injury. Common forms of NSSI include cutting, burning, and scratching that results in injuries ranging from superficial abrasions to severe scarring that requires medical treatment. NSSI occurs at a much higher frequency than suicidal self-injury. Most importantly, NSSI is distinguished from suicidal self-injury by the absence of suicidal intent.

#### Key Point 2: Nonsuicidal Self-Injury Is a Multidetermined Behavior

Clinicians must recognize that NSSI is carried out in the service of multiple functions to comprehensively address the contingencies that reinforce this class of behaviors. The most common reason given for engaging in NSSI behaviors is to experience a sense of relief from a negative cognitive, emotional, or physiological states. Those who engage in NSSI report self-punishment or the generation of desired feelings as the second most common reason for harming themselves. Nonsuicidal self-injurers tend to be highly self-critical and engage in this behaviors to alleviate any cognitive dissonance associated with their perceived sense of self (i.e., deserving of punishment). Individuals also regularly engage in NSSI to influence the behavior of others. Therefore, an individual may engage in NSSI to regulate a distressing cognitive, emotional, physiological state, for self-punishment, and/or to gain attention.

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### **Key Point 3: Methods of Assessing for Non-Suicidal Self-Injury**

Effective treatment of those who engage in NSSI begins with a thorough assessment of the forms, functions, and frequencies of actions associated with NSSI, using both self-report inventories and structured interviews for the assessment. A functional approach to this assessment is a more individualized strategy intended to help the counselor and client understand the antecedents, contingencies, and contextual influences that promote and maintain the behavior. This approach dovetails with *dialectical behavior therapy* (DBT), with its built-in use of chain analysis. Clinicians should consider the purpose of their assessment, the needs of their client, and the context of their practice to select the most appropriate method of assessment.

### **Key Point 4: Evidence-Based Treatment for Non-Suicidal Self-Injury**

DBT has garnered a considerable amount of support for its efficacy in individuals who engage in NSSI. It is perhaps best conceptualized as a cognitive-behavioral approach with enhanced effectiveness in reducing the frequency of self-injurious behaviors. DBT is a highly flexible treatment that may be more effective than treatment-as-usual across multiple clinically relevant variables. Additionally, it has been adapted for use with adolescents. Indeed, its use of a stage model in which NSSI and suicidal behaviors are the first targets of treatment may make it an ideal modality in treating this behavior. Therefore, clinicians working with this population may consider obtaining training in DBT.

# The Association Between Excessive Use of Smartphones, Cognition, Emotion, and the Brain

Aviv Weinstein, PhD

*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Excessive smartphone use • Internet gaming disorder • Brain imaging • Functional MRI (fMRI)

**LEARNING OBJECTIVES:** Upon completing this lesson, the clinician will be able to (1) define excessive use of digital media for children and adolescents, as reported in recent literature; (2) explain the effect of excessive smartphone use on human behavior and mental health; and (3) describe the effects of excessive smartphone use on the brain in adolescents and young adults based on evidence provided by structural and functional brain imaging studies.

**LESSON ABSTRACT:** The effects of the excessive use of digital media—including TV, computers, and smartphones—is raising serious concern among health and education professionals because of recent evidence of its negative effects on children and adolescents. An association between increased digital media use and a decrease in the microstructural integrity of white matter tracts associated with the development of language and literacy skills has been shown in 5-year-old children. Additionally, a negative correlation between the use of digital media and cortical thickness has been observed in adolescents. The use of digital media is pervasive among young adults, as well, contributing to heavy media “multitasking,” which increases susceptibility to interference from irrelevant environmental stimuli and irrelevant representations in memory. Excessive use of smartphones, in particular, has been associated with an increased rate of depression, loneliness, anxiety (including social anxiety), obsessive-compulsive disorder, attention-deficit/hyperactivity disorder, and alcohol use disorder. Excessive smartphone use has also been associated with difficulty in regulating the relationship between cognition and emotions while contributing to impulsivity and impaired cognitive function, addiction to social networking, shyness, and low self-esteem. It may also induce sleep problems, reduce physical fitness, and contribute to unhealthy eating habits while contributing to specific medical conditions such as acquired concomitant esotropia, cervical disk degeneration, and migraine. Excessive smartphone use has been correlated with reduced cognitive control during emotional processing in the brain and a reduction in the amount of lateral orbitofrontal gray matter, especially with overuse of social networking platforms. **A significant negative relationship was found between excessive smartphone use and both gray matter volume and activity in the anterior cingulate cortex.** Prolonged smartphone use at bedtime has been associated with altered insula-centered functional connectivity. We conclude that easy access to the smartphone—which facilitates the ability to send messages, play games, download information, and interact with various social networks—may have deleterious effects on mental and physical health, particularly in individuals who use them excessively from childhood through early adulthood.

**COMPETENCY AREAS:** This lesson addresses the gap in our understanding of the effects of smartphones on cognitive and emotional functioning and on the brain in children, adolescents, and young adults. Upon concluding this lesson, the clinician will be able to describe these mechanisms and assess their effects on young smartphone users.

## Introduction

### The Effects of Excessive Use of Digital Media by Children and Adolescents:

The effects of the excessive use of digital media—including television, computers, and smartphones—are raising serious concerns among healthcare and education professionals because they appear to be particularly deleterious in children and adolescents. It was recently shown in 5-year-old children that an increase in digital media use is associated with a decrease in the microstructural integrity of white matter tracts that are associated with the development of language and literacy skills, particularly during the early years of brain development.<sup>1</sup> In a recent study of 4277 adolescents using the *Adolescent Brain Cognitive Development Scale* and *functional magnetic resonance imaging* (fMRI), investigators discovered a negative correlation between screen media activity and cortical thickness.<sup>2</sup> Because cortical thickness naturally declines with age, these findings suggest that the excessive use of screen media causes the brain to age prematurely. This study also showed that screen media use is associated with crystallized intelligence (general knowledge) and fluid intelligence (ability to handle novel situations) and, thus, results in externalized (but not internalized) psychopathology. The pervasive use of digital media has also been shown to cause young adults and heavy media “multitaskers” to be more susceptible to interference from irrelevant environmental stimuli and irrelevant representations of memory. Indeed, heavy media “multitaskers” performed worse on a test of task-switching ability, possibly because their ability to ignore irrelevant stimuli was impaired.<sup>3-4</sup> The findings so far from early childhood to adolescents emphasize the need to assess the effects of the ever-increasing use of digital media on cognitive function and brain activity in children, adolescents, and young adults.

### Excessive Smartphone Use in Young Adults

#### Predictors of Excessive Smartphone Use:

Studies have shown that the main predictors of excessive smartphones are female gender, preoccupation, conflict, and constant use; protective factors include the use of

smartphones for learning.<sup>5</sup> An application that measures daily smartphone use has indicated that frequency of non-use, duration of use, and an average of all parameters may significantly predict problematic smartphone use.<sup>6</sup> A study of Korean adolescents revealed that impairment in family function and relationships with friends, impulsiveness, and low self-esteem were key contributors to excessive smartphone use.<sup>7</sup> Investigators have suggested that intervention programs (e.g., family communication programs) may help control this disorder.

### Comorbidity With Anxiety, Depression, Obsessive-Compulsive Disorder, Attention-Deficit/Hyperactivity Disorder, and Alcohol-Use Disorder:

Research has shown a relationship between excessive smartphone use and depression, anxiety, poor quality sleep,<sup>8</sup> and social anxiety.<sup>9</sup> The relationship with social anxiety is indicated by addiction to social networking, shyness, and low self-esteem.<sup>10</sup> Turgman and colleagues<sup>9</sup> also investigated the interaction between abstinence and sensation-seeking and compared this interaction with excessive smartphone use among university students. The sample was divided into two groups: one consisting of 30 participants who had been abstinent from smartphone use for 1.5 h and the other consisting of 30 participants had not been abstinent. The investigators reported that abstinence was followed by an increase in the excessive use of smartphones by individuals who had been identified as high sensation-seekers. This interaction may be explained by boredom, an attempt to avoid uncomfortable situations, and the need for entertainment.<sup>10</sup> Easy access to the internet on the smartphone allows the user to easily send messages, play games, download information, and participate in social network interactions; when it is temporarily unavailable, the sense of boredom, the need for entertainment, and fear of missing out may be exacerbated.<sup>11</sup> Indeed, there is evidence that young individuals exhibiting excessive smartphone use have high scores of boredom, sensation-seeking, and extensive use of a wide range of smartphone applications.<sup>12</sup> An important ingredient in sensation-seeking is susceptibility to boredom.<sup>13</sup> An experiment conducted by Ben Yehuda and colleagues,<sup>14</sup> investigated the effects of involvement and interest on excessive smartphone use among university students under three conditions: boredom, involvement in passive activity, and active participation in an activity. The



investigators found (1) a correlation between the frequency of smartphone use and internet addiction, and (2) excessive smartphone use was not influenced by the level of interest or involvement in the lecture. Thus, the overall level of internet addiction or disposition toward sensation-seeking was more likely to contribute to excessive smartphone use than an interest in the activity on the phone itself.

In a study of Lebanese undergraduate students, investigators found that a score indicating depression and anxiety was an independent predictor of excessive smartphone use after adjustment for confounders such as age, personality, and socio-economic status.<sup>15</sup> In a Korean study (n = 4854), researchers also found that depression and anxiety were associated with excessive smartphone use.<sup>16</sup> A similar but negative correlation between excessive smartphone use and psychological well-being was identified in students in Thailand.<sup>17</sup> In a 2017 study based on the *Korean Youth Risk Behavior Survey*, which was used to analyze mental health problems in 54,603 adolescents (26,930 male and 27,673 female), excessive smartphone use correlated with reduced cognitive control during emotional processing in the brain and a reduction in lateral orbitofrontal *gray matter volume* (GMV), especially with the overuse of social networking platforms. A significant negative association between excessive smartphone use and both GMV and activity in the *anterior cingulate cortex* (ACC) was found. Prolonged bedtime smartphone use has been associated with altered insula-centered functional connectivity.<sup>18</sup> The risk for depression symptoms, suicidal thoughts, and suicide attempts tends to increase as the duration of smartphone use increases after analysis of covariance has used conflicts with family members or peers or disturbances in school work as covariates.

An analysis of the 2017 *Korea Youth Risk Behavior Web-Based Survey* of middle- and high-school students (n = 62,276) demonstrated that depressive mood and suicidal ideation were associated with social network smartphone use that resembled addiction (e.g., overuse) and the adverse consequences of addiction.<sup>19</sup> Interestingly, excessive smartphone use predicted increased stress for those who engage in little online self-disclosure but reduced the sense of loneliness and stress among those who communicate their feelings, anxieties, and problems online.<sup>20</sup>

**Excessive smartphone use is associated with symptoms of *obsessive-compulsive disorder* (OCD)<sup>21</sup> and *attention-deficit/hyperactivity disorder* (ADHD).<sup>22</sup>**

In a study of 4512 middle- and high-school students in South Korea, investigators found that the odds of finding ADHD in individuals with excessive smartphone use were 6.43—the highest among all variables.<sup>23</sup> A family history of alcoholism and the father's level of education also helped explain 26% of the variance in problematic smartphone use for 100 undergraduates.<sup>23</sup> In a more extensive study (n = 31,425), problematic smartphone use was associated with a lower grade point average, symptoms of *alcohol use disorder* (AUD), and impulsivity (based on the Barratt scale score and symptoms of ADHD), as well as an increase in *posttraumatic stress syndrome* (PTSD), anxiety, depression, and enhanced social activity.<sup>24</sup>

*In summary*, the effects of excessive smartphone use are similar to those of an internet or gaming disorder, in that they are often comorbid with depression, loneliness, anxiety (including social anxiety), OCD, ADHD, and AUD.

## Insecure Attachment vs Poor Cognitive-Emotional Regulation and Communication

Studies have revealed that an insecure attachment style correlated with problematic smartphone use in students<sup>25</sup> with a dysfunctional family but not with students whose family life was characterized by mother-infant bonding or good maternal mental health.<sup>26</sup> Spanish investigators also found that problematic adolescent smartphone users demonstrate maladaptive *cognitive-emotion regulation*.<sup>27</sup> These users had higher scores for all maladaptive cognitive-emotion strategies, including self-blame, rumination, and catastrophizing, as well as a greater tendency to blame others. These strategies suggest the types of interventions that may be needed for relevant targets. In another study from Spain, experiential avoidance—which is defined as an attempt to avoid thoughts, feelings, memories, physical sensations, and other internal experiences, even when doing so causes harm in the long-run—was associated with excessive smartphone use and social networking in 1176 participants.<sup>28</sup> Worry and anger were frequently reported by severely problematic American college student smartphone users.<sup>29</sup> The authors of the study in which that finding was identified argued that their findings could be explained in terms of use and gratification, as well as by the compensatory internet use theory. Excessive

reassurance-seeking behavior appeared to mediate the relationship between rumination and problematic smartphone use by college students in China.<sup>30</sup> In adolescents in Turkey, emotional maltreatment during childhood was both directly and indirectly associated with problematic smartphone use, as well as body image dissatisfaction, depression, and social anxiety.<sup>31</sup>

Problems with interpersonal relationships were indicated by a preference to communicate emotions through texting rather than through verbal communication by medical students in Pakistan.<sup>32</sup> Celikkalp and colleagues reported a weak negative correlation between communication skills and excessive smartphone use in Turkey.<sup>33</sup> Finally, in a study of 111 US adolescents, emotion regulation difficulties, unregulated eating, restrained eating, food addiction, and a higher percentage of body fat were associated with excessive smartphone use.<sup>34</sup> Furthermore, emotion regulation difficulties mediated the relationship between excessive smartphone use and unregulated eating, restrained eating, and food addiction. These findings imply that excessive smartphone use may increase the risk of abnormal eating behaviors and food addiction through the challenge of regulating emotions.

*In summary*, excessive smartphone use has been associated with difficulty in cognitive-emotion regulation, as well as worry, anger, and excessive reassurance-seeking behavior, all of which can result in poor communication and low self-esteem.

## Impaired Cognitive Function

Inadequate inhibitory control mechanisms have been reported for excessive smartphone users.<sup>35</sup> Researchers have used a modified Go/No-Go task within three contexts (blank, neutral, and smartphone-related) and electrophysiological *event-related potentials* (ERPs) to investigate this issue. The No-Go N2, an ERP component associated with inhibitory control, had more negative results in excessive smartphone users than in the control group. This finding suggests that in the early stage of inhibition processing, excessive smartphone users experience more conflicts and show a general deficit independent of smartphone-related cues. Hadar and colleagues reported impaired attention, reduced numerical processing capacity, and changes in social cognition.<sup>36</sup> They compared participants lacking previous experience with smartphones with heavy

smartphone users based on behavioral and electrophysiological measures recorded by electroencephalogram combined with *transcranial magnetic stimulation* (TMS) over the *right prefrontal cortex* (rPFC). Heavy smartphone users showed an increase in impulsivity, hyperactivity, and negative social concern. Early TMS-evoked potentials were reduced in the rPFC in this group, which correlated with the severity of self-reported inattention problems. Heavy users also demonstrated less accuracy in numerical processing than nonusers. A second experiment, which included a longitudinal intervention, was carried out in a randomly selected sample of the original nonusers who received smartphones to use over 3 months and a control group that did not receive smartphones. The investigators found that both numerical processing and social cognition domains were causally linked to smartphone use, changes in social cognition, and reduced rPFC excitability.

*In summary*, heavy smartphone use appears to lead to impaired inhibitory control mechanisms, a reduction in numerical processing capacity, and changes in social cognition—all impairments that have not been seen before.

## Social Media Use, Personality Impulsivity, and Gambling

**Problematic social media use has been associated with a “fear of missing out” (FOMO).**<sup>37</sup> Furthermore, FOMO mediated a relationship between the fear of a negative and positive evaluation and both problematic and social smartphone use. Withdrawal and FOMO ratings were higher among participants with 72 hours of restricted access to smartphones compared with those without access to smartphones.<sup>38</sup> FOMO also predicted excessive smartphone use by female WhatsApp users.<sup>39</sup> The use of smartphones by American undergraduate students for social purposes was more strongly associated with the severity of problematic smartphone use and FOMO.<sup>40</sup> Furthermore, FOMO mediated a relationship between both depression and anxiety and the severity of problematic smartphone use, which suggested that individuals experiencing social anxiety who desire social contact are likely to use the smartphone for non-social purposes as an avoidance mechanism.

Relatively few studies have addressed the relationship between personality factors and excessive smartphone use. In one study (N = 640), personality factors—such

as low ratings of conscientiousness, openness, emotional stability, and high ratings of narcissism and neuroticism were associated with problematic smartphone use.<sup>41</sup> Eventually, impulsiveness, excessive reassurance-seeking, and depression (but not extraversion) were also associated with problematic smartphone use;<sup>42</sup> age and impulsiveness were identified as independent predictors of problematic smartphone use. Finally, smartphone gaming, coupled with frequent smartphone use, was associated with excessive smartphone use in a study of 880 adolescents in Taiwan.<sup>43</sup>

*In summary*, excessive smartphone use, especially when it involves social media, has been associated with FOMO and certain personality characteristics—specifically low conscientiousness, high openness, and low emotional stability, as well as high sensation-seeking and impulsivity.

## Reduced Sleep Quality, Physical Fitness, and Other Medical Considerations

Several studies have explored the effects of excessive smartphone use on sleep quality and duration in children and adolescents. In their study on the impact of smartphone overuse on sleep in children aged 5 to 8 years in Korea, Kim and colleagues<sup>4</sup> found that the total sleep time for those who used smartphones more than an hour daily was shorter than for the control group. Children in the smartphone overuse group had higher scores on the *Children's Sleep Habits Questionnaire* and on the nocturnal awakening subscale (a parental assessment instrument), which indicates a reduction in the quality of sleep. In a large study of adolescents (N = 362), sleep disturbances partially mediated the relationship between electronic media use in bed before sleep and symptoms of depression.<sup>45</sup> A negative correlation between electronic media use and sleep duration and a positive correlation with sleep difficulties were identified; these, in turn, appeared to be related to symptoms of depression. Sleep difficulties were more important than sleep duration in this regard. Dewi and colleagues provided further evidence of an association between nighttime smartphone use and symptoms of sleep disturbance and depression in adolescents.<sup>46</sup>

A major study of the relationship among changes in sleep-onset difficulties over time, physical activity, and

screen time in adolescents in 33 countries was carried out using data from the last four surveys of *Health Behavior in School-Aged Children*.<sup>47</sup> An increase in the prevalence of sleep-onset difficulties was associated with excessive screen-time exposure and a small but significant increase in physical activity. Adolescents who had more than 2 hours of screen time daily were 20% more likely to report sleep-onset difficulties compared with controls. Still, no relationship was found between sleep-onset difficulties and physical activity. The results of both studies suggest that effective strategies for reducing screen time are key to reversing the disturbing trend in sleep-onset difficulties among adolescents.

An analysis of data from a 2016 U.S. national survey of the caregivers of 43,755 children and adolescents aged 0 to 17 years revealed that children and adolescents who spent more time interacting with digital media slept fewer hours and were more likely than controls to have an insufficient amount of sleep.<sup>48</sup> The relationship between screen time and sleep duration primarily involved the use of portable electronic devices; this relationship remained significant when a diagnosis of anxiety or depression, physical activity, and excessive body mass index were included in the regression model. The results indicate that spending multiple hours each day using electronic devices is associated with shorter sleep duration across all ages, but portable electronic devices have a stronger association with sleep duration than nonportable electronic devices, particularly in children older than 10 years. This finding suggests that future interventions should target portable electronic devices while taking the age of the child into account.

Excessive use of smartphones by medical students in India was associated with poorer sleep quality and higher perceived stress.<sup>49</sup> Poor sleep quality was also reported by Chinese college students, particularly for the male gender, as well as for those who did not have good physical health or were experiencing headache or more severe depressive symptoms, as well as those with more than four years of smartphone use, more than five hours of daily smartphone use, and those with a severe inability to control cravings.<sup>50</sup> An assessment of physical activity among Chinese students in Korea has indicated that those at high risk for excessive smartphone use had less physical activity (as indicated by the total number of steps taken

and the average number of calories consumed each day)<sup>51</sup> and significantly different body composition (in terms of muscle mass and fat mass) compared with those who were not at risk. Excessive smartphone use may, therefore, negatively influence physical health by reducing the amount of physical activity and, consequently, increasing fat mass and a decreasing muscle mass, which can have adverse health consequences.<sup>51</sup>

Other medical conditions associated with excessive smartphone use include *acquired concomitant esotropia* (ACE, an inward turning of the eye); this was observed in 12 adolescents.<sup>52</sup> A higher prevalence of ocular symptoms has been reported for adolescents who have greater exposure to smartphones.<sup>5</sup>

Several studies have reported an association of smartphone use with headaches and migraines. Headache duration and frequency were higher among Turkish university students with a high rate of smartphone use.<sup>54</sup> In a major study of the French i-Share cohort (N = 4927), students with the longest screen-time exposure had an increased risk for migraine than students without headache and a shorter duration of screen-time exposure.<sup>55</sup> Smartphone use has also been associated with an increase in headache duration and frequency in patients with migraine,<sup>56</sup> as well as poor sleep quality and daytime sleepiness, and, thus, a decreased quality of life.

A study of 2438 young patients with chronic neck pain who underwent MRIs of the cervical spine showed that those with smartphone overuse had higher *Cervical Disc Degeneration Scale* scores.<sup>5</sup> Finally, a study of the effect of excessive smartphone use on the clinical and functional status of the hands (N = 120) revealed that the median cross-sectional area of the median nerve was larger in the dominant hand of excessive smartphone users.<sup>58</sup> Measures of excessive smartphone use correlated with subjective measures of pain during movement and at rest, as well as changes in pinch strength. These findings suggest that smartphone overuse enlarges the median nerve, causes pain in the thumb, and decreases pinch strength and hand function.<sup>58</sup>

*In summary*, there is evidence that excessive smartphone use is associated with sleep problems, reduced physical fitness, unhealthy eating habits, and other medical conditions, such as ACE, cervical disk degeneration, and migraine.

## Brain Imaging

A study of facial emotional processing in 25 excessive smartphone users that involved evaluations based on the Behavioral Inhibition System/Behavioral Activation System fMRI findings revealed neural deactivation in the dorsolateral PFC and in the dorsal ACC during the presentation of an angry face and emotional transition compared with controls.<sup>59</sup> Additionally, excessive smartphone use was associated with an increase in neural deactivation of the superior temporal sulcus and temporoparietal junction (which is related to social interaction during emotional transition) compared with controls. **The BAS reward responsiveness level correlated with behavioral responses during repeated exposure to happy faces, which was associated with emotional reward in the excessive smartphone use group compared with control participants. These findings suggest impairment in cognitive control during emotional processing that might be influenced by emotional processing related to social interactions.**<sup>59</sup> In a follow-up study, excessive smartphone users showed less functional connectivity between the right *orbitofrontal cortex* (OFC) and *nucleus accumbens* (NAcc) and between the left OFC and *mid-cingulate cortex* (MCC).<sup>60</sup> Moreover, functional connectivity between the MCC and NAcc was greater in excessive smartphone users. Severe withdrawal symptoms were associated with a higher cortisol concentration and had a negative correlation with OFC-NAcc connectivity. These findings suggest that adolescents with excessive smartphone use had reduced functional connectivity in regions of the brain related to cognitive control of emotional stimuli, including reward.<sup>60</sup>

The frontal cingulate GMV was smaller in the right lateral OFC in 39 problematic smartphone users.<sup>61</sup> There was also a negative correlation between GMV in the right lateral OFC and the *Smartphone Addiction Proneness Scale* (SAPS) score, including the SAPS tolerance subscale in excessive users. These findings suggest that abnormal lateral orbitofrontal gray matter may contribute to problematic smartphone use, especially during the overuse of social networking platforms. Individuals with excessive smartphone use showed a lower GMV in the left anterior insula, inferior temporal, and parahippocampal gyri.<sup>6</sup> Less



activity was reported in the right ACC in individuals with excessive smartphone use.<sup>62</sup> A negative correlation between excessive smartphone use and both GMV and activity in the ACC was also identified. Additionally, a significant negative association between excessive smartphone use scores and left orbitofrontal GMV was observed.<sup>62</sup> Prolonged bedtime smartphone use was associated with a higher SAPS score, but not with a change in sleep quality in adult smartphone users.<sup>63</sup> The strength of resting-state functional connectivity between the left insula and right putamen and between the right insula and left superior frontal, middle temporal, fusiform, inferior orbitofrontal gyrus, and right superior temporal gyrus on fMRI correlated with time spent on the smartphone in bed. These findings suggest that prolonged bedtime smartphone use can be a critical behavioral measure of problematic smartphone use and that altered insula-centered functional connectivity may be associated with it.

Finally, exposure to pictures of smartphones during fMRI appeared to activate the frontal operculum/anterior insula and precentral gyrus in active smartphone users.<sup>64</sup> Investigators also found a negative correlation between medial PFC, ACC, precuneus, and precentral gyrus activity and specific smartphone addiction scores on measures of compulsive behavior, functional impairment, and withdrawal. The results of this study suggest that there are similarities between the activation of smartphone use through exposure to smartphone images and the results of image exposure in other addictive disorders.<sup>64</sup>

In conclusion, excessive smartphone use appears to correlate with reduced cognitive control during emotional processing in the brain and reduced lateral orbitofrontal GMV, especially during the overuse of social networking platforms. A significant negative association was found between excessive smartphone use and both GMV and activity in the ACC. Prolonged bedtime smartphone use has been associated with altered insula-centered functional connectivity.

## Discussion

The potentially negative effects of excessive digital media use on children and adolescents raise serious concerns among healthcare and education professionals. Studies reviewed so far suggest that the more traditional method

of listening to stories facilitates activity in white matter tracts that mediate language development in preschool-aged children more efficiently than digital media. They also provide a grave warning that immersion in digital media makes the cortex thinner, resulting in “older brains.” Finally, the use of digital media typically involves multitasking. Although many people consider multitasking to be a virtue, many studies have shown that it impairs the ability to concentrate on a single task and perform it properly while ignoring irrelevant stimuli, which is cognitively highly disadvantageous.

Excessive mobile phone use is associated with potentially harmful behaviors such as loss of control over daily life activities and problems in relationships and work. Despite the view that excessive or problematic smartphone use is a behavioral addiction, recent reviews suggest that evidence of this is scarce. In particular, Billieux and colleagues have argued that there is a lack of studies that definitively show behavioral and neurobiological similarities between excessive smartphone use other addictive behaviors.<sup>65</sup> Panova and Carbonell also failed to find sufficient evidence that excessive smartphone use constitutes an addiction.<sup>66</sup> The behaviors observed during research into excessive smartphone use could be better labeled problematic or maladaptive rather than evidence of addiction.

Nevertheless, studies reviewed have consistently shown evidence of comorbidity of excessive smartphone use and psychiatric disorders such as depression, anxiety, OCD, and ADHD resembling that found by Weinstein and colleagues in adolescents and young adults diagnosed with internet addiction.<sup>67</sup> This similarity is not surprising, given the strong correlation between measures of internet addiction and excessive smartphone use found through these studies. Both conditions are characterized by the loss of cognitive and emotional control, which is associated with impairment in family function and relationships with friends, as well as with impulsiveness and low self-esteem. Other emotional factors included rumination, catastrophizing, blaming others, experiential avoidance, excessive reassurance-seeking, childhood emotional maltreatment, and difficulty regulating emotions. These may result in impaired emotional attachment and poor communication skills. These factors have also been associated with internet addiction, and the smartphone is a vehicle for internet use.

Excessive use of smartphones has also been associated with impaired inhibition, impaired attention, reduced numerical processing capacity, and changes in social cognition. Cognition and emotion are often intertwined; thus, it is not surprising to find the common cognitive-emotional mechanism resulting in the loss of cognitive-emotional control in excessive smartphone users. Research on impaired personality factors in excessive smartphone users is limited; currently, low scores of conscientiousness, openness, and emotional stability, and high scores of impulsivity and narcissism have been associated with problematic smartphone use. Evidence of internet addiction is mixed and is based on personality factors such as sensation-seeking, high harm avoidance, novelty-seeking, and low reward dependence.<sup>67</sup> Impulsivity and high sensation-seeking seem to be common to internet gaming and excessive smartphone use; indeed, young individuals with excessive smartphone use show high ratings for boredom, sensation-seeking, and impulsivity in their extensive use of the smartphone in a wide range of applications.<sup>9-10</sup>

Several studies have revealed evidence of sleep problems among excessive smartphone users, specifically a reduction in sleep quality rather than in the number of hours of sleep. The availability of digital media and their regular use before bedtime negatively affects the quality of sleep and the ability to disengage from such activity. **Reduced physical fitness, unhealthy eating habits, and other medical conditions—including ACE, cervical disk degeneration, hand pain, and migraine—have all been associated with excessive smartphone use.**

Few brain imaging studies have been conducted to compare the effects of excessive smartphone use with the effects of internet gaming.<sup>68</sup> Excessive smartphone use has been associated with reduced cognitive control during emotional processing in the brain. **A reduction in GMV was observed in the ACC of individuals with excessive smartphone use. This change was similar to that observed in individuals diagnosed with an internet or gaming disorder.**<sup>68</sup> The activation of smartphone

use through exposure to smartphone images occurs similarly to that seen with internet and gaming activities and other addictive disorders upon image exposure. A novel finding has been a reduction in lateral orbitofrontal gray matter, especially during the overuse of social networking platforms. Also, prolonged bedtime smartphone use has been associated with altered insula-centered functional connectivity.

One of the major limitations in studies of excessive smartphone use is that they are mainly cross-sectional studies without baseline measures, and they rely on the relationship between structural and functional changes in the brain and subjective measures. These relationships do not provide any proof that excessive smartphone use affects the development of the adolescent or adult brain. Factors that mediate such associations tend to be educational, cognitive, emotional, and social. Methodological considerations have included age (e.g., use by adolescents and students), culture (most studies were done in the Far East), and lack of comparison with substance use disorder. Finally, very few studies have considered differences in cognitive and brain function in excessive smartphone users between the sexes.

*In summary*, easy access to the smartphone enables users to send messages, play games, download information, and interact on social networks. Unfortunately, this can lead to excessive use and may have deleterious effects on mental and physical health, especially from childhood through early adulthood. Excessive smartphone use correlates strongly with internet addiction; hence, the cognitive, emotional, and social consequences of excessive smartphone use are similar to those of the more general construct of internet addiction. Personal characteristics unique to pre-sleep use of digital media to affect sleep quality include altered emotional communication patterns, a need for constant stimulation, and FOMO. These characteristics should signal an alarm to clinicians and educators to investigate excessive smartphone use as an underlying causative factor, particularly in this age group. ■

### *About the Faculty*

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## Multiple-Choice Questions

- 49. According to this lesson, excessive smartphone use is comorbid with the following psychiatric disorders?**
- A. Anxiety
  - B. Depression
  - C. ADHD
  - D. All of the above
- 50. Which of the following mechanisms is *not* associated with excessive smartphone use?**
- A. Reward
  - B. Cognitive emotion regulation
  - C. Excessive reassurance
  - D. Worry and anger
- 51. Which of the following medical conditions is *not* associated with excessive smartphone use?**
- A. Chest pain
  - B. Migraine
  - C. Thumb pain
  - D. Acquired concomitant esotropia
- 52. Participants with an internet gaming disorder have demonstrated lower gray matter density in which region of the brain?**
- A. Hippocampus
  - B. Cerebellum
  - C. Dorsolateral prefrontal cortex
  - D. Anterior cingulate cortex

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# Best Practices in Continuing Medical Education

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## The Association Between Excessive Use of Smartphones, Cognition, Emotion, and the Brain

By Aviv Weinstein, PhD

ID#: L003455

**This valuable take-home reference translates evidence-based, continuing medical education research and theory, acquired from reading the associated CME lesson, into a stepwise approach that reviews key learning points for easy assimilation into your armamentarium of knowledge practice.**

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### CME Lesson Overview

The information in this lesson will be helpful for medical students, general practitioners, pediatricians, and family physicians who are interested in current knowledge about excessive smartphone use. Knowing the effects of excessive smartphone use on cognitive and emotional function and brain activity can improve our ability to identify and understand the impact of this phenomenon.

#### **Key Point 1: The Effects of Excessive Digital Media Use in Children and Adolescents**

The findings of studies of the effects of excessive smartphone screen use in children and adolescents are summarized in this lesson to help the reader gain familiarity with the consequences of this practice on cognitive development and brain function.

#### **Key Point 2: Comorbidity With Anxiety, Depression, Obsessive-Compulsive Disorder, Attention-Deficit/Hyperactivity Disorder, And Alcohol Use Disorder**

Excessive smartphone use, similar to internet and gaming disorder, has been associated with comorbid conditions such as anxiety, depression, attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, and alcohol use disorder.

#### **Key Point 3: Insecure Attachment and Poor Cognitive-Emotional Regulation and Communication**

There is evidence of an association between excessive smartphone use and attachment and cognitive-emotion regulation. The reader should become familiar with the various cognitive-emotion mechanisms described herein and their clinical implications.

#### **Key Point 4: Cognitive and Personality Factors Affected by Excessive Smartphone Use**

Studies have assessed the cognitive impairments associated with excessive smartphone use. Several studies outline personality factors that are common to excessive smartphone users and individuals with internet gaming disorder.

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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### **Key Point 5: Medical Conditions Affected by Excessive Smartphone Use**

Excessive smartphone use is associated with sleep problems, ophthalmological disorders, pain, and reduced physical fitness.

### **Key Point 6: Brain Imaging Studies of Excessive Smartphone Use**

Several studies have shown an association between excessive smartphone use and changes in gray matter volume, functional connectivity, and cue reactivity in the brain.

# Pediatric Anger Management

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*This continuing medical education lesson was developed free of commercial support.  
Divalproex and lithium are discussed herein which are not approved medications by the FDA for managing anger in the pediatric population.*

**KEY WORDS:** Anger • Irritability • Adolescent anger • Aggression in children

**LEARNING OBJECTIVES:** Upon completion of this lesson, the clinician will be able to (1) describe pediatric anger and irritability, (2) discuss relevant abnormalities in brain structure and function, (3) identify clinical presentations of pediatric anger and irritability, (4) identify risk factors and potential sequelae of untreated conditions, and (5) discuss methods of assessment and treatment of pediatric anger and irritability.

**ABSTRACT:** This review highlights common presentations in the pediatric psychiatric population anger and irritability and discusses their possible origins and risk factors, as well as associated sequelae when they remain untreated. It also discusses underlying neurologic processes and treatment options.

**COMPETENCY STATEMENT:** This lesson addresses the management of irritability, anger, and the related concepts of aggression and frustration in children and adolescents. These are common and often nonspecific presentations in pediatric psychiatric clinics that lack a consistently clear diagnosis or treatment guidelines. Upon the conclusion of this lesson, clinicians will have gained knowledge of pediatric anger and irritability, associated abnormalities in brain structure and function, possible outcomes when untreated, and treatment options in the pediatric psychiatric population.

## Introduction

Pediatric anger and irritability are among the most common reasons children and adolescents are referred for psychiatric care. These symptoms comprise a critical component of the diagnosis of multiple internalizing and externalizing disorders. Irritability occurs on a continuum ranging from normal developmental behavioral outbursts to severe aggressive behavior. Children with chronic nonepisodic anger and irritability have a strong emotional sensitivity to negative events that is often accompanied by a manifestation of anger that is disproportionate to the situation and results in verbally or physically aggressive behaviors that are harmful to themselves, to others, or to property.<sup>1</sup> **Pediatric anger and irritability are predictors of poor psychiatric outcomes, an increased risk for depression, a decrease in overall functioning later in development, and increased psychosocial adversity.**<sup>2</sup> In children, high levels of outward anger expression have also been linked to medical illnesses, increased utilization of medical services, and a worsened health-related quality of life.<sup>3</sup>

The term “irritability” is often used to indicate an increased tendency toward anger, frequent outbursts of anger, and/or a tendency to be easily annoyed. The prevalence of irritability reported in the literature ranges from 3.3% in the *Great Smokey Mountains Study*<sup>4</sup> to 20% in the *Isle of Wight Study*.<sup>5</sup> Outbursts of irritability and anger are nonspecific symptoms. Irritability is observed in multiple mental health pathologies during childhood and adolescence, including neurodevelopmental, mood, anxiety, trauma- and stressor-related, and addictive disorders.

Population-based twin studies show substantial overlap between genetic and environmental factors that influence the risk for irritability and increase the risk of depression and anxiety in childhood.<sup>6</sup> The exhibition of anger and irritability in preschool-aged children, especially when accompanied by aggressive behavior, is often a marker for a poor prognosis. Specifically, it may serve as an early marker for more severe mental health problems and, therefore, is a signal for the need for early intervention. If anger or irritability is treated suboptimally during early childhood, the result could be a trajectory toward significant disruption of family dynamics by the time the child reaches adolescence.

Mental health professionals who are assigned the tasks of assessing and treating children who exhibit irritability and anger must determine the extent to which the behavior is developmentally appropriate and the extent to which it is caused by other factors, e.g., as a response to the psychosocial environment of the child. This lesson provides an overview of the presentation of irritability and anger in children and adolescents, the risks associated with nontreatment, and pharmacological and nonpharmacological treatment options.

## Defining Anger, Irritability, and Related Concepts

Anger and irritability are ubiquitous in mental health conditions. Differences in definition, measurement, and methodologies used to study each condition make it difficult to discuss their multivariate manifestations across multiple mental health conditions in children. Irritability is a mood state that has been defined as having a greater tendency to become angry than one's peers of the same developmental age.<sup>2,7</sup> It has also been described as “excessive reactivity to negative emotional stimuli... having an affective component, anger, and a behavioral component, aggression.”<sup>7</sup>

Spielberger and colleagues refer to anger as “a state of arousal due to threatening or frustrating social situations with associated cognitions and behaviors.”<sup>8</sup> The individual's response to anger, termed “anger expression,” is seen as anger directed inwardly or outwardly.<sup>9</sup> “Anger in” (the inward expression of anger) is experienced internally without overt manifestations; “anger out” is shown by aggressive or hostile behaviors or actions.<sup>9</sup> There is also a third expression of anger: “trait anger,” a dispositional form of anger that is stable over time and characterized by negative cognition and aggressive behaviors.<sup>10</sup> The expression of anger may increase in frequency and severity when it leads to the achievement of desired goals, effectively becoming adaptive and reinforcing.

Frustration is closely related to irritability and anger. It was defined by Perlman and colleagues as “the affective response to the prevention of goal attainment or the absence of expected reward” and often results in outbursts of anger.<sup>11</sup> Frustrative non-reward, a concept used throughout behavioral science literature, occurs when a previously available award is no longer attainable.

## Neuroscience of Irritability, Anger, and Frustration

**The amygdala and *prefrontal cortex* (PFC) are implicated in the regulation of emotion and behavior.**

Epigenetics a process that regulates gene expression has been linked to individual differences in irritability, and in the manifestation of anger and physical aggression.<sup>12</sup> This section discusses abnormal neural structures and functions associated with anger, irritability, and aggression in children and adolescents, touching on epigenetics related to these issues.

### Imaging Studies:

#### Irritability

Literature supporting the role of the amygdala in modulating emotion has revealed that irritable youth tend to respond to angry faces.<sup>13,14,15</sup> Irritable children are more likely than nonirritable children to interpret ambiguous or neutral faces as angry or threatening.<sup>16</sup> Such errors in processing threats may be due to the amygdala having difficulty modulating this response.<sup>17,22</sup> This suggests that irritability shares a pathophysiological link with internalizing disorders such as anxiety and depressive disorders.<sup>13</sup> Deficits in the ability to recognize emotion are associated cross-sectionally and longitudinally with depressive symptoms in children with severe irritability.<sup>18</sup>

Impairment in amygdala responses has also been demonstrated in *functional magnetic resonance imaging* (fMRI) studies. Thijssen and colleagues found a relationship between irritability and abnormalities in the amygdala, striatum, *anterior cingulate cortex* (ACC), and parietal lobe.<sup>19</sup> Aberrant white matter microstructure was also associated with irritability in children and adolescents.<sup>20</sup> Certain structures in the brain diminish in volume with normal maturation specifically the hippocampi, insula, and the medial orbitofrontal and cingulate cortices.<sup>21</sup> In a study of 151 adolescents, less volume contraction was observed in these structures in the more irritable individuals over the same period of development.<sup>21</sup> Interestingly, the internal capsule and putamen were smaller than expected in these individuals.<sup>21</sup>

Perlman and colleagues (2015) studied 26 children aged 6 to 9 years with clinically impairing irritability while they played a video game designed to induce frustration. As in previous reports from the literature, the authors

found decreased activation of the ACC and middle frontal gyrus in these children.<sup>11</sup> Having connections to the PFC and limbic systems, the ACC can influence the regulation of affect and emotions, including frustration. Neural imaging studies have also demonstrated increased activity in the posterior cingulate (an area of the brain that gives emotional salience to stimuli) in these children.<sup>29</sup>

In a similar study, Deveney and colleagues (2013) induced frustration through videogame feedback in 19 severely irritable children aged 8 to 17 years with severe mood dysregulation and 23 healthy controls and compared neural images taken in each group. The fMRI results showed reduced activation of the left amygdala and both the left and right striatum (an area responsible for processing positive and negative emotions) in subjects with severe mood dysregulation.<sup>22</sup>

#### Aggression

Aggression is heritable in humans, but its genetic origins have yet to be determined. Thijssen and colleagues demonstrated a relationship between aggressive behavior and abnormalities in the structure and function of the ACC, amygdala, dorsolateral PFC, orbitofrontal cortex, and hippocampus in children.<sup>19</sup> Imaging showed a reduced amygdala volume, thinning of the sensorimotor cortex, and decreased gyrification of the right hemisphere. There may also be a gender difference in childhood aggression, with girls demonstrating more cortical thickening around the dorsomedial nucleus in the thalamic than their male counterparts.<sup>19</sup>

### Physiologic Correlates:

#### Anger

The style of anger expression is a predictor of future childhood health.<sup>23</sup> Cardiovascular reactivity, in particular, an increase in both systolic and diastolic blood pressure, has been detected in children exhibiting anger-out expressions of anger, specifically angry speech,<sup>24</sup> and in aggressive children whose parents have a history of hypertension.<sup>25</sup> Anger-out expressions also predicted an increase in the number of medical visits, sleep disturbances, and externalizing and internalizing behaviors.<sup>24</sup> Anger-in expressions did not appear to influence any health outcome measures covered by Kidwell and Siegman,<sup>23,24</sup> but Oolop and colleagues<sup>26</sup> found that anger suppression a key feature

of anger-in expression correlated with factors that can predict future cardiovascular pathology, including an increase in glucose, cortisol, and blood pressure.<sup>26</sup>

## Aggression

Childhood aggression has been linked with physiologic underarousal or reactivity.<sup>27</sup> Schneider and colleagues found that aggressive children aged 7 to 13 years had an elevated heart rate at baseline and lower heart rate reactivity compared with controls.<sup>27</sup> Other studies have shown that autonomic reactivity in children with aggression may be modulated by anxiety.<sup>28</sup> For example, physically aggressive, nonanxious boys had autonomic underarousal, whereas physically aggressive anxious boys had elevated cardiac reactivity and increased muscle tension.<sup>28</sup> Adolescents who expressed more anger had significant difficulty regulating their anger; this, in turn, led to more aggressive symptoms.<sup>29</sup>

## Serotonin

Reduced serotonin levels have been associated with aggression;<sup>30</sup> this relationship has been confirmed through fMRI studies. In 2011, Passamonti and colleagues conducted the first fMRI-based study to demonstrate a relationship between low serotonin levels in the central nervous system and decreased communication between the amygdala and PFC, which resulted in impaired anger reactions and responses.<sup>31</sup>

## Dopamine

Dopamine has been associated with aggressive behavior in humans. Epigenetic studies of aggression have associated nongenetic risk factors with modification of the stress response and immune system. In a study of 984 parent-adolescent dyads, adolescents with a long dopamine receptor D4 variant were found to be more susceptible to proactive parental control of aggression.<sup>32</sup> Cecil and colleagues found support for the role of peripheral DRD4 methylation as a potential biomarker of physically aggressive behavior; however, evidence of a causal relationship has not yet been established.<sup>33</sup>

## Cortisol and Amylase

Interactions between the *hypothalamic-pituitary-adrenal* (HPA) axis and the *sympathetic nervous system* (SNS)

have been associated with adolescent aggression. While monitoring HPA cortisol levels and SNS alpha-amylase activity, Gordis and colleagues (2005) found an association between an increase in aggressive adolescent behavior and low cortisol and alpha-amylase levels. They also found that an increase in alpha-amylase levels did not increase aggressive adolescent behavior.<sup>34</sup> Thus, the authors hypothesized that alpha-amylase and the SNS might protect against aggressive adolescent behavior. Similarly, McBurnett and colleagues (2000) reported an association between low cortisol levels (within a limited range) in male children aged 7 to 12 years and a diagnosis of early-onset aggression. Low cortisol levels had a stronger relationship with early-onset aggression than a single low cortisol value.<sup>35</sup>

## Clinical Presentation

The expression of irritability varies with the developmental stage and age of the child. It may be nonpathological (e.g., toddler tantrums or adolescent irritability). Reports of the prevalence of more severe and impairing irritability in children have been inconsistent, however, ranging from 3.8% of children aged 4 to 16 years<sup>2</sup> to 5% to 6% for subjects aged 8 to 19 years<sup>2,36</sup> to 20% of adolescents in the *Isle of Wight Study*.<sup>4,5</sup>

**Irritability or anger may be a sign of psychopathology when it is disproportionate to a given situation or to developmental or chronologic expectations. These symptoms are seen across multiple psychiatric diagnoses.** These are among the most common reasons for psychiatric referrals of children by parents and teachers. They may be the basis for multiple diagnoses or none specifically. For example, anger/irritability is a key feature in childhood *major depressive disorder* (MDD), *intermittent explosive disorder*, *oppositional defiant disorder* (ODD), *conduct disorder* (CD), *disruptive mood dysregulation disorder* (DMDD), *bipolar disorder* (BD), and *borderline personality disorder* (BPD). It is also a manifestation of *autism spectrum disorder* (ASD), *attention-deficit/hyperactivity disorder* (ADHD), *adjustment disorder*, *posttraumatic stress disorder* (PTSD), *Tourette's syndrome*, *intellectual developmental disability*, *premenstrual dysphoric disorder*, and *substance use and dependence*, among other diagnoses, and can also be a symptom of childhood abuse.



Given this, a thorough workup and assessment are imperative. A complete evaluation should include collateral gathered directly from the child as well as from caregivers and teachers. It is also important to note that children typically underreport externalizing symptoms but provide more accurate information about internalized symptoms. By contrast, caregivers and teachers typically report more externalizing symptoms and underreport internalizing symptoms.

## Risk Factors for Elevated Anger and Irritability

A comprehensive review by Mahon and colleagues (2010) produced nine predictors of adolescent anger. Trait anger, a personal history of depression and anxiety, exposure to violence, and stress were associated with the largest effect sizes. Moderate to low effect sizes were seen in children who were hostile and had experienced violence, had low self-esteem, and had poor social support. Age, race/ethnicity, and gender had the smallest effect sizes.<sup>37</sup>

Compared with healthy controls, children with anxiety often have significantly higher levels of irritability.<sup>38</sup> They often present with more severe symptoms and functional impairment across various psychosocial domains.<sup>38</sup> Symptoms of anxiety and irritability often accompany ADHD in children, and ADHD, in turn, is also commonly associated with irritability.<sup>38</sup> Irritability is also a symptom of ODD (a frequent ADHD comorbidity) and seems to be related to internalizing disorders such as anxiety. Maire found that emotional lability is a significant predictor of the severity of hyperactivity, whereas irritability is the most significant predictor of the severity of anxiety and oppositional symptoms.<sup>39</sup> Reduced sleep quality has also been associated with increased irritability and reactive aggression in children.<sup>40</sup> Disturbances in both sleep and circadian rhythm contribute to irritability and behavioral difficulties in children with autism.<sup>41</sup>

Poor emotional support is associated with lower *socioeconomic status* (SES), and members of lower SES households tend to have poorer understanding of emotions and poorer anger management skills than higher SES households.<sup>42</sup> **With the increased risk of exposure to conflict and expression of negative emotion in SES households, children living in such households are at risk of developing impairing anger and poor anger**

**management.**<sup>43</sup> In such circumstances, the adolescent's negative perceptions of the home and family environment increases the risk of developing externalized behaviors and having a diagnosis of depression and anxiety, which are themselves implicated as risk factors for severe anger and irritability.<sup>44</sup> One study revealed a statistically significant difference in home-associated anger/irritability scores for white male and female adolescents compared with African-American and LatinX males.<sup>45</sup> In the same study, a strong correlation between attitude toward the home environment and anger/irritability score was identified for African-American and white female adolescents, which suggests an increased risk for anger and irritability in females of these ethnicities given similar home environments.<sup>64</sup>

Shipman and Zeman observed a relationship between the anger management skills of mothers and those of their children. Specifically, they found that children who had been physically maltreated by their mothers demonstrated a limited range of affect and expression of anger and, as with their mothers, poor anger management skills.<sup>46</sup> Further investigation of the relationship between maternal anger management and pediatric anger revealed that the children of mothers with effective anger management skills were more effective in regulating affect independent of a personal history of physical maltreatment.<sup>46</sup> The response of parents to the child's anger is another important factor in the development of anger in children. **Children whose anger was met with a negative response by their caregivers, (e.g., with anger, belligerence, punishment, or criticism) were as much as four times more likely to exhibit severe anger than their counterparts whose feelings were validated by their caregivers.**<sup>47,48</sup>

Certain parenting styles are also risk factors for the development of severe pediatric anger. The low demand and high responsiveness characteristic of permissive parenting provide few rules, little discipline, and low behavioral expectations of children, who are regarded as equals to their parents. With permissive parenting, the child's behavior is rarely restricted, and poor behaviors are tolerated as children make their own behavioral decisions. Such parenting results in externalizing behaviors, particularly in boys,<sup>49</sup> and can lead to the onset and maintenance of ODD and CD. Similarly, the excessive scolding, corporal punishment, and authoritarian nature

of nonpermissive parenting a style of parenting in which children are expected to follow the rules without discussion or compromise are associated with more negative and aggressive behaviors by children who fail to learn how to manage these feelings.<sup>50,51</sup>

Studies of gender differences in the development of externalizing behaviors conducted by Hosokawa and Katsura (2019) and Chaplin and Aldao (2013) revealed that boys are more prone to expressing anger than girls, particularly outward anger. They also found that boys are more likely to express anger when alone or with their peers from early through middle childhood.<sup>52</sup> Only during adolescence did girls externalize their negative emotions more than their male counterparts.

Finally, the school environment poses an increased risk for anger and irritability in children within the context of negative peer influences, lack of attachment with school staff and teachers, low educational achievement, and cognitive/learning difficulties. Studies have shown this to be particularly evident with females.<sup>45</sup> Conversely, a positive school environment can mitigate or reverse the risk for poor anger management that is associated with a negative home environment. The relationship between scholastic performance, feelings toward school and behaviors in school and anger/irritability scores for African-Americans, whites, and Latinx individuals was significant, but there was no significant difference among females in these ethnic groups. Latinx students were at a slightly higher risk for anger/irritability at school than white males; this finding was hypothesized to be related to cultural and language barriers encountered at school.<sup>45</sup>

## Potential Outcomes of Untreated Anger Expression

Untreated anger-out expression is a risk for sleep pathology, increased medical visits, externalizing and internalizing behaviors, and increased cardiovascular reactivity levels, such as increased blood pressure.<sup>23,24</sup> Unmanaged anger may also result in social difficulties associated with aggressive and bullying behaviors and school-based violence.<sup>53</sup> Children who witness bullying behaviors in the home are more likely to demonstrate similar behaviors at school. Further, those with unregulated externalized anger are at risk for lower social achievement, legal issues,

conduct behaviors such as property damage, and relationship difficulties in the workplace as adults.<sup>54,55</sup>

Finally, externalized expression of anger, particularly when it takes the form of aggression toward another and/or behaviors resulting in school consequences, is a predictor of early initiation of substance use.<sup>56</sup> Substance use by children and adolescents is a risk factor for substance dependence during adulthood. A diagnosis of PTSD, a familial history of substance use, a personal history of physical or sexual assault, and/or witnessing violence increases the risk of illicit substance use by adolescents.

### Academic:

Unmanaged anger expression and irritability increases the risk of repeating a grade, experiencing academic difficulties, and/or dropping out of school.<sup>55</sup> This may lead to poor academic performance and poor interpersonal relationships, thereby creating a negative feedback loop with peers and teachers.

## Assessment and Treatment

**A thorough biopsychosocial clinical evaluation is imperative for the diagnosis and treatment of anger and irritability in children, given that these symptoms range from developmentally normal to impairing and pathological and may fit multiple physical, medical, and psychiatric diagnoses.** Irritability is a criterion for several child mental health conditions, including DMDD, MDD, generalized anxiety disorder, ODD, adjustment disorder, acute stress disorder, and PTSD. Irritable mood may also accompany ASD. Irritability, even when not a specific criterion for certain conditions, often occurs in children with ADHD and addictive disorders.

Determining the symptomatic threshold may help to distinguish normative misbehavior, subthreshold symptoms, and syndromic levels of symptoms accompanied by functional impairment. Identifying antecedents to the behavior is often a key to understanding the child's reasons for outbursts or the deficits that result in outbursts. Identifying the positive and negative consequences of the behavior often helps the clinician understand the factors that reinforce or discourage the behaviors or outbursts. Noting the number and severity of irritable mood or behavior outbursts at baseline and monitoring

this through treatment may help indicate the direction of treatment response, particularly in children with high symptom levels. It is particularly important to assess children with irritability for suicidality, because irritability is associated with suicide-related outcomes and is a risk factor for suicide-related outcomes, including suicidal ideation, attempt, and mortality.<sup>57,58</sup> Table 1 outlines clinical instruments that can be used to facilitate the assessment of these patients and may help guide the clinical evaluation and diagnosis. Although medications are effective against severe anger and irritability, behavioral therapy is often the first-line treatment option. Figure 1 contains an overview of the biopsychosocial management of pediatric anger and irritability.

### Psychosocial Interventions:

First-line treatment of anger and irritability in children and adolescents is multimodal in nature and includes discussion, role play, modeling, and practice.<sup>53</sup> The goals of psychosocial interventions are to promote prosocial

behaviors and improve adaptive coping skills for the child faced with frustration. This section discusses therapeutic interventions for severe anger and irritability in children, including individual, family, parent-based, school, and community-based programs.

### Cognitive-Behavioral Therapy

Most anger treatment outcome studies follow a multimodal, *cognitive-behavioral treatment* (CBT) approach<sup>23</sup> intending to teach children how to identify anger triggers and use cognitive reframing to manage anger responses. Techniques may include relaxation training, including role-play and imagery.

CBT sessions directly involve the child and therapist; parents facilitate the treatment by providing the therapist information about behaviors occurring at home and by encouraging their child to practice learned skills at home. Various *randomized control trials* (RCTs) support CBT approaches to disruptive behaviors.<sup>59-61</sup>

**Table 1:**  
**Instruments for Assessing Irritability**

| Type of Instrument       | Name of Instrument  | Rater                     | Advantages  |
|--------------------------|---|---------------------------|---|
| Questionnaire            | Affective Reactivity Index (ARI)                                      | Self, parent, and teacher | Short by design and good reliability/validity   |
| Questionnaire            | Multidimensional Assessment of Preschool Disruptive Behavior (MAP-DB) | Parent and teacher        | More comprehensive than ARI and covers a broad range of behaviors                         |
| Questionnaire            | Retrospective-Modified Overt Aggression Scale (R-MOAS)                | Parent                    | Good internal consistency and more focused on aggressive behaviors                        |
| Semistructured Interview | Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS)    | Interviewer               | Relies on answers to interview questions rather than only observations                    |
| Structured Interview     | DMDD Module of the Development and Wellbeing Assessment (DAWBA)       | Parent                    | Set up for online completion and provides space for open-ended comments by the respondent |

### Anger Control Training

*Anger control training* (ACT) is a form of CBT that targets emotion regulation and social cognitive deficits associated with aggression. Supported by multiple RCTs for its efficacy in managing disruptive behaviors such as

anger outbursts, aggression, and noncompliance across various diagnoses, **ACT is used to identify internal and external anger triggers by using self-affirmations and coping skills, such as deep breathing and imagery to manage anger, and self-evaluations with rewards for successful anger management.**

## Social Skills Training

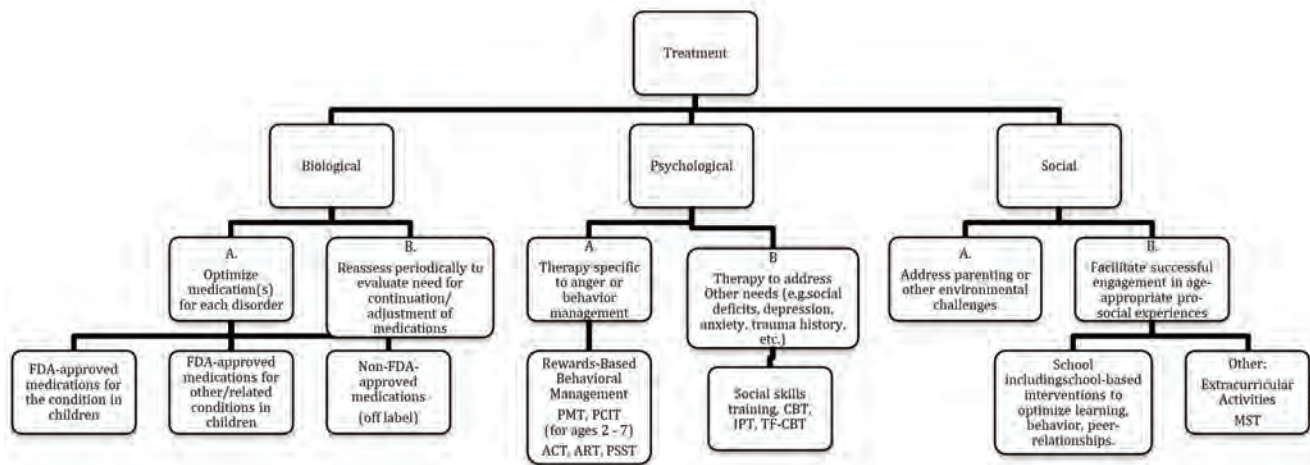
Poor verbal, social, and conflict resolution skills are associated with anger and irritability in children. Social skills training focuses on improving social competence and reducing negative social interactions. Behaviors taught with such training range from basic to advanced skills that include conversation skills, learning to apologize, asking for help, learning to express feelings, finding alternative

responses to anger, developing coping skills, and practicing setting goals and decision making.

## Problem-Solving Skills Training

The goal of problem-solving skills training is to help the child understand the consequences of one's actions by examining interpersonal conflicts and developing alternative solutions to avoid engaging in aggressive behaviors.

**Figure 1:**  
**Overview of Biopsychosocial Management of Pediatric Anger and Irritability**



## Rewards-Based Behavioral Management

Commonly referred to as a “token system,” rewards-based behavioral management allows the patient to earn tokens that can be traded for desired rewards or are returned for undesired behaviors. The child should earn more than is returned to maintain engagement and motivation for behavioral change. Younger children exchange earned tokens throughout the day; older children, based on their ability to maintain motivation and tolerate delayed gratification, earn smaller daily rewards, and await larger rewards at the end of the week.

## Parent Management Training and Parent-Child Interaction Therapy

Behavioral improvements can mitigate or even prevent future antisocial behaviors. *Parent management training* (PMT) and *parent-child interaction therapy* (PCIT) focus on parental management of maladaptive behaviors in their children. PMT therapists use positive reinforcement and operant conditioning framework to teach parents skills to manage their children's problematic behaviors. Parents are taught how to recognize problematic behaviors, how to praise desired behaviors, and how to provide consistent consequences for undesired behaviors.



For children aged 2 to 7 years, PCIT involves the parent-child dyad and focuses on fostering positive parent-child interactions. Its goal is to reduce disruptive behaviors by teaching children effective methods of managing frustration and anger and providing parents real-time feedback via observations made through a one-way mirror during interactions with their children. Feedback focuses on strengthening the parent-child relationship by creating positive interactions, practicing consistent limit-setting, and using appropriate and consistent forms of discipline.

The effectiveness of parent training programs has not been studied in RCTs. In meta-analytic reviews, however, investigators found a larger effect using programs that emphasize parents practicing learned behavior management skills. A larger effect was seen using programs that focus on promoting positive parent-child interactions, improving emotional communication skills, and emphasizing the importance of providing consistent consequences for undesired behaviors.<sup>62</sup>

## **Community-Based Interventions:**

### ***Multisystemic Therapy***

*Multisystemic therapy* (MST) is a wraparound intervention for at-risk children that involves the family and surrounding community including schools, peers, and neighborhood systems to address the multifactorial nature of risk factors for problematic behaviors. Studies demonstrate that family functioning improves and mental health problems decrease in children with severe conduct problems when the MST approach is used.<sup>63</sup>

### ***Aggressive Replacement Training***

*Aggressive replacement training* (ART) is a multimodal treatment program designed to help children replace angry/aggressive behaviors with more desirable, prosocial behaviors. ART encourages the development of prosocial behaviors by helping children build moral reasoning skills and reduce impulsivity and antisocial behaviors.<sup>64</sup> A significant reduction in aggressive behaviors and impulsivity and significant improvement in self-esteem, coping, social skills, and positive thought processes have been demonstrated in adolescents participating in ART.<sup>64</sup>

## **School-Based Interventions**

School-based interventions vary in content and implementation, although most use a cognitive, behavioral, social, and counseling framework for the general student body (universal programs) or for selected students (targeted programs).<sup>65</sup> The greatest effects were seen with behaviorally based interventions.<sup>65</sup> A meta-analysis assessing school-based interventions that targeted aggressive, disruptive behaviors found a statistically significant relationship between aggressive, disruptive behaviors by students in the general school population exposed to universal programs and in students with preexisting problematic behaviors who had been selected for targeted programs. This suggests that either universal or targeted programs implemented in a school environment may garner positive results and that a more important factor may be well implemented programs with consistent student exposure.

## **Pharmacological Treatments:**

Ideally, the decision to use pharmacological agents should be made after psychosocial interventions alone have not resolved the problem. Nevertheless, there are situations in which the symptoms affect functioning significantly or are causing concern for imminent danger. In such cases, it may be wise to switch to pharmacological agents sooner rather than later. The decision to use pharmacological agents in children with symptoms of irritability or anger should be based on criteria for disorders characterized by clear target symptoms. With this approach, single agents should be used to avoid the dangers of polypharmacy and, thus, reduce the risk of their adverse effects. The goal is to treat the child appropriately by addressing the root cause of his/her anger or irritability. Polypharmacy should be avoided in this patient population because of the risk of the child being overmedicated yet undertreated. Failure to include psychotherapy with adequate behavior management interventions can also be considered a form of undertreatment. Combination pharmacotherapy is warranted, however, in some children with severe or resistant symptoms. Several agents effectively treat anger and irritability in children; these are discussed later in this section. The reasons for prescribing off-label medication should be weighed carefully. A safer stepwise approach

is, to begin with medications that have been approved by the U.S. *Food and Drug Administration* (FDA) for children with this disorder, then adding other medications for related disorders in children. These steps should be taken before considering medications that have not been approved by the FDA for children with any disorder (see Figure 1).

### Alpha Agonists

The noradrenergic system is associated with arousal, irritability, and hostility. Alpha agonists can reduce adrenergic tone and, thus, can be effective against pediatric hyperarousal, including hyperactivity, anger, aggression, and irritability (as is seen in patients with ADHD or PTSD). The alpha agonists, clonidine and guanfacine, improve functioning in the PFC associated with executive functioning, mood, and behavior regulation. Their extended-release formulations of these agents have been approved by the FDA specifically as monotherapy in patients with childhood ADHD, which is associated with anger/agitation/aggression/ irritability, and as adjuncts to stimulant therapy.

### Stimulants

Mood lability occurs in children with ADHD at 10 times the rate as in the general population.<sup>66</sup> Stimulants are associated with a high irritability response rate in children with ADHD. Meticulous titration of stimulant medication and concurrent behavioral therapy may avert the need for additional medications. In children with aggressive behavior within the context of ADHD, ODD, or CD, a systematic, closely-monitored titration and optimization of stimulant therapy often reduces aggression and, consequently, the need for additional agents.<sup>67</sup> **Multiple studies have demonstrated that stimulant monotherapy, with or without behavioral management, is more effective than behavioral management alone at reducing core symptoms of ADHD, including symptoms of comorbid ODD, aggressive behavior, and temper outbursts.**<sup>66,68</sup>

### Selective-Serotonin Reuptake Inhibitors

Low levels of serotonin in the CNS have been implicated in intense anger, irritability, and aggressive behavior.<sup>30</sup> **The FDA has approved fluoxetine and escitalopram**

**for pediatric depression, of which anger and/or irritability are core symptoms.** Towbin and colleagues completed the first RCT of an SSRI, citalopram, in the pediatric population, demonstrating the efficacy of citalopram against severe irritability in children aged 7 to 17 years whose symptoms were refractory to stimulant monotherapy.<sup>69</sup>

### Atypical Antipsychotics (Second-Generation Antipsychotics)

*Second-generation antipsychotics* (SGAs) such as risperidone and aripiprazole are routinely prescribed to manage anger, irritability, and aggression in the pediatric psychiatric population. The 5-HT<sub>2A</sub> antagonist activity of these SGAs makes them effective in managing anger/irritability/aggression associated with serotonin deficits. Risperidone has been shown to be effective in reducing aggressive behavior in children with CD.<sup>70</sup> Liquid risperidone was effective in shortening the duration of rage episodes, regardless of diagnosis.<sup>71</sup> Risperidone and aripiprazole are FDA-approved for irritability and aggression in pediatric ASD.<sup>72</sup> When they are used as adjuncts to stimulants in ADHD, however, the findings are varied, with some studies finding risperidone to be effective<sup>73</sup> and others showing no sustained benefit compared with basic treatment.<sup>74</sup> Given the side-effect profile of SGAs which includes weight gain, hyperprolactinemia, metabolic syndrome, and neuromuscular manifestations caution is warranted when prescribing drugs in this pharmacologic class. Consideration should first be given to behavioral therapy and/or other pharmacologic treatments with more benign side-effect profiles.

### Divalproex

Divalproex is used off-label against psychiatric mood lability across various diagnoses. Divalproex is helpful in children and adolescents with impulsive aggression and irritability,<sup>75</sup> explosive temper and mood lability,<sup>76</sup> and CD<sup>77</sup> and as an adjunct to stimulant monotherapy for chronic aggressive behavior refractory in children with ADHD.<sup>68</sup> Studies have shown that divalproex is effective in patient subpopulations with impulsive aggression and irritability,<sup>75</sup> including autism.<sup>78</sup> Given its side-effect profile, however, divalproex is not considered a first-line



treatment for patients with severe anger, irritability, or aggression.

### **Lithium**

Lithium has been used off-label for psychiatric mood lability. There is conflicting support for its use in the behavioral science literature, however. Malone and colleagues found that lithium decreased aggressive behavior in children with CD,<sup>79</sup> whereas, Dickstein and colleagues did not find a significant benefit for lithium versus placebo in reducing severe irritability in children with severe mood dysregulation.<sup>80</sup> In a limited group of studies, lithium provided benefits for irritability in patients with certain neurodevelopmental disorders, including Rett's syndrome,<sup>81</sup> fragile X syndrome,<sup>82</sup> and autism.<sup>83</sup> Similar to divalproex, however, its side-effect profile and narrow therapeutic range indicates that it should not be used as a first-line treatment for patients with severe anger, irritability, or aggression, and consideration should first be given to other treatment options.

### **Conclusion**

Pediatric anger and irritability are complex behaviors with presentations ranging from developmentally normal to pathological impairment. They are among the most common reasons for referral and presentation to child

psychiatry. **Untreated severe anger and irritability place children at risk for long-term sequelae, including substance use, poor social relationships, low academic achievement, and poorer social outcomes.** It can also result in health impairments due to sleep problems and increased blood pressure. Risk factors for impairing pediatric anger and irritability are multifactorial and include race, ethnicity, home environment, SES, gender, and age. Modifiable risk factors such as parenting style, manner of anger expression, school involvement and support, and validation or invalidation of the child's feelings may be targets for intervention in at-risk children or children already demonstrating problematic behaviors. They may also serve to help children build practical social-emotional skills and form healthy relationships with others.

Although multiple treatment options are available for children presenting with impairing anger and irritability (including both behavioral therapies and pharmacotherapies), it is important to remember to conduct a thorough assessment that involves the patient, caregiver(s), and systems closely involved with the child and involve these systems in the treatment. Depending on the child's symptomatology and diagnosis, a combination of pharmacological agents may be needed. In such cases, it is essential to avoid the pitfall of polypharmacy to prevent overmedication while undertreating the child. ■

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## Multiple-Choice Questions

**53. According to this lesson, the best approach to the management of pediatric anger or irritability is:**

- A. Adjusting parenting styles.
- B. Social approaches, such as adjustment of home and school environments.
- C. Biological approaches, such as targeted symptom reduction.
- D. Biopsychosocial management.

**54. Which two neural structures are highly involved in the regulation of emotions and behaviors?**

- A. Amygdala and prefrontal cortex
- B. Amygdala and hippocampus
- C. Hippocampus and prefrontal cortex
- D. Thalamus and amygdala

**55. Anger and irritability are considered signs of psychopathology:**

- A. When they are occasionally excessive.
- B. When they are disproportionate to a given situation, developmental stage, or chronological expectation.
- C. Only when they are associated with a psychiatric diagnosis.
- D. When they result in physical harm.

**56. All the following are risk factors for increased anger in children, *except*:**

- A. Physical maltreatment.
- B. Being in environment with high level of conflicts.
- C. Being cared for by parents with good coping strategies.
- D. Children whose anger was met with negative response.

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# Best Practices in Continuing Medical Education

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## Pediatric Anger Management

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ID#: L003456

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

Severe anger and irritability in children and adolescents are nonspecific yet important clinical presentations in pediatric psychiatry clinics. Their expression may range from normative development to pathologic and often fits across multiple psychiatric diagnoses. It is essential to understand and assess patients for risk factors for this presentation to help identify at-risk children as well as possible targets for intervention. Untreated severe anger and irritability are associated with such sequelae as subsequent socioeconomic, physical, and mental health impairments, including depression, anxiety, and substance use. A biopsychosocial framework is essential to understanding and selecting appropriate treatment for childhood anger and irritability, particularly because the risks associated with untreated anger and irritability follow children into adulthood, with long-term consequences.

### **Key Point 1: Child and Adolescent Irritability and Anger Are Some of the Commonest Reasons for Pediatric Psychiatric Presentations**

Irritability and anger, which vary by developmental stage and biological age, may be nonpathological (e.g., toddler tantrums or adolescent irritability). The current literature suggests that the prevalence of severe, impairing irritability in children ranges from 3.8% to 20% and is an indicator of poor health and psychosocial trajectories later in development. Severe irritability and anger in children may indicate psycho-

pathology when they are disproportionate to a given situation, developmental stage, or chronologic expectation. These symptoms present across multiple psychiatric diagnoses including (but not limited to) ADHD, PTSD, major depression, ODD, conduct disorder, disruptive mood dysregulation disorder, substance use, and autism spectrum disorder and may be symptoms of childhood abuse. Assessment requires a biopsychosocial approach involving the child, parent(s), and any other prominent caregivers or involved systems such as teachers and the school.

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## **Key Point 2: Risk Factors Associated with Severe Youth Anger and Irritability Are Multifactorial**

Risk factors predicting future anger and irritability are biopsychosocial and multivariate in nature. Some are biologic and nonmodifiable such as age, race, ethnicity, and gender; others are psychological (e.g., trait anger, hostility, low self-esteem, and personal history of depression and anxiety). Permissive and authoritarian parenting styles, the invalidation of a child's feelings, and maternal response to anger are also risk factors of severe childhood anger and irritability. It is vital to understand such fixed and modifiable risk factors to assess the child's level of risk and target areas for intervention.

## **Key Point 3: Untreated Anger May Result in Physical and Psychosocial Sequelae**

Children with untreated anger and irritability may experience adverse physical health outcomes, exhibit externalizing behaviors such as bullying others, internalizing behaviors, and a psychiatric diagnosis such as anxiety, depression, or suicidal ideation. They may also turn to illicit substance use at a relatively early age. As adults, they are at increased risk of lower social achievement, legal issues, conduct behaviors, and relationship difficulties in the workplace.

Further, outward anger expression, such as aggressive or hostile behaviors, is associated with reduced sleep quality, elevated systolic and diastolic blood pressures, and increased utilization of healthcare resources.

## **Key Point 4: A Biopsychosocial Approach to Treatment is Important With This Population**

A thorough assessment is needed to accurately diagnose and treat children with severe anger and irritability. Treatment should target the individual and include systems close to the child, such as the family and school. First-line treatment is a multimodal therapy that involves discussion, role-playing, modeling, and practice. Multiple cognitive-behavioral approaches include anger control training, social and problem-solving skills training, and rewards based behavioral management. Children with anger and irritability refractory to therapy alone should receive a combination of therapy and medications. Careful titration to determine the lowest effective dose and medication optimization will mitigate the risk of adverse effects and polypharmacy. During treatment, it is important to assess the child for behavioral improvement and/or decompensation, including the presence of possible thoughts of harm to self or others.

# Sports-Related Concussions in High School Athletes

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**KEY WORDS:** *Sports-related concussion* (SRC) • High school • Student athlete • Adolescent • Concussion • *traumatic brain injury* (TBI)

**LEARNING OBJECTIVES:** Upon completion of this lesson, clinicians will be able to (1) define a *sports-related concussion* (SRC); (2) describe the symptoms of concussion and discuss the mechanisms involved in concussion in adolescents; (3) describe the epidemiology of SRC, the risk and protective factors of SRC, and the reasons for the underreporting of SRC in high school students; and (4) identify the immediate and persistent mental health consequences of SRC.

**LESSON ABSTRACT:** Adolescence is a neurodevelopmental period that confers a great risk for the impact of concussions. Attention to factors related to concussions in high school athletes is pivotal to mitigating the risk and long-term effects of this injury. A *sports-related concussion* (SRC) is a significant cause of traumatic brain injury in this group. Although healthcare professionals are increasingly aware of the long-term impact of SRCs, including conditions such as chronic traumatic encephalopathy in professional athletes, the impact on nonprofessional and high school athletes is less researched. In this review, the authors provide an up-to-date synthesis of the available data regarding SRCs in high school students. Risk factors for SRCs in different high school sports are discussed, and the sequelae of SRCs, which encompass a spectrum of somatic and neuropsychiatric symptoms. SRC is associated with neurocognitive impairment, depression, anxiety, and behavioral changes. In some recent studies, SRC has been identified as a risk factor for suicide attempts and completion, as well as neurodegenerative conditions like chronic traumatic encephalopathy. Although there are physical, emotional, and psychological benefits to engaging in sporting activities in high school, understanding the factors associated with the SRCs that can occur in these activities is essential to effectively mitigate the associated risks and sequelae.

**COMPETENCY STATEMENT:** This lesson addresses gaps in learning, particularly among mental healthcare providers working with the pediatric patient population. Many healthcare providers are not fully aware of the occurrence and consequences of concussions in high school athletes. With limited information, providers are not cognizant of the factors involved and are therefore less equipped to advise patients and their caregivers on ways to minimize the risks, identify the symptoms and changes in behavior that can occur in young patients with SRCs, and take effective action to mitigate these factors. Furthermore, many providers are not well informed about the mental health risks, including the immediate and lingering mental health symptoms, nor about the longer-term impact of SRC on high school athletes. The authors suggest practice implications for clinicians to monitor the mental health sequelae of SRC and also recommend screening student athletes for a history of concussions as part of their medical history.

## Introduction

The extracurricular activities in which adolescents and high school students choose to participate can be influential in shaping their identities, behavior, life philosophies, and future achievement. Involvement in sports also provides a sense of belonging to a peer group, which is vital for healthy adolescent development.<sup>1</sup> Engagement in sporting activities promotes physical well-being. However, compared to nonathletic high school activities, high school athletics predisposes adolescents to a higher risk of sports-related injuries, including concussions.<sup>2</sup>

**Sports-related concussion (SRC), classified as a mild traumatic brain injury (TBI), is a significant neurological condition that involves complex pathophysiological processes affecting the brain, induced by biomechanical forces encountered during sporting activities.**<sup>3</sup> SRC is the second most common cause of head injuries in the adolescent age group after motor vehicle accidents,<sup>4</sup> accounting for up to 40% of TBI in adolescents.<sup>5</sup> The clinical incidence of SRCs for all sports is estimated to be about 2.36 per 100 student athletes,<sup>6</sup> and as many as 9.1% of high school students report having had a concussive experience in the preceding 12 months.<sup>7</sup>

The American Academy of Neurology describes concussions as “a clinical syndrome of biomechanically induced alteration of brain function, typically affecting memory and orientation, which may involve loss of consciousness.”<sup>8</sup> Generally, concussions occur when a blow to the head causes rapid “acceleration-deceleration” of an individual’s head, causing the brain to slam against the skull, stretching the neurons and causing neuronal dysfunction.<sup>9</sup> **This produces a wide variety of symptoms ranging from less severe signs such as altered awareness of surroundings, disorientation, headache, drowsiness, irritability, and light sensitivity to more severe symptoms such as loss of consciousness and amnesia.**<sup>10</sup>

Concussions can cause more subtle difficulties with daily neurocognitive functioning, including trouble focusing and problems with memory, concentration, learning, judgment, speech, and sleep.<sup>9,11</sup> These symptoms may occur in varying degrees in the patient. In general, concussions with higher severity of symptoms following the injury tend to last longer and manifest broader symptomatic profiles.<sup>12</sup> Similarly, the number

of concussions can affect the duration of the symptoms. Concussed high school student athletes with a history of three or more concussions take longer to recover than those with one or none.<sup>13</sup> As a result, affected athletes are sometimes advised to entirely forgo further engagement in competitive high-contact sports.

A subconcussion is a cranial impact that does not result in a known or diagnosed concussion based on clinical findings.<sup>14</sup> Following a subconcussion, an individual may have brain changes that are similar but less severe than with a concussion.<sup>14</sup> Although most sports-related head impacts do not result in a concussion, these subconcussive hits can affect brain structure, function, and performance.<sup>15,16,17</sup>

**Second impact syndrome occurs when two concussions occur within a relatively short time, and the second concussion is inflicted before the first has fully healed.** Although rare, studies support that the majority occur in high school athletes who play high-impact sports.<sup>18</sup> Having a concussion increases the risk of experiencing a second one, and the risk increases with each additional concussion.<sup>19</sup>

Post-concussion syndrome is a “constellation of sometimes disabling symptoms, mainly headache, dizziness, and trouble concentrating, in the days and weeks following a concussion.”<sup>20</sup> Risk factors for post-concussion syndrome include sex, high-contact sports, and a high number of symptoms experienced following the injury. Identifying students with post-concussion syndrome and avoiding a return to sporting activities is critical because a reinjury during this period results in poorer outcomes.<sup>21</sup>

*Chronic traumatic encephalopathy* (CTE) is “a progressive neurodegenerative syndrome caused by single, episodic, or repetitive blunt force impacts to the head and transfer of acceleration-deceleration forces to the brain.”<sup>22</sup> Clinical signs and symptoms of CTE include a progressive decline of memory and cognition, irritability, aggression, depression, heightened suicidality, and death, which may, in advanced forms, be preceded by dementia and parkinsonism.<sup>23</sup> CTE occurs in professional athletes with a history of repeated head impact exposure over years of playing contact or collision sports, with boxers, football players, hockey players, and wrestlers being at the highest risk.<sup>23</sup>

SRCs in high school students vary by sport, gender, and type of exposure. The immediate and long-term



effects of concussions can affect the students' cognitive performance and mental health with potential consequences for their future education and career paths.

## Mechanisms Involved in Concussions in Adolescents

The biomechanics of SRCs involve the interplay among the forces encountered during impact, head and neck movements, stiffness of the head and neck area, deformation and rebound of brain structures at the macroscopic and microscopic level, and the physiological responses to the various loading conditions imposed on the head. The biological responses may be anatomical or structural (e.g., disrupted vessels or neurons and tissue distortion) or physiologic or functional (e.g., changes in blood flow or neurological status). These changes may also be immediate, delayed, or protracted.<sup>19</sup> Data are limited for older youth regarding brain and skull tissue stiffness and the ability to resist external force, although data exist for young children (infants and toddlers) and adults.<sup>19</sup> Available data demonstrate that adults, compared to children, sustain more axonal injuries from brain tissue distortions and more skull fractures from mechanical forces on the skull. However, these data do not exist for older youth.<sup>19</sup>

Concussive injuries in adolescents are associated with varying degrees of diffuse neuroinflammation, myelinated axonopathy, metabolic impairment, alterations in neuronal activation, cerebral blood flow perturbations, and disruption to the blood-brain barrier.<sup>24</sup> Adolescents may have a high sensitivity to the amino acids (glutamate and N-methyl-D-aspartate) that are released in the brain following a concussion.<sup>25</sup> These amino acids stimulate intracellular and extracellular metabolic changes that result in increased glucose breakdown along with decreased cerebral blood flow. This, in turn, reduces cerebral blood flow and prevents much-needed nutrients, including oxygen and glucose, from reaching the injured tissue.<sup>25</sup> This mismatch between the demand for and supply of the increased metabolic requirements in the injured parts of the brain further compromises neuronal function and recovery, which can last from 1 to 10 days or more following the concussion. During this time, the brain is even more vulnerable to further injury, including the effects of repeat concussion with additional cranial hits.

Second impact syndrome causes the brain to lose its ability to regulate blood flow, resulting in rapid brain swelling and further neurocognitive sequelae.<sup>26</sup> Although rare and associated with some controversy, second impact syndrome can lead to epidural hemorrhages and fatalities.<sup>18</sup> The epidemiology of sudden death in high school athletes suggests that fatalities are most frequent in football, and a significant number have been associated with a recent history of symptomatic concussion.<sup>18</sup>

High school athletes with multiple subconcussive head blows showed significant changes in the percentage of their white matter, which, in one study, was more than three times higher than in controls. However, the clinical significance of this is unknown.<sup>27</sup> Concussive injuries in high school and collegiate athletes affected brain functioning when measured within 72 hours of the concussions. Still, these changes were no longer observed 45 days after the injury, suggesting recovery.<sup>28</sup> Initial levels of *glial fibrillary acidic protein* (GFAP), a vital neuroprotein responder to central nervous system inflammation and necessary for the repair of central nervous system injuries, are associated with the degree of symptoms immediately following the injury and up to one month afterward. This has prompted the suggestion that GFAP may offer an objective measure of trauma and recovery after pediatric concussions.<sup>29</sup> Altered signaling pathways of the c-Jun N-terminal kinase pathway involved in axonal injury and the role of the dopaminergic system in working memory deficits have also been implicated in concussion neuropathology.<sup>30</sup>

**Proposed reasons for adolescent susceptibility to concussions include a larger head-to-body ratio, decreased neck strength, reduced cerebral blood volume, a larger subarachnoid space, and a less mature brain and physical system.**<sup>25,31</sup> Neuromaturation processes occurring in the developing adolescent increase their vulnerability to the effects of concussive and re-concussive injuries.<sup>32</sup>

## Gender-Related Differences in Concussion Risk and Effects

In sports played by both genders, research shows that girls have a higher incidence rate of concussion than their male counterparts.<sup>2,33,34</sup> **According to a study by Gessel et al., the concussion rate for girls is 68% higher than for**

boys.<sup>35</sup> Of note is that girls are more likely to disclose concussion events than boys.<sup>36</sup>

Possible factors that increase the risk of concussions among female soccer players include a larger ball-to-head size ratio, reduced protective forces owing to decreased head-neck segment mass, and reduced girth and neck strength.<sup>2,33</sup> Several studies have shown that girls have a significantly higher risk of concussion than boys in other sports besides soccer.<sup>2</sup> Lincoln et al. reported that the concussion incidence rate during basketball and baseball/softball for girls (0.16 and 0.11 respectively) was significantly higher than the rate for boys (0.10 and 0.06 respectively).<sup>33</sup>

Self-reported symptoms differ by gender.<sup>2</sup> Relative to baseline, females experience more discomfort and report more acute post-concussive symptoms and higher severity scores immediately following SRC when compared to males.<sup>37,38</sup> Females tend to complain more about drowsiness and noise sensitivity, while males complain of cognitive deficits and amnesia.<sup>39</sup> Females also have a higher post-concussion symptom score at three months post-injury.<sup>40</sup>

Post-concussion sequelae also appear to differ by gender. Researchers propose that with SRCs, females have more neurological deficits; a different symptom constellation; and a delayed resolution of symptoms owing to disparities in the neck musculature and head and neck stability, lower biomechanical thresholds, and hormonal factors.<sup>41</sup> Although both males and females manifest a decline in cognitive testing compared to their baseline, visual memory tasks are more affected in female students than males.<sup>38</sup> Some studies suggest that female students with a history of concussions perform worse on visual memory tasks and experience more severe consequences after suffering a concussion than their male counterparts. Female lacrosse and soccer high school athletes were also found to report more symptoms and perform significantly worse than males across all neurocognitive measures.<sup>38,42</sup> Notably, and to the contrary, several scholars found no sex-based differences.<sup>39,43</sup>

## Concussions in High School Sports

The incidence of SRCs in high school sports has increased over the years, partly due to increased awareness and

identification and improved policies and response protocols for concussions in youth and high school sports.<sup>2,33</sup> Contact sports have higher concussion rates than noncontact sports, and concussion rates are generally higher during competition than in practice.<sup>44</sup> Despite the advancements in policies and response protocols, the 2017 national *Youth Risk Behavior Survey* found that as many as 15% of all high school athletes would sustain a concussion during the season.<sup>7</sup> Given that one study revealed that only 40% of concussion events were reported among high school athletes, this is likely to be an underestimate.<sup>45</sup>

## Concussions in High School Football

Football is associated with the highest incidence of SRC.<sup>33</sup> Despite research and improvements in technology in recent years, concussion rates have increased over time across all sports, with the highest rate in football.<sup>33</sup> This finding is likely the outcome of the increase in concussion detection and treatment awareness,<sup>4</sup> resulting in increased reporting. The use of a helmet and other protective equipment does not appear to affect the risk of concussion in football athletes.<sup>33</sup> **The highest percentage of concussion injuries occur during a tackle while playing.**<sup>34</sup> Linebackers (accounting for 58.9% of all concussions among defensive players) and running backs (accounting for 46% of all concussions sustained by offensive players) face the most significant risk.<sup>34</sup>

## Concussions in High School Soccer

High school soccer is associated with a comparatively high concussion rate (3.6 per 10,000 athletic exposures),<sup>46</sup> and girls are at higher risk than boys.<sup>33,35</sup> In a 3-year study from 2008 to 2010 in which the authors evaluated 20 high school sports, female soccer players had a higher rate of concussions per 10,000 athlete exposures (3.4) compared to males (1.9).<sup>34</sup> Risk factors for concussions in soccer include attempting and receiving a slide tackle, ball dribbling, blocking a shot, chasing a loose ball, defending, heading a soccer ball, and receiving a pass.<sup>35</sup> Heading a ball was the most frequent activity associated with concussions among boys and girls. However, girls

were more likely than boys to suffer a concussion when receiving a slide tackle, defending, chasing a loose ball, or dribbling. Boys were more likely than girls to suffer a concussion when receiving a pass, goaltending, or attempting a slide tackle.<sup>35</sup> As in football, playing during competition increased the likelihood of a concussion compared to practice, and the location on the field was a factor, with most injuries occurring “between the top of the goal box and centerline on the offensive side of the field.”<sup>46</sup> Midfielders, defenders, and forwards, were more likely than goalkeepers to experience a concussion.<sup>46</sup>

## Concussions in Other Traditional High School Sports

The concussion rate for cheerleading varies from the mid to low range.<sup>47</sup> Girls’ volleyball ranks low among noncontact sports in most studies.<sup>2,33,34</sup> Often overlooked, wrestling poses many threats similar to traditional contact sports such as football, hockey, and soccer. SRCs sustained during scholastic wrestling are subject to the

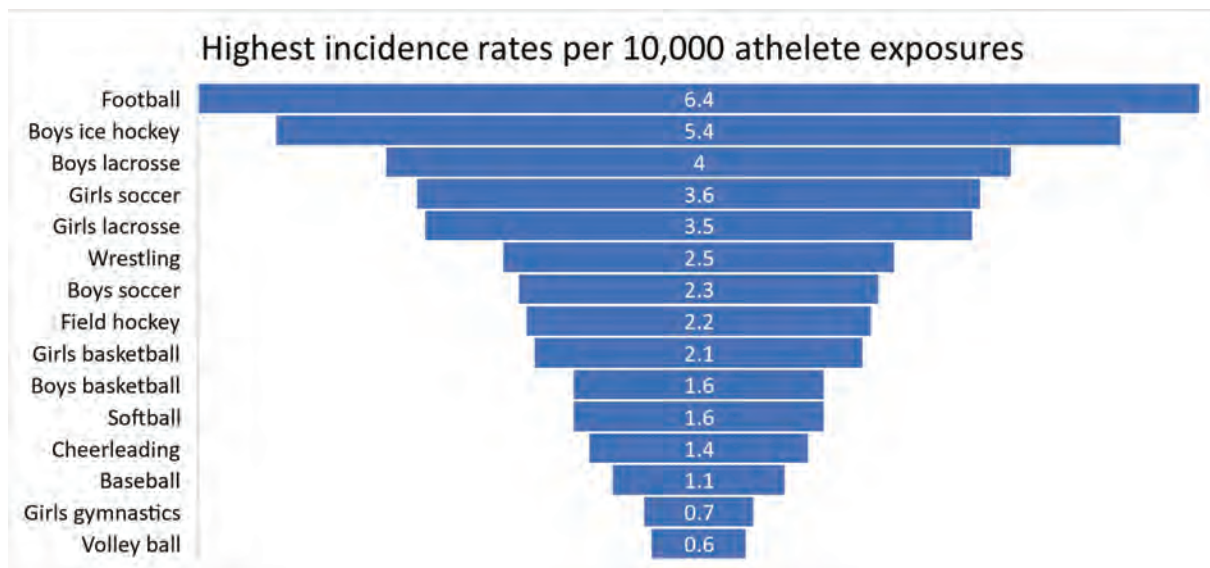
same strain and shearing forces, leading to similar degrees of diffuse neuroinflammation, myelinated axonopathy, and blood–brain barrier disruption.<sup>48</sup> Because the risk of reinjury is high in wrestling, athletes should recognize this and allow enough time for proper recovery to avoid a worse brain injury.<sup>48</sup>

## Concussions in Popular High School Club Sports:

Though not played traditionally in many high schools, certain sports are associated with a high incidence of concussions. Boys’ lacrosse, girls’ lacrosse, and ice hockey have been associated with high incidences of concussion (See Figure 1). Although girls usually have higher concussion rates than boys in similar sports, the different rules, protective equipment, and nature of play in the boy’s game are cited as reasons the concussion rate in lacrosse is lower for girls.<sup>49</sup> In a study that included boys’ ice hockey, the authors reported that this sport had the second-highest rate of concussions per 10,000 athletic exposures followed by boys’ lacrosse.<sup>34</sup>

**Figure 1:**

**Highest Incidence Rates per 10,000 Athlete Exposures: Created from data provided by Powell and Barber-Foss 1999, Schultz et al. 2004, Gessel et al. 2007, Lincoln et al. 2011, and Mirar et al. 2012.**



## Underreporting of Sports-Related Concussions

Studies indicate that as many as 40% of recalled concussion events are not reported to a supervising adult.<sup>50,51</sup> Nearly a quarter of football players continued to engage in sporting activities while experiencing concussion symptoms, thereby placing themselves at higher risk of repeat concussions.<sup>25</sup> In the same study, it was also found that among high school football athletes, only 54% had discussed concussions with their parents or guardians, while 25% reported that they had not received education about concussions.<sup>25</sup>

High school student athletes lack understanding of the severity and seriousness of concussions and often do not see the need to disclose hits encountered during practice or play.<sup>52</sup> **Although girls tend to self-report concussions more than boys, both males and females reasoned that concussion is not a serious enough injury to warrant reporting to a medical professional.**<sup>36</sup> Up to 69% of concussed athletes reported playing with symptoms, and 40% said their coach was not aware of their concussion.<sup>53</sup> **Interestingly, measures of coach concussion education were not associated with coach awareness of concussions in their athletes.**<sup>53</sup>

**Reasons for underreporting SRCs include the fear of losing game time, the perception that the injury is not serious, a lack of knowledge about concussions, the concern about letting teammates down, the situation wherein the injury occurred (e.g., during practice versus during a game), the attitude of coaches, and lack of availability of medical personnel in the school.**<sup>54</sup> Student athletes are incentivized to play actively and may mask their symptoms, causing underreporting. Other identified reasons for nondisclosure include internal conflicts over divulging, previous concussion history, perceived peer influence, and family factors.<sup>55</sup> Sports subcultures, policies such as concussion-related legislation, and, most importantly, access to concussion prevention materials all influence reporting.<sup>54,55</sup>

**Studies show the level of athletic trainer availability in high school sports influences the number of reported SRC and post-SRC management activities.**<sup>50</sup> Athletes in schools with low athletic trainer availability (the athletic trainer only spends one hour at the school per week and is present on the sidelines during home

varsity football games) are less likely to be treated in line with evidence-based guidelines.<sup>50</sup>

These factors highlight the need for improved education of high school athletes and their families pertaining to the knowledge, awareness, detection, and treatment of SRCs in young athletes. The use of multiple sources of concussion education in concussion-related decision-making is effective.<sup>51</sup> School administrators, sports personnel, and sports authorities should make concussion education a priority; ensure that students, families, and coaches are up to date about concussions; and promote an optimal reporting environment to improve management and prevent concussive injuries in young athletes. Moreover, informed clinicians should routinely inquire about SRCs in high school athletes.

## Clinical Manifestations of Concussions

Concussions can have immediate, short-term, and longer-lasting effects. The immediate effects are often more readily recognizable, as are the short-term effects. However, some symptoms may last months to years or cause permanent changes (Table 1). Beyond the immediate symptoms, patients may experience post-concussion syndrome or post-traumatic nervous instability. **In one study, 80–90% of athletes with post-concussion symptoms reported that symptoms resolved in one to two weeks.**<sup>4</sup> However, for some, the symptoms tended to persist.

The most frequently observed physical symptom for identifying post-concussion syndrome is a headache.<sup>4</sup> Conversely, post-concussion treatment can lead to persistent headaches due to medication overuse, making it essential to accurately diagnose and identify the cause of the headache, because the approach to treatment will differ.<sup>4</sup> Statistics for post-concussion syndrome vary. However, it is commonly stated that if symptoms have not been resolved within a few weeks, they will most likely persist for months and tend to resist treatment.<sup>20</sup> In one study, a third of patients with persistent post-concussion symptoms complained of anxiety and depression, though it is unclear if those symptoms preceded the injury.<sup>20</sup> The post-concussion syndrome occurs in 30–80% of patients following a concussion, and 20% of patients will have persistent symptoms.<sup>4</sup>



**Table 1:**  
**Symptoms and Signs of Concussions and Danger Signs**

|                           | General  | Cognitive   | Central Nervous System   | Musculoskeletal   | Mood and Behavior   |
|---------------------------|--|---|--|---|---|
| <b>Symptoms and Signs</b> | <ul style="list-style-type: none"> <li>– Fatigue</li> <li>– Nausea</li> <li>– Vomiting</li> <li>– Feeling sluggish</li> </ul>  | <ul style="list-style-type: none"> <li>– Difficulty concentrating</li> <li>– Difficulty thinking clearly</li> <li>– Anterograde amnesia</li> <li>– Learning problems</li> </ul> | <ul style="list-style-type: none"> <li>– Headache</li> <li>– Dizziness</li> <li>– Hazy or blurry vision</li> <li>– Photophobia</li> <li>– Phonophobia</li> <li>– Hypersomnia</li> <li>– Insomnia</li> </ul>  | <ul style="list-style-type: none"> <li>– Lack or loss of coordination</li> <li>– Lack or loss of balance</li> <li>– Numbness</li> </ul> | <ul style="list-style-type: none"> <li>– Increased emotionality</li> <li>– Irritability</li> <li>– Depression</li> <li>– Anxiety</li> <li>– Emotional lability</li> </ul> |
| <b>Danger Signs</b>       | <ul style="list-style-type: none"> <li>– Recurrent nausea</li> <li>– Recurrent vomiting</li> <li>– Increasing confusion</li> <li>– Increasing restlessness</li> <li>– Agitation</li> </ul> | <ul style="list-style-type: none"> <li>– Recurrent disorientation</li> <li>– Excessive forgetfulness (relative to baseline)</li> <li>– Memory loss</li> </ul>                   | <ul style="list-style-type: none"> <li>– Slurred speech</li> <li>– Worsening or unresolved headache</li> <li>– Drowsiness</li> <li>– Difficulty maintaining alertness</li> <li>– Inability to wake up from sleep</li> <li>– Loss of consciousness</li> <li>– Anisocoria</li> <li>– Seizures</li> </ul> | <ul style="list-style-type: none"> <li>– Impaired coordination</li> <li>– Muscle jerks or twitches</li> <li>– Numbness</li> </ul>       | <ul style="list-style-type: none"> <li>– Unusual behavior</li> <li>– Erratic behavior</li> <li>– Sudden rages</li> <li>– Change in personality</li> </ul>                 |

The long-term effects of concussions in high school athletes are understudied. However, research has shown that a history of multiple concussions can lead to long-term mental and cognitive problems that may reduce quality of life. Some scholars have found that three or more concussions make the outcomes worse. In contrast, others have found no difference in outcomes after two concussions.<sup>56</sup> In the long term, a concussion can have many potentially permanent effects if the initial injury is not treated properly. **A 2007 study showed that athletes with multiple concussion histories exhibited a three-fold increase in depression compared to athletes with no concussion history.**<sup>57</sup> Other long-term outcomes include mild cognitive impairment, memory deficits, and executive dysfunction.<sup>57</sup> Although longitudinal investigations are still needed, authors of some cross-sectional studies did not identify any observable effect of adolescent concussion history on cognition or motor performance with age.<sup>57</sup>

## Mental Health Symptoms

Although studies on the mental health outcomes that follow concussions among high school students are limited, researchers have demonstrated that high school athletes with a history of concussions are at increased risk for psychological problems. Multiple concussions are a risk factor for cognitive impairment as well as mental health problems.<sup>58</sup> In a study of high school hockey players, the authors found that concussions were associated with depression, problems with attention, somatization, anxiety, and a poorer sense of control over external events.<sup>59</sup>

Depression is one of the most frequently reported mental health sequelae of TBI and is seen in approximately 25–40% of cases of moderate-to-severe TBI.<sup>60</sup> **Youths who reported a history of SRCs were at higher risk for feeling sad or hopeless, experiencing suicidal ideations, and making a suicide attempt.**<sup>61,62</sup> Boys and

girls with a history of concussions were associated with higher odds of behavioral risk factors for completed suicide.<sup>61</sup> Yang et al., in a population-based study, also found that high school students who had experienced a concussion were 59% more likely to engage in self-harm, were 48% more likely to experience depressive symptoms, and had three-times-higher odds of attempted suicide.<sup>63</sup>

A systematic review examining the association between concussions and mental health outcomes (depression, anxiety, ADHD, PTSD, disruptive disorders, autism, and schizophrenia) showed that the likelihood of adverse mental health outcomes was higher with the following factors: hospitalization following a concussion, proximity of the assessment to the injury, reliance on recall, young age, preexisting psychiatric illness, and multiple concussions.<sup>64</sup> Most research on mental health outcomes has been carried out in populations of adult professional athletes. Many studies among high school students are short-term investigations, which highlights the need for more longitudinal long-term studies.

## Neurocognitive Symptoms

Analyzing how high school athletes generally perform in the classroom is essential because this can have a significant impact on psychosocial outcomes. The findings are mixed regarding the cognitive effects of concussions on high school athletes, and most studies have been short-term follow-ups.<sup>65</sup> Brain MRI changes are detectable in as little as a single season of football and are associated with changes in the verbal memory subscore of the ImPact (*Immediate Post-Concussion Assessment and Cognitive Testing*) scores.<sup>1,2</sup> Some researchers find evidence of poorer performance in neurocognitive tests, while others do not. For example, Rieger et al. did not find any evidence of poor neurocognitive performance following a concussion, although their sample size was small.<sup>66</sup> Importantly, they found that students' perceptions about academic performance following a concussion differed from their actual performance on a range of neurocognitive battery tests and that the presence of somatization and worry symptoms following concussion affected their perceptions of academic performance.<sup>66</sup>

Russel et al. found that SRCs may be associated with lower grade point average scores but do not appear to affect the likelihood of graduation from high school.<sup>67</sup> Ilie et al. found that adolescent TBI was associated with poorer academic performance, particularly if there had been frequent hits to the head.<sup>5</sup> Charek et al. found that adolescents who were removed from play did better on post-concussion cognitive assessments than adolescents who continued to play.<sup>68</sup>

Post-concussion states, including CTE, are associated with persistent cognitive dysfunction and emotional and behavioral dysregulation. Concussions are also associated with a higher risk of mental health symptoms, including depression and anxiety.<sup>20</sup> Although these symptoms do not directly affect academic performance, they negatively affect the individual's ability to function properly in a classroom setting.

## Symptoms Associated with Prolonged Recovery

In pediatric SRC patients treated in concussion clinics, the median length of recovery was about 17 days. Only 16.3% of such patients recovered within one week, while 26.4% took longer than four weeks to recover.<sup>69</sup>

**The most consistent predictor of slower recovery from concussion is the severity of the acute and subacute symptoms.<sup>70</sup> High symptom scores at injury and initial visit, the time to the initial clinical presentation, the presence of two or more previous concussions, and being female are associated with prolonged concussion recovery.<sup>69</sup> In one study, concussed high school athletes with persistent foggiess experienced a higher number of other post-concussion symptoms, slower reaction times, reduced memory performance, and slower processing speed when compared to athletes with no reported foggiess.<sup>71</sup>**

Athletes with self-reported foggiess at one week post-injury are more likely to experience adverse effects from their concussions in multiple domains.<sup>71</sup> The development of subacute problems with headaches or depression is a possible risk factor for persistent symptoms lasting more than a month. Patients with a preinjury history of mental health problems appear to be at higher risk for persistent symptoms.<sup>71,72</sup>



## Assessment and Management

### Assessment:

With increasing attention paid to the effects of concussions, several organizations have put together guidelines and consensus statements that help guide the management of SRC.<sup>73,74</sup> In addition, the *Centers for Disease Control and Prevention* (CDC) website has training modules available to healthcare professionals. Several assessment tools outline how to assess symptoms and signs following a concussion, including tools that can be used on the field and healthcare professionals.<sup>19</sup> The *acute concussion evaluation* (ACE) form is a tool for clinicians to assess symptoms immediately following a concussion and track symptoms over time. Moreover, the ACE care plan form provides a working plan to enable the athlete to monitor recovery and return to sporting activities.

**Following a suspected sport-related concussion or brain injury, the CDC recommends the ABC: Assess the situation; Be alert for signs and symptoms; Consult a medical professional.** It is crucial to have the high school athlete examined by a healthcare professional, preferably one who is familiar with the child and can detect subtle changes. The assisting adult must be alert for danger symptoms and signs (Table 1) that require immediate transportation to the emergency room. The youth sport concussion laws that have been passed in all states mandate that youths cannot return to play on the day of the injury and need written clearance by a healthcare professional trained in assessing and managing concussions.<sup>75</sup> However, there is a suggestion that changes in legislation alone will not result in increased reporting.<sup>53</sup>

When assessing the student, it is essential to inquire about the history of concussions as well as to evaluate any underlying physical or psychiatric symptoms. A PHQ-9 or other brief screening tool can be used to assess underlying psychiatric signs and to initiate a referral for treatment if indicated. **In addition to a thorough history, a complete physical exam that includes a neurological assessment and tests of vision, balance, and cognition is essential in conducting a comprehensive appraisal.** Imaging studies such as a CT scan or an MRI may be carried out if clinically indicated (by suspicion of a brain bleed or presence of a danger sign; see Table 1).

## Management

Proper care of athletes with SRCs requires a high index of suspicion and appropriate management to optimize the young athlete's outcome. Several helpful decision trees have been suggested to assist healthcare workers in managing concussions and return-to-play decisions.<sup>31</sup> Adequate protocols should be established and actively implemented. Following a concussion, the athlete should be removed from play and assessed for any symptoms and signs because the risk of a worse outcome is high if another injury occurs while an athlete is still recovering. Students should be allowed to rest, which includes sleep and limiting contact and physical activity. Incorporating a gradual return to full activity as the student feels progressively better is strongly recommended.<sup>31</sup> A recent study noted that athletes who were engaged in "moderate-to-heavy" physical activity at the time of the initial concussion assessment at a specialty concussion clinic had a quicker trajectory toward recovery.<sup>3</sup> Academic work may need to be modified or reduced to accommodate any initial difficulties the students may encounter following a concussion. A full return to regular activity should only occur when the student can carry out activities without experiencing any symptoms. Some students may require symptomatic treatment for headaches with nonsteroidal anti-inflammatory drugs or treatment for insomnia with melatonin. Regular appointment attendance with the corresponding medical providers is essential to monitor recovery and receive clearance to return to sporting activities. Part of the management includes educating parents and students about expected improvement and providing recommendations about how to aid healing.

## Preventing Sports-Related Concussions in High School

The rates of concussion have been increasing over time, and this may be reflective of the increase in protocols and the awareness of concussion, resulting in increased education, identification, and treatment. **However, despite this increased reporting, underreporting remains a concern with up to 40% of high school athletes failing to report their concussions.**

Increased knowledge and awareness of concussions is essential for informing the improvements made to rules

and protective equipment, as well as for the availability of medically trained personnel. Training, knowledge, and recognition at the individual, parental, and scholastic levels are essential in preventing and mitigating the risks of concussions. Recognizing the proper symptoms is necessary for adequate treatment and care of concussions.<sup>73</sup>

Decreasing concussion risk across all sports is a multifaceted issue. Protective gear such as helmets has shown conflicting results and, in some cases, does not appear to reduce the risk of concussions. However, helmets should certainly be recommended because they prevent the more severe forms of TBI. As newer designs of helmets are produced, studies will be needed to determine their impact in reducing the incidence of concussions. Rule changes in several sports, including football, have resulted in a significant reduction in concussions.<sup>76</sup>

Practice and competitive play can be adjusted to decrease the overall exposure to head impacts. During practice, head impact exposure may be reduced by limiting contact plays.<sup>77</sup> The rate of SRCs sustained in high school football practice decreased by 57% after a rule change limiting the number and duration of full-contact activities, with no change in the competition concussion rate.<sup>76</sup> Rotating playing positions between high- and low-impact positions may further reduce the rate. Preventing repeat concussions is a vital component of treatment. Recognizing barriers to reporting is critical in addressing and mitigating the effects of concussions. Given that the risk of reinjury following a concussion is higher and can result in worse functional outcomes if an athlete experiences another insult while still recovering, any incentives that keep injured players in active play should be discouraged.

## Practice Implications

Clinicians should be aware that knowledge and attitudes of high school students influence SRC reporting. Clinicians should reinforce the message that concussions can occur in any sport and educate patients on the relevant symptoms and signs. Screening for a history of concussions in student athletes will make their medical history more complete. To obtain a complete medical history, primary care providers should screen patients for concussions by asking if they engage in high school or collegiate

athletics and by asking them to describe their hardest hits to the head.<sup>78</sup> Given that most prior SRCs go unreported in this patient population, it is essential to screen for past concussions when a patient presents with a “first” concussion. Closer monitoring for mental health symptoms in high school students with concussions should be emphasized and conducted. Mental healthcare workers should perform more in-depth clinical assessments of high school students with SRCs and monitor them more closely following concussive events to identify and treat any emerging mental health symptoms with medications if indicated.

## Conclusion

The developing adolescent brain may be more vulnerable to the effects of SRCs. Concussion detection, treatment, and prevention are vital in reducing the immediate and long-term sequelae in high school sports. While the reporting of SRCs is increasing, underreporting is still a problem. Girls appear to have a higher incidence of SRCs. The risk of post-concussive sequelae can be mitigated by prompt attention to concussion events and the prevention of further concussions.

Educating athletes, parents, coaches, and school administrators is critically important for preventing, detecting, and avoiding further concussion. Identifying and addressing factors related to nonreporting cultures and attitudes would be helpful. Implementing effective strategies during practice and competitive play, such as rules promoting player safety and improved technology of protective gear, could decrease the incidence and severity of concussive events.

Clinically, healthcare workers should screen student athletes for histories of concussions as part of their medical history and advise on the necessary steps to mitigate the effects and prevent additional injuries. Mental health workers should monitor students with SRCs more closely for emerging mental health symptoms and treat them accordingly. Finally, high school athletes are a particularly vulnerable population necessitating a significant increase in research focused on protecting them against SRCs, promptly identifying and treating SRCs, preventing concussions, and mitigating their long-term deficits. ■

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## Multiple-Choice Questions

**57. All concussions are serious. A *sports-related concussion* (SRC) is classified as a:**

- A. Severe traumatic brain injury.
- B. Moderate to severe brain injury.
- C. Mild to moderate brain injury.
- D. Mild traumatic brain injury.

**58. All of the following are less severe symptoms of concussion, *except*:**

- A. Altered awareness of surroundings.
- B. Loss of consciousness lasting a few minutes to hours.
- C. Disorientation.
- D. Drowsiness.

**59. Which of the following are proposed reasons for adolescent susceptibility to concussions?**

- A. Smaller head-to-body ratio
- B. Increased neck strength
- C. Larger subarachnoid space
- D. Increased cerebral blood volume

**60. A possible explanation of why females are at higher risk of concussions when compared to boys in soccer and other sports includes:**

- A. Increased disclosure of concussions.
- B. Smaller ball-to-head size ratio.
- C. Reduced head-neck segment mass.
- D. Differences in discipline and technique.

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# Best Practices in Continuing Medical Education

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## Sports-Related Concussions in High School Athletes

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**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

*Sports-related concussion* (SRC) is the second-most-common cause of head injury in the adolescent age group, accounting for up to 40% of *traumatic brain injuries* (TBI) in adolescents. SRCs among high school students occur more frequently during participation in high-contact sports such as soccer and football. Gender differences exist, with girls more likely to experience a concussion. Concussions increase the risk of developing neurocognitive and mental health disorders. It is crucial to identify and evaluate athletes who experience a concussion because the risk of poorer outcomes increases if an athlete experiences another concussion while still recovering from the previous hit to the brain. Athletes, caregivers, and school officials need to be aware of the risk of concussions so that they may implement practices to mitigate the risk. Following a concussion, an athlete should be evaluated and then fully recover before being allowed to return to sporting activities.

#### Key Point 1: SRC Is Common Among High School Athletes

Up to 9% of high school athletes report experiencing a concussion annually. Football is associated with the highest incidence of SRC in boys, while soccer is associated with the highest incidence of SRC in girls. Concussion rates have increased over time, likely as a result of increased surveillance. Factors that increase the risk of concussion include high contact sports, the player's location and position on the field, and particular sporting activities such as heading a ball, dribbling, and receiving a slide tackle.

#### Key Point 2: Girls Are More Susceptible to SRC

Girls have a higher incidence of concussions. Females also experience more discomfort

and higher post-concussive symptoms and severity. The factors that may increase susceptibility to concussions in female athletes include larger ball-to-head size ratio, reduced neck strength and girth, and differences in protective gear in certain sports.

#### Key Point 3: Underreporting of SRCs is High in Both Male and Female Athletes

As many as 40% of recalled concussion events are not reported. One in four players continues to play while experiencing symptoms of a concussion, which unfortunately increases the risk of subsequent concussions and second impact syndrome. High school athletes tend to underplay the significance of a concussion and worry that reporting a concussion will cause them to lose game time or let their team down. The availabil-

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ity of healthcare personnel among school staff increases the likelihood of reporting a concussion. Screening high school athletes for a history of reported and unreported concussions should be part of their medical history.

**Key Point 4: SRC is Associated with Mental Health Problems, Including Depression, Anxiety, Attentional Problems, and Suicidal Behavior**

High school athletes who have experienced a concussion are more likely to report depression or suicidal ideations and to engage in self-harm or suicide attempts. Concussion increases the risk of problems with attention, anxiety, posttraumatic stress disorder, and disruptive disorders. High school athletes with a history of SRCs should be monitored more closely for mental health symptoms following a concussion.

**Key Point 5: Youth Sports Concussion Laws Mandate that Athletes Cannot Return to Play on the Day of the Injury and Require that Athletes Be Evaluated and Provided with a Written Clearance to Return to Play**

Athletes who have experienced a concussion need to be assessed for the presence and severity of symptoms. They may not return to play on the day of injury even when they report no symptoms. Ideally, written clearance to return to sporting activities should be completed by a healthcare professional who is familiar with the athlete. Athletes who experience symptoms typically recover in 10–14 days, although some may take longer. Factors associated with protracted recovery include the severity of the post-concussion symptoms, a previous concussion, being female, and a preinjury history of mental health problems.



# A Review of the Impact of Wearing Masks on COVID-19 Transmission and the Psychology behind Resistance to Wearing Masks

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*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** COVID-19 • Mask • Psychology • Resistance

**LEARNING OBJECTIVES:** Upon completion of this lesson, the clinicians will be able to (1) recognize the benefits of wearing masks in slowing down and preventing the spread of *coronavirus disease 2019* (COVID-19), (2) identify populations vulnerable to COVID-19 and the importance of wearing masks, and (3) recognize the psychological factors associated with resistance to wearing masks.

**LESSON ABSTRACT:** COVID-19, which started in late 2019 in Wuhan, China, has quickly become a challenging global health crisis in recent history. The pandemic has caused tremendous medical, social, economic, and psychological impacts worldwide. In the early phase of this pandemic, major lockdowns were implemented in heavily affected countries, including the *United States* (US), to flatten the curve. With the reopening, long-term and sustainable strategies are needed to prevent the spread of COVID-19. The current strategies of the Centers for Disease Control and Prevention include general precautions such as social distancing, contact tracing, expansion and clarification of the role of public health, and case investigation. While the benefits of wearing masks in healthcare facilities are well established and enforced, wearing masks in public settings remains a debatable topic and stirs up controversies in the US despite being recommended by the country's top health experts and considering its benefits. This review highlights the benefits of wearing masks in preventing the spread of COVID-19 and the psychology behind the resistance to wearing masks in the US.

**COMPETENCY AREAS:** This lesson addresses the benefits of wearing masks, especially in public settings, in slowing down and preventing the spread of COVID-19 and the psychological factors behind the resistance to this health practice. Upon reading this manuscript, readers may gain in-depth psychological knowledge associated with the resistance to wearing masks.

## Introduction

*Coronavirus disease 2019* (COVID-19) is a novel disease caused by *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) that originated in Wuhan, China, toward the end of 2019 before spreading worldwide. By August 2020, the *Centers for Disease Control and Prevention* (CDC) reported that COVID-19 had affected over 17 million people in over 200 countries, with a mortality rate of 8.6%. The US alone had more than 4.6 million cases and 150,000 deaths from COVID-19. As of December 2020, the CDC reported over 13.2 million cases and more than 266,000 deaths in the US.<sup>1</sup> Although SARS-CoV-2 does not cause the highest mortality rate, its dangers lie in its high transmissibility and ability to affect anyone of any age. The US is on the cusp of COVID-19 vaccine approvals for widespread vaccination, which is not yet available to combat the virus; therefore, everyone is vulnerable to contracting the disease.

In an initial response to the pandemic, a major lockdown across the country occurred in early March 2020 until the end of April—during which time, the CDC ramped up its efforts to combat the spread of the virus, including contact tracing and travel restrictions. Wearing masks was recommended but not required; however, when the US decided to begin a phased reopening, wearing masks became an important and required short-term prevention method to minimize viral transmission. By late October 2020, the number of daily new COVID-19 cases in the US had already exceeded 80,000, breaking the record high set in July 2020.<sup>2</sup> Hospital resources rapidly diminished when the pandemic heavily hit the Southern and Western states in July. Texas, California, and Florida became the new hotspots of COVID-19, each with more than 50,000 new cases during the week of July 29 and all with more than 60% ICU capacity.<sup>3,4</sup>

Given the current situation in the US, it is imperative that individuals all practice appropriate public health methods to minimize viral transmission. Because the ideal situation of zeroing all contact between individuals to prevent any chance of transmission is impossible and preserving human well-being is of the utmost importance in society, much attention and effort are given to developing correct precautionary approaches to minimize the spread of COVID-19. A central public practice encouraged by healthcare professionals is wearing face masks during

times where the number of COVID-19 cases in the US is resurging, combined with the need for people to leave their homes for their occupations and daily activities.<sup>5</sup>

Why is wearing masks to prevent the spread of COVID-19 a responsibility of the public? Wearing masks is accessible, simple, and highly effective in preventing COVID-19 transmission. Although wearing masks does not guarantee others' transmission prevention to the individual, appropriately masked individuals decrease the chances of transmission for everyone around them, including themselves. Further, wearing masks provides more than improving the physical well-being of the public. Wearing masks provides a sense of comfort for the public and fosters an altruistic environment where individuals can resume regular public activities without the constant worry of transmission and infection.<sup>6</sup> With daily reports of terrifying statistics, constant reminders of the dangers of COVID-19, and countless stories of families getting broken by the pandemic, comfortably resuming normal lives is becoming increasingly harder for the public. The necessity of wearing masks stems from not only its physical protection of everyone's safety but also its positive psychological effects on the population as a whole.<sup>7</sup>

Because COVID-19 spreads primarily when people are in close contact via small droplets and possibly through aerosols, prevention methods are similar to those against other viral infections, including SARS and the 1918 flu. Therefore, incorporating what we have learned from the past into the present is important for the public. In the current state of wearing masks across the US, a unified message on how to best prevent COVID-19 spread is lacking, evidenced by a gap between expert recommendations and state and federal approaches, causing unnecessary confusion and public mistrust. Furthermore, the vulnerability of individuals to COVID-19 varies depending on age, pre-existing conditions, socioeconomic status, and access to health care; therefore, certain populations are more at risk than others. The differences in masking behaviors among various populations may lead to differences in viral transmission rates.

In summary, this review explores aspects of public health surrounding wearing masks during the COVID-19 pandemic—including the appropriate method to wearing masks, which explains the best practices and types of masks; the general effectiveness of wearing masks,

specifically examining population studies conducted on COVID-19 and other past pandemics; masking practices and impacts in different populations, where locations and socioeconomic differences may indirectly impact the prevalence of COVID-19; and the psychology behind the resistance to wearing masks, exploring possible reasons why some Americans are hesitant to use a helpful method for mitigating the pandemic.

## Appropriate Masking Methods, Need for Masks, and Scientific Evidence

### A Need for Wearing Masks:

COVID-19 is an illness caused by SARS-CoV-2 and transmitted by both direct contact and large pathogen-containing respiratory droplets. There is an ongoing discussion about whether COVID-19 can be spread through aerosols—which are smaller respiratory droplets that can either stay suspended in the air for several hours or evaporate very quickly, leaving the remaining solid particulate to travel large distances through the air.<sup>8</sup> Regardless of whether COVID-19 is transmitted through large or small respiratory droplets, it is still imperative that the public take steps to minimize the spread of the virus. Current U.S. guidelines call for six-foot social distancing and wearing masks. However, a recent MIT study concluded that 2 people need to be 27 feet apart from each other to guarantee that there will be no transmission of respiratory droplets between the two individuals.<sup>9</sup> As a result, the next step to protecting the public from COVID-19 is wearing masks. In August 2020, Robert Redfield, the director of the CDC, told reporters that “we could drive this epidemic to the ground” if everyone wore a face cover for the next four to six weeks.<sup>10</sup> There is, undoubtedly, an urgent need for the public to wear masks.

**Several studies for both SARS-CoV-2 and other past influenza-like viruses have demonstrated the measurable benefits of wearing masks for both the individual and public.** During the 2003 SARS outbreak, where *severe acute respiratory syndrome coronavirus 1* (SARS-CoV-1) affected over 8,000 people in 26 countries, Hong Kong was one of the hardest-hit areas in the world, accounting for nearly 40% of the world’s cases of SARS.<sup>11</sup> As a result, China heavily mandated the use of

face masks—where Hong Kong residents demonstrated a 90% mask-adherence rate during the epidemic, which successfully curbed the spread rate.<sup>12</sup> A 2004 study demonstrated that wearing masks, among other protective health measures in Hong Kong during the SARS outbreak, was effective in reducing the risk of transmission.<sup>13</sup> Those who wore masks had a 70% lower risk of being diagnosed with SARS, allowing for a significant decrease in the transmission of SARS-CoV-1.<sup>14</sup> Another 2009 Hong Kong study demonstrated that the combination of hand washing and wearing masks significantly decreased the transmission of the influenza virus within 36 hours.<sup>15</sup> More recently, a 2020 study on the COVID-19 pandemic discussed how Taiwan enforced preventive measures of hand washing and wearing masks to successfully flatten the curve of the virus; as of May 2020, Taiwan reported only 440 cases and 7 deaths, which are small numbers compared with the 1,761,503 aggregated reported cases and 103,700 deaths in the US. The number of cases represents 0.0018% of Taiwan’s population and 0.53% of the U.S. population, a percentage of over 288 times that of Taiwan.<sup>16,17</sup> Evidently, data from both the past SARS outbreak and the current COVID-19 pandemic demonstrate that widespread masks wearing is imperative for public health, especially during an outbreak.

Widespread mask wearing is not only important but choosing the proper mask material can significantly increase its effectiveness, as different materials provide varying degrees of protection against infection. Although the precise quantitative benefit of wearing masks differs between studies, with only moderate evidence of wearing masks in preventing transmission in community settings, the overarching conclusion is that wearing masks is undoubtedly critical for public health and contributes to minimizing the spread of infection.<sup>18</sup> Wearing a mask protects the wearer both from being infected by inhaling droplets and from spreading the infection by exhaling the droplets into the air. A 2008 experiment demonstrated that although homemade tea cloth masks were shown to be only half as effective as surgical masks, both types could still reduce the transmission of the droplets.<sup>19</sup> A 2013 study went a little further and examined the efficacy of 100% cotton T-shirt material, a double layer of tea towels, and surgical masks, among others. Their results indicated that all three types of masks protect the wearer

from infection, with the surgical masks having the highest filtration efficiency. However, all mask types could protect the wearer from respiratory droplets.<sup>20</sup> Furthermore, a 2020 study concluded that homemade masks made of four-layer kitchen paper and one-layer cloth, surgical masks, and N95 masks could all block over 95% of the avian influenza virus, an influenza-like virus that spreads in similar ways to COVID-19.<sup>21</sup> **Although N95 masks are the most effective at blocking respiratory particles, they were in low supply.**<sup>22</sup> As a result, these masks should be kept for healthcare workers who fight the pandemic on the frontlines. If the general public uses well-made homemade masks properly, this already can and will immensely help flatten the spread curve of COVID-19. A recent peer-reviewed study demonstrated that countries enforcing wearing masks of any type see a much flatter growth rate curve compared with those that do not.<sup>23</sup> Anecdotal evidence from the current pandemic shows that wearing face masks reduces the risk of contracting the virus significantly, as well as the severity of the infection. Recent studies with more rigorous analyses have also offered further direct evidence. “A preprint study posted in early August (and not yet peer reviewed) found that weekly increases in per-capita mortality were four times lower in places where masks were the norm or recommended by the government, compared with other regions.”<sup>24</sup> However, despite the mounting evidence that wearing masks is critical in slowing the spread of the virus, masking policies still differ within and among countries.

Unfortunately, there is no unified policy on general COVID-19 procedures implemented by the U.S. government. Instead, individual states are responsible for managing their own response to COVID-19, resulting in differing efforts across the nation. Some states mandated that wearing masks be enforced in public, while others only required employees to wear masks during their working hours. A 2020 study measured the COVID-19 growth rate differences between these two groups and discovered that the states mandating wearing masks in public demonstrated a significant decline in the COVID-19 growth rate of 2.0% within three weeks after signing the mandate; models predict that as many as 230,000–450,000 cases have been prevented by these mandates. However, the other states, which only required employees to wear masks, had no decline in the COVID-19 growth

rate.<sup>25</sup> It is important that all Americans, rather than only a subset of the population, contribute to public health by wearing face masks. Fortunately, the US is becoming more open to adopting widespread use of face masks; an internet survey by the CDC demonstrated that the percentage of adults who endorsed wearing masks increased from 62% to over 76% within five weeks between April and May 2020.<sup>26</sup>

Outside the US, wearing masks is also becoming a popular option. By August 2020, France required face masks in all public areas, and England required masks inside all shops and supermarkets.<sup>27</sup> Hong Kong strongly encouraged wearing masks at all times, while Singapore only required people who present respiratory symptoms to wear masks.<sup>28</sup> In April 2020, the data between Hong Kong and Singapore indicated a sharp difference between their number of COVID-19 cases; Hong Kong had just over 1,000 cases, while Singapore had over 10,000.<sup>29</sup> Although wearing masks may not have been the sole factor for this difference, it likely played a significant role.

## Current CDC Guidelines on Wearing Masks

**The current guidelines from the CDC recommend wearing masks in public because it is more effective to reduce the spread of COVID-19 when widely practiced.** However, masks should never be worn by children under the age of two, those who suffer from breathing issues, those who are unconscious or incapacitated, and those who are unable to remove their masks without assistance. Further, not all masks should be worn in public; masks that have exhalation valves or vents are not effective in preventing the spread of COVID-19.

The CDC outlines the proper way of wearing a mask by following these steps: (1) wash your hands; (2) place the mask over your nose and mouth, securing it under your chin; (3) fit the mask snugly against the sides of your face; and (4) make sure you can breathe easily.<sup>30</sup>

## Overview of the Population

COVID-19 presents with mild symptoms only or remains asymptomatic in most patients but disproportionately affects the elderly and those with pre-existing chronic health conditions.<sup>31</sup> According to the CDC, those with



cancer, chronic kidney disease, chronic obstructive pulmonary disease, a weakened immune system from a solid organ transplant, obesity, serious heart conditions, sickle cell disease, and type 2 diabetes mellitus are at an increased risk of severe illness from COVID-19. Patients with other illnesses—such as moderate-to-severe asthma, cerebrovascular disease, cystic fibrosis, hypertension, a weakened immune system from blood or bone marrow transplant, immune deficiencies, human immunodeficiency virus, dementia, liver disease, pulmonary fibrosis, thalassemia, and type 1 diabetes mellitus, as well as patients who use corticosteroids and other immune-weakening medicines, are pregnant, or smoke—may be at an increased risk for severe illness from COVID-19.<sup>32</sup>

However, these traits are not the only qualities that describe those who are more at risk; factors such as socioeconomic status play a big role in determining those who are more susceptible to the infection. Addressing the healthcare disparity and allocating appropriate resources, including masks, should be conducted depending on the population's needs and issues with precautionary practices. The population at risk in America consists of healthcare workers and those living in group homes, shelters, and nursing homes.

### **The Homeless:**

There are an estimated 553,742 people who are homeless in the US on any given night and are at a much higher risk of contracting and spreading COVID-19 than the average individual. In May 2020, in Houston, Texas, 77 of the reported 183 new COVID-19 cases came from homeless shelters—a grossly disproportionate amount of over 42%, given that only 3,900 of its 2.3 million residents are homeless.<sup>33,34,35</sup> Socioeconomic status is a huge factor in COVID-19 transmission. **Accessibility to resources allows proper sanitary practices such as wearing masks, handwashing, and social distancing, which are critical in minimizing the risk of infection. As a result, homeless individuals, unfortunately, are unable to protect themselves from COVID-19.<sup>31</sup> In addition, this population has higher rates of chronic illnesses and compromised immune systems due to the lack of healthcare access.<sup>36</sup> A lack of appropriate prevention techniques, combined with a higher rate of health complications, makes homeless individuals most vulnerable to COVID-19, with a mortality rate**

**that is 5–10 times higher than that of the general population.<sup>37</sup>**

**Challenges faced by homeless individuals were presented in a recent study by Tobolowsky et al., where they found that the viral transmission among residents and staff members of the studied homeless shelters could be attributed to crowding, challenges to enforcing physical distancing, and the unavailability of face masks. Because the unavailability of surgical face masks for this population is a difficult problem to solve, service sites for the homeless have introduced proactive testing for all residents and staff members and required prompt isolation of infected individuals.** However, these tests and other health interventions are limited as well.<sup>38</sup> Conclusively, proper education of the enforcement of social distancing and mask wearing using other materials is a possible solution for these service sites while they have limited resources.

### **Healthcare Workers:**

Healthcare workers working during the COVID-19 pandemic are among those populations at the highest risk of contracting the infection. In a report from China during the spread of the pandemic in January 2020, 29% of 138 hospitalized patients were healthcare workers.<sup>39</sup> Though proper mask wearing is not an issue as it is with other high-risk populations, appropriate personal protective equipment is limited.

It is advised that healthcare workers use N95 face masks when treating suspected or confirmed COVID-19 patients, while the general public uses non-N95 face masks.<sup>40</sup> As such, a critical shortage of N95 face masks in hospital settings has caused healthcare workers to use masks longer than their intended use.<sup>41</sup> In a series of randomized controlled trials in a hospital setting, researchers found that there are no significant differences between surgical masks and N95 masks in protecting healthcare workers against COVID-19 transmission, with N95 being slightly more effective.<sup>42</sup> Thus, a shift to preserving N95 masks while producing surgical masks for healthcare workers may be a method in preparing for critical situations in the future.

### **The General Public:**

The controversy of wearing masks in public areas applies mostly to the general public. Overall, 65% of U.S. adults

reported in a study conducted in early June that they wore masks in public all the time a month prior to the study.<sup>43</sup> This percentage significantly increases or decreases depending on the population's political affiliation, race and ethnicity, and age. **In summary, Democrats are more likely to wear masks than Republicans; Caucasians are the least likely to wear masks, followed by African Americans, Hispanics, and finally, Asians. Americans living in suburban communities are more likely to wear masks than those living in rural regions.** Furthermore, older adults tend to wear masks more often in public places than younger adults.<sup>43</sup> The elderly and those with pre-existing chronic health conditions are more susceptible to severe health consequences from COVID-19; thus, these vulnerable groups are more encouraged to wear facial masks in public. It is more difficult to encourage the rest of the public to practice proper wearing of masks. In particular, Americans seem to wear masks more often if they understand the importance of wearing masks and believe the extent of the pandemic.

Observing other societies, specifically in East Asia, wearing masks, in many cases, is mandated by the government. However, in Europe and North America, wearing masks was not initially recommended for general use. In Hong Kong, a study was conducted during the 2014 influenza pandemic, where researchers found that with a lack of mandatory mask-wearing regulations, citizens showed “a low level of anxiety, fewer misconceptions regarding the novel strains, and less *[sic]* gaps between perceived usefulness and practice of preventive measures toward influenza outbreaks.”<sup>44</sup> The study suggested that increasing public awareness of current issues and best preventive measures should be done through media.

Despite a lack of evidence associating wearing masks with a significant decrease in the transmission rates in East Asia, healthcare professionals have agreed that wearing masks benefits the general public. **As mentioned earlier in this review, although wearing masks does not guarantee the prevention of COVID-19 transmission, it has no harm and can only provide benefits for the physical well-being of the public.** To address the controversy about whether people should wear masks or not, numerous studies have been conducted but showed no evidence that wearing masks offers significant protection from COVID-19 transmission. However, a review done

by Javid et al. suggests that many of these studies “were underpowered and failed to measure adherence”—where adherence to the proper wearing of masks is more significant during a pandemic, given that the public is educated on how to wear masks properly. Further, the review states that more reliable studies modeling transmission rates of other viral diseases that have been better studied give significant results demonstrating the importance of masking.<sup>5</sup>

The priority for encouraging the general public to contribute to the mitigation of COVID-19 transmission is proper education on techniques and practices that are both sustainable and simple to learn. Proper health practices will likely result in significant improvement in the number of COVID-19 cases in the future.

## The Psychology behind Wearing Masks

Although we live in a pandemic-struck world and continually hear from medical experts about the importance of wearing masks, 29% of the U.S. population does not believe that wearing masks should be done at all times.<sup>45</sup> While this percentage is partially attributed to a lack of education and improper dissemination of information, it is also important to consider the psychological aspect as to why individuals refuse to wear masks. Despite encouraging the use of masks, a cluster-randomized 2009 trial showed that after five days, participants wearing masks dropped from nearly 50% to under 25%. **Some participants stated that the discomfort of wearing masks was the biggest factor why they decided not to wear one,** while others mentioned it is the impracticality during mealtimes and the inability to fit the mask to their face.<sup>46</sup> For some, wearing a mask can trigger a false alarm of suffocating or claustrophobia that may result in anxiety.<sup>47</sup>

Different countries have employed different mask-wearing mandates. East Asian governments require wearing masks, while Europe and North American governments only recommend wearing masks in public.<sup>5</sup> In America, some people interpret the government's enforcement of wearing masks as a loss of personal liberty. The idea of wearing masks shifted from a public health method to political propaganda. America's political scene has also been exacerbating the public's negative view on wearing masks, as federal officials recommended against wearing



masks at the beginning of the pandemic and then began to propose wearing masks as the pandemic grew worse. Moreover, the public became confused when the president and other officials were seen not wearing masks despite earlier recommendations. Political power struggles, such as Georgia's governor fighting against an Atlanta mandate requiring mask wearing, created more tensions and further polarized the public in their opinions on mask wearing.<sup>48</sup>

To investigate possible solutions to unify the public's views on wearing masks, Carbon et al. showed that during the COVID-19 pandemic, people feel more comfortable and encouraged to wear masks when people around them also wear masks. This study suggests that social discomfort is a major factor in preventing individuals from wearing masks; thus, encouraging more people to wear masks lessens social discomfort.<sup>7</sup>

These studies have not only highlighted the importance of studying how psychological mechanisms affect preventative behavior during pandemics but also suggested effective ways for implementing pro-masking public campaigns. Despite the debate behind why masks are not effective and provide a false sense of security and the argument that masks are of limited supply and should be reserved for healthcare workers, wearing masks is undeniably a reliable way for source control (keeping infections within individuals) and, therefore, transmission reduction.<sup>6</sup> Furthermore, a population study performed in China found that those who wore masks regularly had lower levels of anxiety and depression compared with those who did not wear masks, regardless of the presence of symptoms. Wang further argued that any confusion or anxiety caused by wearing masks and not wearing masks were the results of an unbalanced distribution of information and a lack of clear guidelines established for appropriate masking techniques.<sup>38</sup> With the ease of access to information in current times through mobile devices and media platforms, conspiracy and misinformation spread quickly, inappropriately introducing biased thinking and politicizing into a scientific approach. A unified encouragement of correct masking using policies, along with better regulation and dissemination of information, will lead to eventual acceptance by the public, with lasting benefits in both health- and psychology-related aspects.

From a strict medical stance, wearing masks is a relatively low-cost, effective method that can reduce the

need for other costly measures (such as testing, contact tracing, and complete isolation). Furthermore, by considering the psychological perspective, wearing masks may successfully shift the focus from debates with social norms to an instilled sense of altruism and serve as a unifying mechanism for the world to act against the pandemic.

## Conclusion

The COVID-19 pandemic has caused unprecedented medical, social, and economic costs globally in just a matter of months. Millions of Americans were infected, and the number of COVID-19-related deaths already passed 266,000 at the time of writing. Until an effective treatment or widespread vaccination becomes available, effective public health measures are our best method to slow down and prevent the spread of COVID-19. The current strategies of the CDC strongly recommend that all people two years of age and older wear a mask in public settings where social distancing is challenging to maintain. Due to the lack of a unified approach in preventing the spread of COVID-19, the U.S. top public health agency strongly urged a national need for a clear and consistent message about the mandatory wearing of masks. While several European and Asian countries already implemented masking mandates in March and April 2020, the US is still debating the need for a national mandate for people to wear masks despite evidence of benefits and a strong recommendation from the country's top health experts. It is clear that the majority of Americans are in favor of wearing masks when going out and believe in its benefit. There is still a significant number of people who are resistant to cloth face coverings and against the idea of mandated mask wearing. Across the country, counties and states continue to take their own approaches in dealing with the resurgence of new COVID-19 cases. The resistance from a minority of Americans against a broad adoption of cloth face coverings seems to be associated with their political affiliations and centers on the belief that their personal liberty is being taken away. In addition, many view not wearing a mask as a cultural and political symbol of freedom. While issuing a limited mandate of public masking remains a political debate, the public clearly needs a consistent message across all levels of government regarding wearing masks when going out

or being close to others in public. A broad adoption of cloth mask wearing should be viewed as a civic duty and cost-effective intervention that can slow down and prevent the spread of COVID-19. Several leading public health experts believe that nationwide adoption of public cloth mask wearing for everyone would effectively control this epidemic in a matter of weeks. As a result,

it is important for our public health system to continue their efforts in educating the public about the benefits of wearing masks. Equally important, Americans need a unified and consistent message from our leaders to avoid any unnecessary confusion in our fight against COVID-19 to protect all of us, especially our vulnerable populations. ▮

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## Multiple-Choice Questions

**61. Which population is the most vulnerable to COVID-19?**

- A. People in low socioeconomic classes
- B. The homeless
- C. People with a high school diploma
- D. People with a college degree

**62. Which of the following is *not* a psychological factor behind the resistance to wearing masks in public?**

- A. Political affiliation
- B. Not wearing masks as a symbol of freedom
- C. Personal liberty being taken away
- D. Discomfort

**63. According to the lesson, what is the current recommendation by the Centers for Disease Control regarding the use of masks in public settings?**

- A. For it
- B. Against it
- C. Neither for nor against
- D. Defer to the local government

**64. What is the current evidence showing the benefits of wearing masks in preventing the spread of COVID-19?**

- A. No evidence
- B. Strong evidence
- C. Some evidence
- D. No studies done yet

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# Best Practices in Continuing Medical Education

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## A Review of the Impact of Wearing Masks on COVID-19 Transmission and the Psychology behind Resistance to Wearing Masks

By Hai Le, MD; Harvey Zhou; Brittany Nguyen; Asim A. Shah, MD

ID#: L003458

**This valuable take-home reference translates research and theory presented in the accompanying continuing medical education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

The information in this lesson is meant to educate mental health professionals, primary care providers, and public health professionals about the COVID-19 pandemic and the benefits of face mask wearing in preventing the spread of the virus and lowering the severity of the COVID-19. The other aim of this lesson is to provide an overview of the benefits of different types of face masks in different settings and current CDC guidelines on masking in public. While the benefits of wearing face masks in public have been increasingly emphasized by the nation's top public health and infectious disease experts, the practice continues to stir up debates and controversies. This lesson also highlights the psychology of resistance of a part of the public in the United States against mandated face mask wearing in public.

#### **Key Point 1: COVID-19 Pandemic and the Role of Face Mask Wearing in Preventing the Spread of the Virus**

**The COVID-19 pandemic requires a comprehensive approach from the public health perspective to contain and control the further spread and damage of this deadly virus. The benefits of mask wearing in public have been established; however, the practice is not well enforced or implemented in the United States, as evidenced by the lack of concerted effort from different government levels.**

#### **Key Point 2: Evidence of the Benefits of Mask Wearing in the Public and the Current Guidelines from the CDC**

**Multiple studies of past epidemics and the current pandemic have suggested the benefits of wearing face masks in public as one of the most helpful tools in preventing the spread of SARS-CoV-2 and limiting the disease damage. Current CDC guidelines also strongly recommend the proper use of face masks when individuals are in public.**

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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### **Key Point 3: Vulnerable Populations That Are at Higher Risk of Contracting COVID-19**

**COVID-19 affects everyone across the country but not equally. Public health data show that a disproportionate number of people in vulnerable populations are at a substantially higher risk of contracting the virus; among them are homeless people, individuals in crowded settings such as nursing homes and shelters, healthcare workers, and people in low socioeconomic classes.**

### **Key Point 4: The Psychology behind Resistance against Wearing Masks in the Public**

**Although some individuals find wearing face masks as a cause of anxiety due to claustrophobia and a false alarm of suffocating, the primary resistance to mask wearing, at least in a part of the U.S. population, stems from cultural and political ideologies.**

# Neuropsychiatric Complications of COVID-19

Mohammad F. Naqvi, MD; Syed Z. Iqbal, MD; Hai Le, MD;  
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*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** COVID-19 pandemic • Intensive care unit • Neuropsychiatric sequelae • Delirium • Posttraumatic stress disorder

**LEARNING OBJECTIVES:** Upon completion of this lesson, the clinician will be able to (1) describe the effects of COVID-19 on the central nervous system; (2) delineate the neuropsychiatric manifestations during previous viral epidemics and pandemics; and (3) explain methods of treating patients with the neuropsychiatric complications of COVID-19 and managing the disease.

**LESSON ABSTRACT:** There is an increasing amount of evidence of neuropsychiatric disorders in patients with COVID-19 both during and after the infection. Symptoms of these disorders—which have included mood lability, fatigue, depression, and anxiety—were also seen during previous coronavirus outbreaks. Delirium and posttraumatic stress disorder have been observed in patients with severe COVID-19 who required admission to an intensive care unit. The increasing global burden of this disease will likely lead to a greater need for attention to its neuropsychiatric effects after the disease has ended. Currently, the chronic neuropsychiatric aspects of COVID-19 require additional study. This review explores the neuropsychiatric sequelae of COVID-19 as they have been observed globally and suggests optimal methods for identifying and managing such complications.

**COMPETENCY AREAS:** This lesson addresses the gaps in learning in the areas of knowledge, patient care, and practice-based learning related to the neuropsychiatric complications of COVID-19. Since much is still being learned about this virus, several clinicians lack an understanding of the short- and long-term effects of COVID-19 on the neuropsychiatric wellness of patients. Upon conclusion of this lesson, readers will have a better understanding of how COVID-19 infects patients, and affects the central nervous system, the neuropsychiatric complications observed in previous pandemics and epidemics, the neuropsychiatric manifestations of COVID-19, and how to prevent, treat, and manage these complications.

## Introduction

At one point, COVID-19 had the entire world on lockdown. Flights have been restricted, businesses have been shut down, schools are operating online, and almost everyone is (or should be) practicing “social distancing.” Formally referred to as SARS-CoV-2, the coronavirus responsible for the COVID-19 pandemic is similar to the viruses responsible for *severe acute respiratory syndrome* (SARS) and *Middle East respiratory syndrome* (MERS);<sup>1</sup> each was responsible for its own pandemic (SARS: 2002-2004; MERS: 2012). Since the initial outbreak of COVID-19 in December 2019, the virus responsible for this disorder has spread from its site of origin in Wuhan, China, to more than 200 other countries and territories across the globe. As of August 2020, more than 17 million cases of this disease have been confirmed, and it has been responsible for approximately 680,000 deaths.<sup>2</sup> The first confirmed case in the United States was reported on January 20, 2020; since then, more than 12.1 million cases and 255,958 deaths have been reported in the United States alone.<sup>3</sup>

Compared with previous viral outbreaks, the COVID-19 pandemic has been one of the most infectious and has spread the fastest across the globe. Interestingly, it has thus far been relatively less deadly than other pandemics. For example, the SARS and MERS outbreaks involved significantly fewer cases than COVID-19 (8439 and 2519, respectfully, vs 680,000 with COVID-19) but resulted in considerably higher death rates (9.6% and 34.3%, respectively, vs an estimated 1.38%-3.40% with COVID-19).<sup>4</sup> As of August 2020, it had not reached the severity of the 2009 H1N1 flu pandemic, which resulted in 60.8 million cases, or the 1918 influenza outbreak, which resulted in 500 million cases and 50 million deaths. Even the seasonal flu is much more severe, infecting approximately 1 billion individuals annually across the globe, with 5 million cases categorized as severe, and resulting in 291,000 to 646,000 deaths.<sup>5</sup> These comparisons are not absolutely reliable, however, given that the COVID-19 pandemic is still ongoing.

The coronavirus is thought to spread primarily from person to person in respiratory droplets released by an infected individual when that person sneezes or coughs. These droplets can land in the mouth or nose of another individual, who may readily inhale them into the lungs.

The risk of viral spread is high when the recipient of these droplets is within six feet of the infected individual. There is a two-week incubation period, although most individuals develop the initial symptoms within five days of being infected. Hosts with preexisting conditions such as diabetes, hypertension, and obesity are at increased risk of infection. It was initially thought that individuals aged 50 years or older are also at an increased risk, but the virus has also infected younger individuals with no preexisting conditions, and even children.

The primary symptoms of the virus include fever, cough, loss of appetite, fatigue, and muscle pain; thus, it is difficult to distinguish COVID-19 from the flu or the common cold.<sup>6</sup> In severe cases, the individual has difficulty breathing and shortness of breath and, as a result, requires prolonged hospitalization. In a case series based on 5,700 patients admitted to multiple hospitals in New York City with a confirmed diagnosis of COVID-19, 14.2% were treated in the *intensive care unit* (ICU), 12.2% received invasive mechanical ventilation, 3.2% received a kidney transplant, and 21% died.<sup>7</sup>

The virus mainly attacks the upper respiratory system however, in severe cases, it has affected multiple organ systems. Reports show that one in three patients exposed to COVID-19 could experience neurological or psychological consequences from their infection, including symptoms such as headache, dizziness, loss of smell or taste, and even stroke.<sup>8,9</sup> Prolonged hospitalization and possible encephalitis caused by viral infection have been associated with neuropsychiatric complications. This lesson provides information that may be helpful to healthcare providers in determining how COVID-19 affects the *central nervous system* (CNS) by recognizing its neuropsychiatric manifestations (as presented in previous viral epidemics and pandemics), developing methods of treating patients with this infection, and managing the neuropsychiatric complications of the disease.

## How COVID-19 Affects the Central Nervous System

The coronavirus is a single-stranded RNA virus with an outer envelope characterized by a distinct crown-like morphology.<sup>8</sup> The clinical expression of infection with the SARS-CoV-2 virus—the coronavirus responsible for COVID-19—depends on the angiotensin II converter

enzyme (ACE-II) acting as an internalization receptor.<sup>9</sup> The clinical expression of this virus occurs in three phases: The initial phase involves a large replication of the virus and manifests as fever and cough;<sup>9</sup> the second phase is associated with a high fever, hypoxia, and the production of bilateral respiratory infiltrates (pneumonia), as well as a decrease in viral load toward the end of this phase;<sup>9</sup> the third phase is characterized by a continued decrease in viral load and an exaggerated immune response called a “cytokine storm,”<sup>9</sup> which results in approximately 20% of patients developing *acute respiratory distress syndrome* (ARDS) and an increase in mortality.<sup>9</sup> **In addition to the respiratory symptoms associated with this virus (which range in severity from symptoms of the common cold to a severe case of ARDS),<sup>10</sup> SARS-CoV-2 can affect the CNS directly by interacting with CNS tissue and indirectly by triggering cytokine network dysregulation, peripheral immune cell transmigration, and postinfection autoimmune damage.<sup>11</sup> Its direct effect may occur when it binds to ACE-II receptors—which are present on glial cells, neurons, and brain vascular endothelium<sup>9</sup>—and then spreads to the CNS directly from the cribriform plate toward the olfactory bulbs, causing anosmia and hyposmia.<sup>12</sup> The virus can also reach the CNS hemodynamically, damaging endothelial cells along the way and causing intracranial bleeding during the acute phase of the infection.<sup>9,10</sup> SARS-CoV-2 may also spread to the CNS through anterograde or retrograde transport being carried by the motor proteins kinesin and dynein through sensory and motor nerve endings.<sup>11</sup> The acute respiratory failure associated with COVID-19 may occur, in part, as a result of direct viral damage to the brainstem.<sup>11</sup> Its indirect effects may occur due to chronic neuroinflammation caused by high levels of cytokines released during the immunological response, as is seen during the pathogenesis of neurodegenerative disorders such as multiple sclerosis or Parkinson’s, Huntington, or Alzheimer’s disease.<sup>9</sup> Thus, the cytokine storm associated with ARDS may be a result of a neurodegenerative disorder.<sup>9</sup>**

## Neuropsychiatric Disorders Observed during Previous Epidemics/Pandemics

Studies of the two previous coronavirus pandemics (SARS and MERS) have revealed that delirium was common

during the acute stage of each infection.<sup>12</sup> Insomnia, emotional lability, irritability, pressured speech, and euphoria were relatively common,<sup>12</sup> but these symptoms could have been related to the use of corticosteroids to treat these patients.<sup>12</sup> The infection may also be associated with depression, anxiety, fatigue, *posttraumatic stress disorder* (PTSD), mania, and psychosis, although the incidence of mania and psychosis has been minimal. The one-year pooled prevalence of depression, anxiety, and PTSD in patients who survived the critical phase of the illness was 29%, 34%, and 34%, respectively.<sup>12</sup> **Post-infection recovery periods ranged from 6 weeks to 39 months. Fifteen percent of patients during this recovery period exhibited symptoms of PTSD, sleep disorders, emotional lability, poor concentration, fatigue, and memory impairment.<sup>12</sup>** Overall, health-related quality-of-life measures were lower in patients with SARS compared with controls.<sup>12</sup>

Reports of the appearance of various neuropsychiatric symptoms (including depression, anxiety, mania, psychosis, and delirium) during influenza pandemics date back as far as the 18th and 19th century.<sup>13</sup> The Spanish flu (1918-1919)<sup>12</sup> was associated with an inflammatory disorder called encephalitis lethargica, which was associated with hypersomnolence, psychosis, catatonia, and Parkinsonism.<sup>13</sup> An increase in the prevalence of narcolepsy, seizures, encephalitis, encephalopathy, Guillain-Barré syndrome, and other neurological and neuromuscular disorders was observed following the 2009 H1N1 influenza pandemic and other coronavirus pandemics, including the SARS and MERS pandemics.<sup>13</sup>

Neurocognitive impairment could develop following admission to an ICU.<sup>12</sup> In Hong Kong, 110 patients with SARS who had been treated in the ICU were followed up on an outpatient basis after being discharged from the hospital to be monitored for lung function capacity and functional disability.<sup>14</sup> No difference in lung function, exercise capacity, or health status was identified between intubated and nonintubated patients one year after discharge.<sup>14</sup> Functional disability seemed to be out of proportion with the degree of lung function impairment, however.<sup>14</sup> Persistence of abnormal lung function was seen in only one-third of patients one year after recovery.<sup>14</sup> Despite the improvement in lung function, patients were not as physically active as they were before their illness



because of extrapulmonary factors, including steroid- or virus-induced myopathy or polyneuropathy, as well as psychosocial stressors.

Prolonged isolation and uncertain treatment due to a lack of prior knowledge of these novel illnesses may increase the risk for mood disturbances and psychosis in some patients.<sup>14</sup> The seropositivity of other human coronavirus strains (e.g., HCoV-NL63) has been associated with a history of mood disorder and suicide attempts.<sup>13</sup>

**Studies of the SARS-CoV-1 pandemic have shown that 54.5% of survivors were diagnosed with PTSD,** 39% with depression, 36.4% with pain disorder, 32.5% with panic disorder, and 15.6% with obsessive-compulsive disorder lasting 31 to 50 months post infection.<sup>13</sup> By comparison, the preinfection prevalence rate was 3%.<sup>13</sup> Studies have established a relationship between a history of influenza and risk for psychosis.<sup>13</sup> In two studies, antibodies against several strains of coronavirus were found in patients with symptoms of psychosis.<sup>13</sup> Conclusions about the neuropsychiatric outcomes of infection should be drawn cautiously in the current COVID-19 pandemic, however, because data regarding its acute effects are still preliminary and only a limited amount of data are available regarding the postillness phase.

## Neuropsychiatric Manifestation of COVID-19

The clinical manifestation of COVID-19 can range from asymptomatic or mild symptoms to severe symptoms, including symptoms of pneumonia, ARDS, myocarditis, acute kidney injury, stroke, encephalitis, and multi-organ failure.<sup>10</sup> A severe infection is anticipated in 15% to 20% of the population, and 5% will develop ARDS.<sup>15</sup> The fatality rate ranges from 2% to 3%.<sup>15</sup> The neuropsychiatric presentations of COVID-19 can be divided into acute, subacute, and chronic manifestations, depending on the progression of the disease.<sup>13</sup>

Neurological disorders that have appeared during the current pandemic include anosmia, stroke, encephalopathy, encephalitis, meningitis, seizures, dysexecutive syndrome, neuromuscular disorders, and Guillain–Barré syndrome.<sup>15</sup> Anosmia and hyposmia are often the only presenting symptoms.<sup>11</sup> In a retrospective study (N = 114), almost half (47%; n = 54) of the patients reported symptoms of

anosmia.<sup>11</sup> This may be the most common neurological presentation in otherwise asymptomatic patients in their early 20s.<sup>11</sup> Acute cerebrovascular disease, which is often responsible for ischemic (and less often hemorrhagic) stroke, may be seen following tissue damage caused by ACE-II depletion, particularly when this depletion is triggered by sepsis-induced coagulopathy. Studies have shown that only 5.7% of patients with severe COVID-19 symptoms develop a stroke, however.

In case studies from Wuhan, China, one out of five individuals with COVID-19 who were admitted to hospital presented with encephalopathy. These included patients exhibiting a change in mental status lasting longer than 24 hours.<sup>13</sup> Delirium accompanied by significant agitation, rigidity, abulia, and alogia is another important sequela of COVID-19 infection.<sup>16</sup>

Studies of the prevalence of neuropsychiatric manifestations in patients with COVID-19 have been carried out based on data obtained from the global health collaborative research platform. In a study of 40,496 patients with COVID-19, 9086 (22.5%) showed evidence of neurologic conditions,<sup>10</sup> including headache (3.7%), sleep disorders (3.4%), encephalopathy (2.3%), myalgia (2%), loss of taste and smell (1.2%), stroke and transient ischemic attacks (1%), dizziness (0.9%), movement disorders (0.7%), seizures (0.6%), polyneuropathy (0.6%), and nerve root and plexus disorder (0.4%).<sup>10</sup> The most common psychiatric disorders included anxiety disorders (4.6%), and mood disorders (3.8%).<sup>10</sup>

In a study conducted in the Netherlands involving 187 ICU patients, 31% developed thromboembolic complications; of these, pulmonary embolism was the most common thrombotic complication, affecting 81%.<sup>17</sup> In a UK-based surveillance study of 153 patients diagnosed with COVID-19, of whom 125 produced a complete data set, 77 (62%) experienced a cerebrovascular event.<sup>18</sup> Of these patients, 57 (74%) had an ischemic stroke, 9 (12%) experienced an intracerebral hemorrhage, and 1 (1%) developed CNS vasculitis.<sup>18</sup> Interestingly, 39 (31%) patients presented with an altered mental status, including 9 (23%) with unspecified encephalopathy and 7 (18%) with encephalitis.<sup>18</sup> The remaining 23 (59%) patients with an altered mental status received a psychiatric diagnosis,<sup>11</sup> which included: new-onset psychosis (n = 10; 43%), neurocognitive dementia-like syndrome



( $n = 6$ ; 26%), and an affective disorder ( $n = 4$ ; 17%).<sup>18</sup> Thus, after stroke, altered mental status was the most common presentation.<sup>18</sup> Retrospective case series studies conducted in Wuhan, China, also revealed neurological symptoms in patients with severe COVID-19; these included acute cerebrovascular accidents and altered level of consciousness.<sup>11</sup> A study of deceased individuals in China showed that they had experienced altered sensorium (22%) and hypoxic encephalopathy (20%).<sup>15</sup> As with other human coronaviruses, SARS-CoV-2 can result in postinfectious acute disseminated encephalomyelitis/brain stem encephalitis over time.<sup>11</sup> This is of particular concern, given that SARS-CoV-2 RNA was detected in the cerebrospinal fluid of a patient in Japan with clinically proven meningoencephalitis.<sup>11</sup>

Data from various sources—including postmortem, in vitro, and animal studies—suggest that coronavirus exposure can result in psychiatric symptoms such as auditory and visual hallucinations, mania, and depressive disorder.<sup>8</sup> The relationship between coronavirus and mental health disorders was studied by measuring the response of IgG production to four human coronavirus strains (229E, HKU1, NL63, and OC43) in 106 patients with recent-onset symptoms of psychosis and 196 non-psychiatric controls.<sup>8</sup> IgG levels were significantly higher than controls in patients with the HKU1 strain ( $P = \leq 0.002$ ) and NL63 strain ( $P = \leq .00001$ ),<sup>8</sup> the latter being associated with schizophrenia-spectrum disorder (OR = 3.10; 95% CI: 1.27-7.58;  $P = \leq .013$ ).<sup>8</sup> Evidence suggests that 0.9% to 4.0% of patients infected with COVID-19 develop a psychotic spectrum disorder.<sup>15</sup> Symptoms of psychosis may develop secondary to viral illness or psychosocial stress or as a side effect of the treatment provided.<sup>15</sup>

Because the pandemic is ongoing, only limited data are available regarding the relationship between COVID-19 and psychiatric symptoms.<sup>13</sup> Long-term follow-up of survivors of this illness is crucial to determine the neuropsychiatric effects of this disease.

## Prevention, Treatment, and Management of Neuropsychiatric Complications of COVID-19

Early detection and identification of neuropsychiatric conditions and their consequences in patients with

COVID-19 will be helpful for the effective management of these complications.<sup>19</sup>

### Olfactory and Gustatory Dysfunction:

The American Academy of Otolaryngology–Head and Neck Surgery suggests that patients with an acute onset of smell or taste dysfunction, even in the absence of other COVID-19 symptoms, should either self-isolate or be tested for the virus. When possible, a psychophysical assessment that includes the use of odorants or tastants is recommended to diagnose impairment or assess improvement of olfactory function. **Specific treatment for olfactory dysfunction is not required because most COVID-19–related symptoms usually improve and resolve spontaneously within two weeks.** If the impairment lasts longer than two weeks, treatment should be considered, even though the efficacy of current treatments for COVID-19–related olfactory dysfunction has not been well established. Treatments for postinfection olfactory dysfunction may be beneficial for COVID-19 patients. Studies have shown improved olfaction after three months of olfactory training, which consists of repeated and deliberate sniffing of a set of odorants (such as lemon or cloves) for 20 seconds each, twice a day. Because of the potential risk of harm and the lack of evidence of any benefit, oral and intranasal corticosteroids are not currently recommended for patients with postinfectious olfactory dysfunction. Medications such as sodium citrate, intranasal vitamin A, and systemic omega-3 have shown promise against postinfectious olfactory dysfunction, but there is no clear evidence that they are effective against olfactory dysfunction in COVID-19 patients.<sup>20</sup>

### Impaired Consciousness and Delirium:

A change in mental status can be a presenting feature of COVID-19; therefore, hospitals should include tests for this phenomenon as part of their diagnostic procedure.<sup>16</sup> An easy but validated method of screening for delirium should be used to identify delirium as early as possible in patients with COVID-19. **Hospitalized patients with COVID-19 should be screened routinely for delirium using dedicated psychometric tools, such as the *Confusion Assessment Method*.** Management of delirium in critically ill ICU patients is exceedingly challenging. Delirium rates among mechanically ventilated ICU patients are particularly high—as much as 75%. Delirium is an

independent predictor of the duration of hospital stay, as well as mortality, cost of care, and risk of dementia. **No pharmacological interventions are recommended for preventing and treating ICU patients with delirium.** The use or overuse of sedatives and anticholinergic agents should be avoided in such patients, as well as prolonged time in the ICU or on a ventilator. Delirium should be managed empirically because it is an immediate indicator of worse survival and affects the cost of care and quality of survival. Nonpharmacological interventions are vital, even in the context of the social distancing required during this pandemic. **The Society of Critical Care Medicine recommends implementing a safety bundle called the ABCDEFs (Assessment/treatment of pain, Both Spontaneous Awakening Trials and Spontaneous Breathing Trials, Choice of sedation, Delirium, Early mobility, and Family presence), which has been shown to reduce the delirium rate among patients on mechanical ventilation by 50%.** It is also recommended that providers follow well-established delirium treatment guidelines such as eCASH (early Comfort using Analgesia, minimal Sedatives, and maximal Humane care) and the Society of Critical Care Medicine guidelines.<sup>21</sup>

### Ischemic Stroke:

The discovery of acute stroke by neuroimaging is a strong indicator of a poor prognosis.<sup>22</sup> A recent study involving New York City cases revealed an unusually high incidence of new-onset, large-vessel stroke in patients with COVID-19: five cases were diagnosed during a two-week period in March 2020 in patients younger than 50 years of age. When a procoagulant pattern is seen in patients with COVID-19—especially in severe cases, in which fibrinogen and D-dimer elevation correlate with the severity of the disease—antithrombotic therapy is recommended.<sup>23</sup>

### Post-ICU PTSD:

Traumatic events in the ICU may include having delirium-related hallucinations, witnessing distress in other patients, seeing or hearing (or learning about) other patients dying, experiencing invasive medical procedures, receiving bad news about diagnosis and prognosis, or experiencing perceived mistreatment. Seeing institutional staff members wearing personal protective equipment can make patients feel more anxious and frightened, especially

when the patient is delirious. Restriction of family visits further increases the sense of isolation and helplessness and removes opportunities for much-needed reassurance and support. Symptoms of PTSD may emerge immediately after the ICU stay or may be delayed in onset and, thus, may become less of a primary focus of care, given that physical recovery remains a priority.<sup>24</sup>

In a randomized clinical trial of the effect of a nurse-led preventive psychological intervention on symptoms of PTSD in critically ill patients in the United Kingdom, researchers found that complex psychological interventions did not significantly reduce the severity of PTSD symptoms reported by patients six months after their ICU stay.<sup>25</sup>

Early interventions by clinical psychologists may reduce the probability of a diagnosis of PTSD 12 months after discharge. Studies have provided evidence that such interventions may help critically ill trauma patients recover from acute and stressful experiences. Early intervention programs may be the most effective ways to prevent PTSD in survivors of critical illness. The UK National Institute for Health and Care Excellence recommends trauma-focused cognitive-behavioral therapy to reduce subsequent trauma symptoms.<sup>26</sup>

### Guillain–Barré Syndrome, Polyneuritis, and Encephalitis:

Critically ill COVID-19 patients are at high risk of polyneuropathy due to prolonged periods of immobilization, sedation, and ventilation. Polyneuropathy, as well as sepsis and multiorgan dysfunction, may also occur secondary to the administration of neuromuscular blocks and corticosteroids. Neuropathic pain may arise as an adverse effect of disease-modifying investigational medications such as lopinavir, ritonavir, and hydroxychloroquine. There have also been case reports of Guillain–Barré syndrome arising as a complication of COVID-19. These patients were treated using intravenous immunoglobulin, with some evidence of success.<sup>27</sup>

The number of cases of COVID-19–related encephalitis remains low. This condition is usually caused by infection or by the body's immune defenses. It usually presents with typical neurological symptoms of encephalitis such as irritability, confusion, and reduced consciousness. No specific treatment is recommended, and a clinical trial is unlikely because of the low number of cases.<sup>28</sup>

## Headache:

In a meta-analysis of 61 studies, headache was present in 12% of patients with COVID-19, making it the fifth most common clinical feature of this infection. Headache was reported more frequently by females than males, and it was more prevalent in young patients than in older patients. No particular treatment is recommended for COVID-19–related headaches. It is suggested that providers consider a careful pain management approach to provide relief.<sup>5</sup>

## Psychosis:

If a COVID-19–psychosis relationship is proven to exist, then effective treatment of the viral infection and management of the inflammation associated with it would be as important as the use of antipsychotics in patients with symptoms of psychosis.<sup>29</sup> In some cases, the onset of psychotic symptoms in patients with COVID-19 appears to be related to the administration of steroids to treat the

infection. There has been limited evidence that a low dose of an antipsychotic medication, such as aripiprazole, is effective against psychosis associated with the infectious disease or its psychosocial stressor.<sup>30</sup>

## Conclusion

The rising incidence of COVID-19 may be distressful, but it will allow us to learn more about the neuropsychiatric complications of this disease. Anosmia appears to be the most common neurologic sequela of this infection; other neuropsychiatric complications that have been seen with this disease include delirium, cerebrovascular events, and PTSD. Many of these complications are a direct result of the effect of the virus on body tissues or the effects of medications used to treat the disease; however, some occur as a result of prolonged hospitalization and quarantine. Early detection and management of these neuropsychiatric sequelae may help prevent their long-term negative effects. ■

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## Multiple-Choice Questions

**65. All of the following statements about the human coronavirus are true, *except*:**

- A. Symptoms of the human coronavirus can progress from mild illness such as the common cold to severe acute respiratory distress syndrome.
- B. They are double-stranded DNA viruses.
- C. SARS-CoV-2 has affected a large proportion of the population because of its high infectivity and pathogenicity.
- D. The human coronavirus mediates its effects by acting on the angiotensin enzyme inhibitor angiotensin-converting enzyme II.

**66. All of the following statements about the clinical expression of SARS-CoV-2 are true, *except*:**

- A. It involves angiotensin-converting enzyme II receptors, which are present on glial cells, neurons, and the vascular endothelium.
- B. Its clinical expression involves three phases, of which the initial phase includes large-scale replication of the virus manifesting as fever and cough.
- C. Ten percent of patients develop acute respiratory distress syndrome.
- D. It can affect the central nervous system both directly and indirectly.

**67. Which of the following statements about the previous pandemics and epidemics is true?**

- A. Delirium was not commonly observed in the acute stage of SARS and MERS infection.
- B. Mania and psychosis were observed in the majority of patients.
- C. SARS infection did not affect health-related quality-of-life measures compared with controls.
- D. During the recovery period following SARS and MERS infections (6 weeks - 39 months), 15% of patients exhibited symptoms of PTSD and other disorders.

**68. Studies of neuropsychiatric symptoms in SARS CoV-1 survivors revealed the following:**

- A. Depression was the most common sequela in survivors.
- B. About 54.5% of patients develop PTSD symptoms.
- C. Twenty-five percent of patients develop a panic disorder.
- D. Twenty percent of patients develop obsessive compulsive disorder.

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# Best Practices in Continuing Medical Education

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## Neuropsychiatric Complications of COVID-19

By Mohammad F. Naqvi, MD; Syed Z. Iqbal, MD; Hai Le, MD;

Komal Nathani, MD; Asim Shah, MD

ID#: L003459

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

The information in this lesson is intended to educate mental health professionals, primary care providers, psychologists, and anyone else who works with patients infected with COVID-19 about the significant neuropsychiatric complications of this infection and the influence of prolonged hospitalization on the incidence of such complications. There is an increasing amount of evidence of neuropsychiatric presentations in COVID-19 patients, both during and after the infection. These symptoms—which have included mood lability, fatigue, depression, and anxiety—were also seen during previous coronavirus outbreaks. COVID-19 patients with severe illness who require admission into an ICU appear to be at a particularly high risk for post-ICU PTSD. The increasing burden of COVID-19 across the globe will likely lead to a greater need for attention to its neuropsychiatric effects after recovery from the illness. Currently, the chronic neuropsychiatric aspects of COVID-19 require additional study. The aim of this review is to detail the neuropsychiatric sequelae of COVID-19 as they have been observed thus far and suggest methods healthcare providers can use to identify and manage such complications today and in the future.

### Key Point 1: COVID-19 Central Nervous System Involvement

**The spread of COVID-19 to the central nervous system likely leads to complications through its direct effect on the brainstem and indirectly through neuroinflammation caused by high levels of cytokines. The clinical expression of angiotensin-converting enzyme II helps facilitate the direct invasion of the central nervous system, which may lead to acute respiratory distress syndrome.**

### Key Point 2: Past Epidemic Neuropsychiatric Manifestations

**Previous coronavirus outbreaks suggest that neurocognitive impairments may be sequelae following ICU admission. The limited availability of data obscures mental illness issues after recovery; however, they include increased incidence of depression, anxiety, and PTSD.**

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The information presented herein is based upon the content in the associated CME lesson. If you have comments or feedback about this page, please send your feedback via email to: [editorial@hatherleighpress.com](mailto:editorial@hatherleighpress.com) and reference the ID number under the title to which you are referring. We will review your commentary which may be used for publication.

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### **Key Point 3: Observed Neuropsychiatric Manifestations of COVID-19**

Neuropsychiatric presentations occur in three phases: acute, subacute, and chronic. The acute phase is characterized by symptoms such as stroke, encephalopathy, hypercoagulable state, and neuropathy. The subacute stage is characterized by anosmia (which is seen in approximately half of patients) and delirium. The chronic phase may be characterized by postviral acute disseminated encephalomyelitis and psychotic symptoms that arise secondary

to psychological stress or as side effects of treatment. Chronic issues will need further study to determine the neurocognitive effects of COVID-19 in survivors.

### **Key Point 4: Need for Long-Term Follow-Up with COVID-19 Patients**

At this time, more observation of the neuropsychiatric consequences of COVID-19 is essential, given the growing global burden of this disease. Patients with COVID-19 should be observed for the development of chronic issues, such as ICU-related PTSD, neuromuscular disorders, and dementia.

# A Review of Psychopharmacotherapy for Geriatric Depression, Part 1

Mujeeb U. Shad, MD, MSCS

*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Pharmacotherapy • Geriatric • Depression • Review

**LEARNING OBJECTIVES:** This lesson is a review of currently available antidepressants to manage geriatric depression, followed by an evidence-based discussion of the efficacy and tolerability of antidepressants in older adults. Moreover, this review lays the foundation for the mechanism of action-based learning to promote safe and effective use of antidepressants, especially those without formal studies in the geriatric population. This foundation will allow clinicians various options for selecting antidepressants in a high-risk population known for suboptimal response, treatment resistance, increased vulnerability from adverse effects, age-related changes in drug disposition, and high prevalence of polypharmacy. Augmentation strategies in managing *treatment-resistant depression in older adults* (TRDOA), including strategies in major depression with cognitive dysfunction, are also reviewed in this lesson.

**LESSON ABSTRACT:** The geriatric population is at significant risk for *major depressive disorder* (MDD), which may frequently offer a treatment challenge due to age-related changes in drug disposition, frequent medical and substance use comorbidities, and high prevalence of polypharmacy with increased risk for drug interactions. A large number of older adults may be treatment-refractory and may require a trial of antidepressants that are relatively new and/or not investigated in this patient population, although several evidence-based antidepressant treatment options exist to manage MDD. Therefore, this review presents findings from major antidepressant clinical trials and reviews clinically relevant and mechanism-based psychopharmacology of antidepressants, including those that have not been studied in the geriatric population. Consequently, augmentation strategies will also be reviewed for TRDOA, including those with cognitive dysfunction. Lastly, this review facilitates a better understanding of basic psychopharmacological concepts to optimally and effectively use antidepressants in a psychiatrically and medically vulnerable geriatric population.

**COMPETENCY AREAS:** Readers will have gained knowledge of the clinical pros and cons of using different mechanism-based classes of antidepressants in older adults with MDD upon the conclusion of this lesson. Thus, the audience will not only learn current evidence-based antidepressant treatment for MDD but also gain knowledge on how to safely and effectively use these antidepressants in a patient population with age-related vulnerabilities and polypharmacy. Readers will learn to distinguish each class of antidepressants' potential adverse effects, which may be of high clinical relevance in a highly vulnerable geriatric population with comorbidities, age-related changes in drug disposition, and polypharmacy. Finally, readers will learn evidence-based augmentation strategies to manage TRDOA, as well as pharmacotherapy of major depression compromised by cognitive dysfunction, frequently reported in older adults.

## Introduction

Geriatric depression is one of the most common psychiatric disorders that not only diminishes the quality of life of depressed elderly but also that of their families.<sup>1,2</sup> Also, depression in a rapidly growing population of older adults is associated with a significant cost burden for the entire community. Some older adults, especially those with late onset and presenting symptoms of anhedonia and cognitive dysfunction, may have a delayed and less robust response with antidepressants, although studies have shown similar response rates between young and elderly patients with depression.<sup>3,4</sup> Another complexity is the diagnosis of depression in the geriatric population, which can be challenging due to social isolation, communication difficulties caused by hearing or cognitive impairments, medical or other comorbidities with physical symptoms similar to those of depression, and the mental illness stigma limiting self-reporting of depressive symptoms. Major depression in this population may be associated with female gender, somatic illness, cognitive and functional impairments, social isolation, premorbid personality traits, stress, and a previous history of depression.<sup>5,6</sup> No significant age-related differences exist in the treatment of depression, and antidepressants provide first-line treatment being the most-studied treatment option. The antidepressant response can be enhanced by psychotherapy, a healthy diet, physical and social activity, and sleep hygiene, although not discussed in this review. However, electroconvulsive therapy may be the only effective option for older adults with treatment-refractory severe depression.

Multiple studies have supported antidepressant use in geriatric depression.<sup>7-17</sup> Further, a meta-analysis of 51 *randomized clinical trials* (RCTs) showed evidence to support similar response or remission rates in older versus younger adults.<sup>14,18,19</sup> Similarly, 6.7 and 6.1 older and younger adults, respectively, are needed to obtain a response to antidepressants compared with placebo.<sup>14, 19</sup> However, most studies have produced a modest response despite documenting the beneficial effects of antidepressants in older depressed patients. One meta-analysis of 15 RCTs showed that antidepressants were not found to be effective in the subgroup of patients older than 65 years.<sup>13</sup> A larger meta-analysis of

34 RCTs found an inverse correlation between increasing age and antidepressant response.<sup>15</sup> A greater burden of cardiovascular diseases, ischemic brain changes, and frequent use of suboptimal doses of antidepressants to some extent, may explain the lesser antidepressant response in older compared with younger patients.<sup>13,20,21</sup> Nevertheless, even the modest antidepressant response justifies using antidepressants in older adults due to a significant decrease in quality of life, suicidality, and high cost burden of this illness in a rapidly growing elderly population.

Although evidence-based treatment with antidepressants should be the first choice, it may be useful to have a fundamental, preferably mechanism-based, knowledge of antidepressants to facilitate its safe and effective use, even those which are relatively new and are not studied in older adults. A combination of evidence- and mechanism-based antidepressant psychopharmacology may help address the age-related vulnerabilities, comorbidities, and frequent polypharmacy in this population. This review is an effort to synthesize evidence- as well as mechanism-based information for currently approved antidepressants in the geriatric population. The following section reviews the clinical and psychopharmacological information for each class of antidepressants.

## Tertiary Amine Tricyclic Antidepressants or Nonselective Norepinephrine and Serotonin Reuptake Inhibitors

Imipramine was the first effective antidepressant serendipitously discovered in the mid-1950s, followed by a similar mechanism of action antidepressants, amitriptyline, clomipramine, doxepin, and trimipramine. This class of antidepressants has not been formally studied in the geriatric population primarily because they target multiple receptors with undesirable and nuisance adverse effects (e.g., anticholinergic, antihistaminic,  $\alpha 1$  receptor blockade, and membrane-stabilizing effects), resulting in QTc prolongation, which can be lethal in any age group, especially older adults. The adverse effects are especially problematic in the geriatric population and include orthostatic hypotension resulting in risk for falls due to  $\alpha 1$ -blocking activity; risk of a complete atrioventricular block resulting in QTc prolongation due



to membrane-stabilizing effects; and dryness of mouth, retention of urine, cognitive deficits, loss of sweating, confusion, and blurring of vision due to anticholinergic effects. Membrane stabilization is one of the main reasons for significantly narrower therapeutic indices for *tricyclic antidepressants* (TCAs) compared with other classes of antidepressants.<sup>22</sup> Consequently, the clinical use of these antidepressants even in young adults significantly declines despite their proven efficacy not only as antidepressants but also as anxiolytics.

## Secondary Amine Tricyclic Antidepressants

These antidepressants include desipramine and nortriptyline, which are the metabolites of *tertiary amine tricyclic antidepressants* (TATCAs) imipramine and amitriptyline, respectively. However, contrary to the multitarget profile of TATCAs, *secondary amine tricyclic antidepressants* (SATCAs) are relatively selective for the norepinephrine reuptake pump with a significantly lower potency to block cholinergic, histaminergic, and  $\alpha$ 1adrenergic receptors compared with TATCAs, which means that SATCAs have better tolerability even in the older population. Unfortunately, QTc prolongation persists with these metabolites, which can be as lethal as the parent compounds. A 10 times higher dose of TCA can be fatal due to a complete heart block or ventricular reentry arrhythmias.<sup>23</sup> Both nortriptyline and desipramine are almost exclusively metabolized by CYP2D6. Thus, caution is required when using these antidepressants with any drug that inhibits CYP2D6 due to increased risk for QTc prolongation.<sup>22</sup> Nortriptyline and desipramine are the only antidepressants with a therapeutic window of 50–150 and 115 ng/mL for nortriptyline and desipramine, respectively.<sup>24</sup> The clinical relevance of therapeutic drug monitoring for these antidepressants is further underscored by the reduction in the first-pass metabolism in older adults, resulting in higher plasma levels of the drugs compared with the younger population. However, in general, **SATCAs can be recommended as the second- or third-line agents for use in older adults with electrocardiogram (EKG) monitoring given the low potential for adverse effects and the advantage of dosing guided by therapeutic drug monitoring.**

## Monoamine Oxidase Inhibitors

Like the TCAs, this class of antidepressants was also a serendipitous discovery in the mid-1950s. These antidepressants inhibit monoamine oxidase A (MOA-A) and/or B (MOA-B). Although in vivo selectivity of these two isoenzymes is unclear, a mice knockout study has revealed that MAO-A preferentially oxidizes serotonin and norepinephrine, whereas MAO-B preferentially oxidizes phenylethylamine and can oxidize dopamine.<sup>25</sup> Both enzymes are found intrasynaptically in the brain and catabolize dopamine and tyramine. Further, MAO-A and MAO-B are present in the gastrointestinal system and platelets, respectively. In general, the inhibition of one of the two MAO isoenzymes is not as effective in the treatment of MDD compared with the inhibition of both. Thus, MAO-A-selective moclobemide (only available in Europe) may be less effective than nonselective *monoamine oxidase inhibitors* (MAOIs) despite some evidence of similar efficacy when compared with non-MAOIs in active-controlled studies.<sup>26</sup> **The low-dose selegiline is selective for MAO-B.** However, low-dose selegiline works in Parkinson's disease but not depression. Thus, only the higher selegiline dose, which inhibits both MAO enzymes, has been found effective for depression management as supported by the *Food and Drug Administration* (FDA) approval of a selegiline transdermal patch at nonselective doses.<sup>27</sup>

In addition to their selectivity, MAOIs are also subclassified on the reversibility of their action. Moclobemide is the only reversible MAOI, while tranylcypromine and phenelzine are irreversible and are some of the few nonselective MAOIs still in widespread clinical use. **Tranylcypromine is more activating than phenelzine because it was initially developed as an amphetamine analog and has some stimulant effects.** These irreversible MAOIs require a two-week drug-free period when switching between MAOIs and other antidepressants, including when switching to another MAOI<sup>28</sup> because the enzyme takes about two weeks to regenerate.

Despite their broad-spectrum efficacy, MAOIs have not been used as the first-line treatment for MDD due to several adverse effects, including weight gain, sexual dysfunction, headache, dizziness, and insomnia, as well as a large number of pharmacodynamics drug interactions.<sup>29</sup> **However, one of the most likely reasons for the**

**reduced use of MAOIs is the food–drug interaction between foods containing a high amount of tyramine (aged cheeses and meats, draft beer, concentrated yeast extract [marmite], sauerkraut, and soy sauce) and MAO-induced inhibition of MAO-A in the gastrointestinal tract (GI) tract, resulting in potentially fatal hypertensive crises, especially in the elderly population.** Only the nonselective doses of MAOI (inhibiting both MAO-A and MAO-B) have been found effective in the treatment of MDD, and the risk for food–drug interaction due to MAO inhibition cannot be averted. **However, moclobemide, being a reversible inhibitor of MAO-A, does not displace tyramine but is instead displaced by the tyramine, thereby averting a tyramine reaction. Consequently, moclobemide can be administered much more safely in older adults than the irreversible MAOIs.**<sup>30</sup> However, the risk of interaction with ingested tyramine may become clinically relevant with moclobemide doses >900 mg/day.<sup>26</sup> Similarly, the low-dose transdermal selegiline patch, which bypasses the GI tract despite being an irreversible MAOI, averts a tyramine reaction to require dietary restrictions but only at the lowest dose of 6 mg/day transdermal patch.<sup>27</sup> Another serious adverse effect that has minimized the use of MAOIs is the risk for serotonin syndrome when any MAOI is concomitantly used with a serotonergic drug, such as a selective *serotonin reuptake inhibitor* (SSRI) or serotonin–norepinephrine reuptake inhibitor (SNRI).<sup>31</sup> Serotonin syndrome can be clinically serious and further limits MAOI use, especially in the elderly population despite their robust efficacy.

## Selective–Serotonin Reuptake Inhibitors

Researchers were motivated to develop antidepressants that are selective for the putative mechanisms mediating their antidepressant effects (e.g., inhibitors of the serotonin transporter) to develop cleaner antidepressants to avoid the nuisance adverse effects of TATCAs and MAOIs. SSRIs do not have the adverse effects associated with TATCAs, and postmarketing experience has revealed several clinically serious adverse effects with SSRIs, especially in older adults.

Fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, and escitalopram are currently available SSRIs

frequently used primarily due to their excellent safety profile. Clinical differences between efficacy and tolerability exist, although the six SSRIs share the same mechanism of action, which is the blockade of the *serotonin transporter* (SERT). These differences can best be explained by each SSRI having different secondary pharmacologic actions other than SERT blockade, depending on their binding affinities and selectivity for these secondary targets. This concept has not been tested formally, but it is one of the very few that provides a logical explanation for these differences in efficacy and tolerability in individual patients. **For example, discouraging the use of paroxetine, especially in the geriatric population, is primarily due to its most potent secondary mechanism, which is the muscarinic blockade.**<sup>32</sup>

Different SSRIs have slightly different FDA-approved indications based on the indications submitted for approval by pharmaceutical companies. In general, this does not imply that another drug from the same class and mechanism of action will not be similarly effective for the same indication. The choice of an appropriate SSRI should include the potential for drug interactions and elimination half-life. Fluoxetine has the longest half-life of 4–6 days after chronic administration, while norfluoxetine, its primary metabolite, has a half-life of 7–15 days after acute and chronic administration.<sup>33</sup> Therefore, fluoxetine can be given once a week, preferably at a higher dose. Its long half-life allows occasional missed doses even at the usual doses without significantly affecting serum concentrations. Furthermore, with an antidepressant such as fluoxetine, few, if any, withdrawal symptoms may happen upon abrupt fluoxetine discontinuation. **However, the long half-life also means that it takes five or more weeks for the drug and its active metabolite to wash out completely. Thus, any adverse effects or drug interactions involving fluoxetine can persist up to several weeks even after the medication is abruptly discontinued.**<sup>34</sup> **A five-week drug washout period is also needed before switching from fluoxetine to an MAOI.**

In addition to half-life, age-related changes in drug disposition should also be considered when prescribing antidepressants in elderly subjects. A study reported two-fold higher plasma levels for citalopram, escitalopram, and fluvoxamine and 1.5-fold higher plasma levels for sertraline than those in younger adults. The study also

found higher plasma levels in women than in men.<sup>35</sup> A recent meta-analysis of 19 RCTs and two observational studies showed that SSRIs are better tolerated than *serotonin–norepinephrine reuptake inhibitors* (SNRIs) for acute treatment of MDD in older adults.<sup>36</sup> Citalopram, escitalopram, or sertraline should be tried first for its safety and tolerability due to a relatively lower risk for drug interactions. However, cardiotoxicity remains a concern with citalopram and its S-enantiomer, escitalopram. The dose–response curve of the SSRIs remains relatively flat once a minimal effective dose is reached, which results in 60%–80% serotonin transporter blockade. The results of a meta-analysis of studies in mixed-age patients found that slightly higher doses of SSRIs appear to be more effective,<sup>37</sup> which may not apply to an older population due to reduced tolerability.

### Adverse Effects of SSRIs:

One of the most clinically serious adverse effects associated with SSRIs is the risk of suicide, which is already high in older adults. However, unlike package insert warnings for younger patients taking antidepressants, evidence shows that antidepressants decrease the risk of suicide in the older adult population, regardless of drug class, as seen in a meta-analysis of 372 double-blind RCTs that were submitted to the FDA.<sup>38</sup> Another meta-analysis, including more than 200,000 older adults with moderate or severe depression, reported a protective effect of SSRIs on completed suicides.<sup>39</sup>

Hyponatremia (sodium levels <135 mmol/L) has been reported with SSRIs regardless of the presence or absence of clinical symptoms. Induction of syndrome of inappropriate antidiuretic hormone hypersecretion by several antidepressants, especially SSRIs and venlafaxine, appears to be the main reason for hyponatremia although its exact mechanism is unknown.<sup>40</sup> In a retrospective controlled study, about 40% of older psychiatric inpatients (average age, ~74 years) who were treated with an SSRI or venlafaxine developed hyponatremia compared with only 10% of controls.<sup>41</sup> Even mild asymptomatic hyponatremia may cause cognitive changes (e.g., attention deficits, unsteady gait, and falls), while severe hyponatremia may result in seizures, coma, and respiratory arrest.<sup>42,43</sup> Hyponatremia may be more clinically severe in older adults than the younger population. Polypharmacy makes it even worse if antidepressant-induced hyponatremia is enhanced

by concomitant use of natriuretic drugs (e.g., thiazide diuretics, carbamazepine, and oxcarbazepine)<sup>44</sup> in elderly patients. Obtaining a baseline sodium level in such high-risk patients is a good practice before starting an antidepressant associated with hyponatremia, such as SSRIs, venlafaxine (an SNRI), and vortioxetine (a multimodal antidepressant). The baseline assessment will prevent hyponatremia from being automatically attributed to the antidepressant, which may lead the patient or the provider to stop the antidepressant prematurely because several other causes for hyponatremia exist.<sup>45</sup> **A switch to a less hyponatremia-prone antidepressant (e.g., bupropion or mirtazapine) may be logical after ruling out other causes for hyponatremia.** However, bupropion carries a risk for lowering the seizure threshold and should not be used in the presence of hyponatremia, which can persist for some time after initiating the switch. Management may include fluid restriction and a gradual infusion of hypertonic saline in more severe cases of hyponatremia.

SSRI-induced osteoporosis is another adverse effect, which is mostly studied and reported with fluoxetine, resulting in hip fracture in patients with an average age of 80 years. A large cohort study found that antidepressant users sustained more than twice as many hip fractures than nonusers in the year before and the year after therapy initiation.<sup>46</sup> Antidepressants may also independently contribute to the increased risk of bone fractures, although the increased risk for fractures has been attributed to the confounding effect of depression itself. This may be caused by SSRI-induced hyperprolactinemia resulting in osteoporosis and, in turn, fractures.<sup>47</sup> The Fluoxetine Or Control Under Supervision<sup>48</sup> trial randomized acute poststroke patients (average age, 71 years) to fluoxetine 20 mg/day or placebo for 6 months and found that bone fractures were 1.4% higher in the fluoxetine compared with the placebo group.<sup>49</sup> Thus, concomitant use of serotonergic antidepressants with other drugs that have histamine type 1 (H1)-, muscarinic, and  $\alpha$ 1-receptor blocking effects may be risky in elderly subjects because these effects can increase the risk for falls and fractures.<sup>50</sup> If serotonergic antidepressants cause osteoporosis, antidepressants with a nonserotonergic mechanism of action (e.g., nortriptyline, desipramine, mirtazapine, or trazodone) should be used because untreated depression itself can contribute to low bone mass and accelerated bone

loss, thus increasing the risk for fractures regardless of the antidepressant class or mechanism of action.<sup>51</sup>

Another potentially lethal adverse effect associated with serotonergic antidepressants is an increase in bleeding risk consistently shown with SSRIs.<sup>52</sup> A meta-analysis of observational studies found that the increased bleeding risk with SSRIs ranged from 12% to 64% across studies.<sup>53</sup> **Therefore, SSRIs should be used cautiously in older adults receiving concurrent administration of nonsteroidal anti-inflammatory drugs, antiplatelet therapy (aspirin and clopidogrel), or anticoagulants and in those with preexisting bleeding risk or an anticipated increase in bleeding (e.g., following dental or other surgeries).** Similar caution is required with concomitant use of any of the above drugs with high doses of vitamin E, which has anticoagulant properties.<sup>54</sup> One retrospective cohort study showed that concurrent use of SSRIs and dual antiplatelet therapy with aspirin and clopidogrel increased the risk of bleeding by 60% compared with dual antiplatelet therapy alone in post-acute myocardial infarction patients.<sup>55</sup> Dual antiplatelet therapy is used in post-acute coronary syndrome<sup>56</sup> and poststroke<sup>57</sup> patients, and SSRIs are the first-line treatment to manage frequently observed depression in both patient groups.<sup>58,59</sup>

SSRIs are not the only class of antidepressants that increases the risk of bleeding. A large population-based cohort study found that the risk of upper GI bleeding increased with the use of all antidepressant classes than with their nonuse.<sup>60</sup> A meta-analysis of 22 studies also looked at the impact of medications on falls in older adults and found an increased risk with antidepressants as a drug class.<sup>61</sup> Moreover, a recent Austrian retrospective analysis of patient charts of predominantly older adults found an increased risk of bleeding with all antidepressants.<sup>62</sup> The increased risk for bleeding has also been reported with higher doses of fish oil, and the FDA-approved package inserts for fish oil products, as well as literature review, do not support this claim.<sup>63</sup> The upper GI tract is the most common site of bleeding, and the use of acid-suppressant drugs may be advisable.<sup>64</sup> However, omeprazole should be avoided in conjunction with the prodrug clopidogrel because it inhibits its conversion to the active metabolite via the CYP2C19 inhibition.

Falls have been reported with more selective antidepressants (e.g., SSRIs) although the risk of falling is

much higher with antidepressants (e.g., TATCAs) that cause cardiovascular side-effects, insomnia, excessive sedation, confusion, and dizziness secondary to orthostatic hypotension.<sup>65,66</sup> However, the association between SSRI use and falls in older adults was observational only, and the direction of the association remains undetermined. A longitudinal analysis of older adults (mean age, 73.6 years at baseline) over 7 years found a 48% greater likelihood of recurrent falls among antidepressant users compared with nonusers even after adjusting for potential confounders.<sup>67</sup> The increased risk of falling with SSRIs was noted even during the early part of treatment initiation and at moderate doses.

The FDA advised in 2011 that older patients should not receive >20 mg/day of citalopram due to the dose-dependent increase in QTc interval, with an update 1 year later to avoid citalopram in patients with congenital long QT syndrome, bradycardia, hypokalemia, hypomagnesemia, recent acute myocardial infarction, or uncompensated heart failure because of the cardiovascular adverse effects of SSRIs. Moreover, escitalopram may also prolong the QTc interval.<sup>68</sup> Thus, Canadian and European health agencies have issued warnings regarding dose-dependent QT prolongation with escitalopram.<sup>69</sup> The FDA issued in 2013 a similar safety warning for fluoxetine.

Abrupt discontinuation of antidepressants can also be problematic, especially with antidepressants having a short half-life (e.g., paroxetine among SSRIs and venlafaxine among SNRIs).<sup>70,71</sup> Withdrawal symptoms may present as flu-like syndrome, insomnia, nausea, imbalance, sensory disturbances, and hyperarousal. It is important to differentiate between these discontinuation symptoms and relapse in depressive symptoms due to the inherent similarities between the two. A systematic review of medication withdrawal in older patients identified only one double-blind RCT and one open-label RCT of SSRI discontinuation. Both studies found no major discontinuation symptoms.<sup>72,73,74</sup>

## Conclusion

Except for SSRIs, none of the earlier classes of antidepressants discussed in part 1 (TATCAs, SATCAs, and MAOIs) are the first-line treatment of geriatric depression primarily due to their undesirable adverse effects which can be fatal in older adults. SSRIs remain the most frequently



prescribed antidepressants among all age groups, including geriatric depression, primarily due to their safety and relative selectivity for serotonergic receptors even after almost three decades of their first use. Nevertheless, some level of monitoring is still required in this age group due to age-related changes, polypharmacy, and comorbidities, especially concerning increased risk for drug interactions, bleeding, osteoporosis, and discontinuation symptoms. However, it should be noted that these risks are not *class* effects of SSRIs, and the selection of an SSRI should be personalized based on the profile of each patient.

Part 2 of this lesson will expound on serotonin and norepinephrine reuptake inhibitors and adverse effects, serotonin antagonist and reuptake inhibitors, norepinephrine and dopamine reuptake inhibitors, noradrenergic  $\alpha_2$  and selective-serotonin antagonist, serotonin partial agonist and reuptake inhibitors, multimodal antidepressants, and augmentation strategies for treatment-resistant depression in older adults.

*Editor's Note: References are listed at the end of Part 2 of this lesson. 📖*

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## Multiple-Choice Questions

**69. All of the following statements are true, *except*:**

- A. Fluoxetine can be started after two weeks of MAOI discontinuation.
- B. Vortioxetine is the only antidepressant improving psychomotor speed.
- C. Low-dose selegiline is relatively selective for MAO-B.
- D. Secondary-amine tricyclic antidepressants can be recommended as second- or third-line agents for use in older adults with EKG monitoring.

**70. Which of the following MAOI has stimulatory effects?**

- A. Tranylcypromine
- B. Moclobemide
- C. Phenelzine
- D. Selegiline

**71. Which of the following is relatively safe with tyramine-containing foods?**

- A. High-dose selegiline patch
- B. Phenelzine
- C. Tranylcypromine
- D. Moclobemide

**72. Which of the following SSRIs has the highest risk for cognitive adverse effects?**

- A. Fluoxetine
- B. Paroxetine
- C. Escitalopram
- D. Fluvoxamine

[illegible]

# A Review of Psychopharmacotherapy for Geriatric Depression, Part 2

Mujeeb U. Shad, MD, MSCS

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**KEY WORDS:** Pharmacotherapy • Geriatric • Depression • Review

**LEARNING OBJECTIVES:** This lesson is a review of currently available antidepressants to manage geriatric depression, followed by an evidence-based discussion of the efficacy and tolerability of antidepressants in older adults. Moreover, this review lays the foundation for the mechanism of action-based learning to promote safe and effective use of antidepressants, especially those without formal studies in the geriatric population. This foundation will allow clinicians various options for selecting antidepressants in a high-risk population known for suboptimal response, treatment resistance, increased vulnerability from adverse effects, age-related changes in drug disposition, and high prevalence of polypharmacy. Augmentation strategies in managing *treatment-resistant depression in older adults* (TRDOA), including strategies in major depression with cognitive dysfunction, are also reviewed in this lesson.

**LESSON ABSTRACT:** The geriatric population is at significant risk for *major depressive disorder* (MDD), which may frequently offer a treatment challenge due to age-related changes in drug disposition, frequent medical and substance use comorbidities, and high prevalence of polypharmacy with increased risk for drug interactions. A large number of older adults may be treatment-refractory and may require a trial of antidepressants that are relatively new and/or not investigated in this patient population, although several evidence-based antidepressant treatment options exist to manage MDD. Therefore, this review presents findings from major antidepressant clinical trials and reviews clinically relevant and mechanism-based psychopharmacology of antidepressants, including those that have not been studied in the geriatric population. Consequently, augmentation strategies will also be reviewed for TRDOA, including those with cognitive dysfunction. Lastly, this review facilitates a better understanding of basic psychopharmacological concepts to optimally and effectively use antidepressants in a psychiatrically and medically vulnerable geriatric population.

**COMPETENCY AREAS:** Readers will have gained knowledge of the clinical pros and cons of using different mechanism-based classes of antidepressants in older adults with MDD upon the conclusion of this lesson. Thus, the audience will not only learn current evidence-based antidepressant treatment for MDD but also gain knowledge on how to safely and effectively use these antidepressants in a patient population with age-related vulnerabilities and polypharmacy. Readers will learn to distinguish each class of antidepressants' potential adverse effects, which may be of high clinical relevance in a highly vulnerable geriatric population with comorbidities, age-related changes in drug disposition, and polypharmacy. Finally, readers will learn evidence-based augmentation strategies to manage TRDOA, as well as pharmacotherapy of major depression compromised by cognitive dysfunction, frequently reported in older adults.

## Introduction

Part 2 of this lesson reviews clinical information on antidepressant classes that followed SSRIs.

## Serotonin–Norepinephrine Reuptake Inhibitors

This class of antidepressants started with venlafaxine primarily in an attempt to create the desired profile of TATCAs (i.e., serotonin and norepinephrine reuptake pump blockade), putatively mediating its efficacy, but without the adverse effect burden due to undesirable multitarget involvement with TATCAs. Thus, SNRIs can also be referred to as *selective* SNRIs compared with the nonselectivity of TATCAs. **SNRIs may slightly be more effective in SSRI nonresponders because they enhance the activity of two (i.e., serotonin and norepinephrine) out of three core neurotransmitter systems.**<sup>75</sup>

Venlafaxine was followed by its metabolite, **desvenlafaxine, which has more noradrenergic activity than its parent compound venlafaxine.** Duloxetine, another SNRI, has a similar balance between serotonin and noradrenergic activity as desvenlafaxine. **However, the newest SNRI, levomilnacipran, is the only SNRI that has more noradrenergic than serotonergic activity.** The different serotonin to norepinephrine ratios may be clinically meaningful. For example, only desvenlafaxine and duloxetine are approved for the treatment of fibromyalgia due to more balanced activity between serotonin and norepinephrine activity compared with venlafaxine, which at doses <225 mg/day may primarily be like an SSRI.<sup>76</sup>

Like SSRIs, SNRIs are one of the most commonly used antidepressants sharing similar indications and adverse effects with few exceptions. In addition, the choice of an appropriate SNRI should also be based on the elimination half-life and potential for drug interactions. **Although the dose-adjusted serum concentrations for venlafaxine and duloxetine were less elevated than most SSRIs,<sup>35</sup> a need for dose adjustments in elderly subjects still exists.** In a similar context, the use of supratherapeutic doses in older subjects is usually not advisable due to age-related changes in plasma levels, receptor sensitivities, and increased prevalence of medical and other comorbidities and polypharmacy. **Thus, the evidence**

**from studies in mixed-age populations supporting higher than recommended doses of venlafaxine and perhaps MAOI (tranylcypromine) to treat drug-resistant depression<sup>77</sup> should be applied cautiously to the geriatric population. Also, higher venlafaxine doses may increase the risk of tachycardia and hypertension.** However, switching strategies from a meta-analysis of four clinical trials in mixed-age adults may have a modest advantage in switching patients with SSRI-resistant depression to a non-SSRI antidepressant, including an SNRI, rather than switching within the class.<sup>75</sup>

### Adverse Effects of SNRIs:

Venlafaxine appears to have a similar adverse effects profile as SSRIs, probably because it is predominantly serotonergic. Noradrenergic effects start to appear at >225 mg/day in most patients.<sup>78</sup> **In terms of suicide risk, venlafaxine seems to have one of the highest risks for suicide risk among both SSRIs and SNRIs.**<sup>79</sup> Venlafaxine has also been associated with hyponatremia. A retrospective controlled study showed that about 40% of older psychiatric inpatients (mean age, 74.2 years) treated with an SSRI or venlafaxine developed hyponatremia compared with only 10% of controls.<sup>41</sup> However, the incidence of hyponatremia has not been studied in large studies with other SNRIs (e.g., duloxetine and desvenlafaxine) and may be lower than SSRIs and venlafaxine. In general, FDA labels caution providers about hyponatremia not only with SSRIs but also SNRIs and the multimodal antidepressant, vortioxetine. As with SSRIs, the use of venlafaxine concomitantly with sodium-lowering drugs (e.g., thiazide diuretics, carbamazepine, and oxcarbazepine) requires caution.<sup>44</sup> A baseline sodium level may be highly desirable in older adults. Although the most evidence for bleeding risk is with SSRI,<sup>55</sup> other studies have reported an increased risk of bleeding common to all antidepressants).<sup>62</sup> Similarly, all antidepressants have been observed to increase the risk of falling.<sup>66</sup> As expected with noradrenergic drugs, SNRIs were found to have a modest but higher risk of tachycardia and hypertension than SSRIs.<sup>80</sup>

## Serotonin Antagonist and Reuptake Inhibitors

Some of the long-term adverse effects of SSRIs (e.g., sexual dysfunction, cognitive haze, and sleep problems)

appear to be mediated by activation of specific subtypes of serotonin receptors, including serotonin type 2 (5HT<sub>2</sub>) receptors.<sup>81, 82, 83</sup> Thus, a drug that selectively blocks 5HT<sub>2</sub> receptors can neutralize some of these adverse effects. This concept is supported by trazodone and nefazodone, which have a higher affinity to block 5HT<sub>2</sub> receptors than the serotonin transporter,<sup>84</sup> which may be the reason that depressed patients receiving *serotonin antagonist and reuptake inhibitors* (SARIs) are less likely to experience sexual dysfunction,<sup>83, 85</sup> sleep disruptions,<sup>82</sup> and cognitive blunting.<sup>81, 86</sup> **Despite these advantages, SARIs are used less because of their potent blockade of H<sub>1</sub> and adrenergic  $\alpha$ <sub>1</sub> receptor, resulting in oversedation, dizziness, and falls, which may be potentially disastrous in elderly patients.** A slow titration may be able to reduce these effects, but it may take a long time to reach the effective antidepressant dose, which can be around 200–300 mg/day. Nevertheless, trazodone-induced sedation is one of the most frequently used sedating agents across different patient populations with a definite benefit of not having any significant anticholinergic effects over antihistaminic drugs (e.g., diphenhydramine and doxepin). The lack of anticholinergic effects is of high clinical relevance in the cognitively impaired elderly depressed population. Recent evidence exists to support that trazodone may delay cognitive decline in elderly depressed patients.<sup>86</sup> Due to the 5HT<sub>2</sub> blockade, trazodone has also been used to manage the adverse effects caused by SSRIs as aforementioned. Nefazodone is still available as a generic but has been minimally used after it became the only antidepressant to carry an FDA black box warning for hepatic failure following a World Health Organization analysis showing a high number of reports of liver injury.<sup>87</sup>

## Norepinephrine and Dopamine Reuptake Inhibitors

This antidepressant class was the first to provide a combination of primarily noradrenergic and some dopaminergic mechanisms to target depressive symptoms. However, bupropion is the only antidepressant representing this class. One naturalistic study<sup>88</sup> and three RCTs have been done with bupropion in older adults with depression although data with bupropion

in older adults is scarce.<sup>89, 90, 91</sup> The naturalistic study compared the efficacy of bupropion monotherapy versus bupropion combination with SSRIs.<sup>88</sup> A significantly higher response rate was noticed with the combined use of bupropion and an SSRI (81%) than with bupropion monotherapy (61%). The study by Hewett et al. reported significantly better efficacy for bupropion *extended-release* (XR) than placebo.<sup>89</sup> Moreover, the study by Weihs et al. reported similar efficacy between bupropion and paroxetine groups.<sup>90</sup> The latest RCT compared the efficacy and safety of switching to bupropion, augmentation with bupropion, or augmentation with aripiprazole for 12 weeks with a 36-week follow-up in a large sample of 1,522 veterans with MDD and an average age of 54.4 (*VA Augmentation and Switching Treatments for Improving Depression Outcomes*, VAST-D).<sup>91</sup> This study failed to find any benefits of switching to bupropion or augmentation with bupropion over augmentation with aripiprazole.<sup>91</sup> The two bupropion groups did show significant treatment-emergent anxiety although bupropion was slightly better tolerated than aripiprazole. Despite some positive results from earlier studies in geriatric depression and the potential benefits of having less risk for hyponatremia and a precognitive profile, bupropion should be used cautiously in the geriatric population especially in those who have lost weight and those with hyponatremia due to high-risk seizures with bupropion.

## Noradrenergic Alpha-2 and Selective Serotonin Antagonist (e.g., Mirtazapine)

Mirtazapine is the only drug represented in this antidepressant class. It is a unique drug in many ways with multimodal mechanisms, including an increase in noradrenergic and serotonergic activity via  $\alpha$ <sub>2</sub>-adrenoceptor antagonism<sup>92, 93</sup> and serotonin 5-HT<sub>2A</sub>, 5HT<sub>2C</sub>, and 5-HT<sub>3</sub> antagonism.<sup>92</sup> These are desirable mechanisms to have in an antidepressant especially in older adults with MDD. An increase in noradrenergic activity may be beneficial in low-energy, anhedonic, and low-motivation depression frequently observed in geriatric depression. Further, the serotonin boost via blockade of *alpha-2* ( $\alpha$ <sub>2</sub>) heteroreceptors may address the serotonin deficiency seen in depressed patients along with 5HT<sub>2A</sub> receptor

blockade resulting in anxiolytic effects, 5HT<sub>2C</sub> receptor blockade causing long-term weight gain (which may be highly desirable in medically ill depressed older adults, especially in nursing homes), and 5HT<sub>3</sub> receptor blockade preventing serotonin-mediated GI upset.<sup>84</sup> Moreover, mirtazapine does not have any significant activity at the dopamine receptors, muscarinic receptors, or the monoamine transporters,<sup>94,95</sup> which gives it a favorable adverse effect profile.

However, despite these advantages in older adults, few studies have investigated this antidepressant in this patient population. An open-label trial of mirtazapine in 16 elderly patients with MDD with one or more serious medical comorbidity reported improved depression, insomnia, anxiety, somatic symptoms, and quality of life with mirtazapine treatment.<sup>96</sup> Another open-label trial suggested that the rapidly-dissolving mirtazapine tablets were effective and well-tolerated in depressed nursing home residents aged >85 years.<sup>97</sup> A comparison study between mirtazapine and paroxetine found both antidepressants to be effective. The mirtazapine group demonstrated an earlier response (i.e., 26 days) as well as a greater reduction in anxiety, somatization, and insomnia compared with the paroxetine group (i.e., 40 days).<sup>98</sup> In addition, mirtazapine and amitriptyline were found to have similar efficacy and safety in the treatment of MDD in older adults.<sup>99</sup> In elderly patients with hyponatremia, mirtazapine may offer a safer alternative than bupropion because mirtazapine does not lower the seizure threshold, unlike bupropion. Dose adjustments may be needed for mirtazapine as required for other antidepressants in older adults with MDD due to age-related changes in drug disposition.<sup>35</sup>

## Serotonin Partial Agonist and Reuptake Inhibitors (e.g., Vilazodone)

Vilazodone is the first member of the *serotonin partial agonist and reuptake inhibitors* (SPARI), combining serotonin reuptake inhibition with 5-HT<sub>1A</sub> partial agonism. This drug offers a unique combination for the first time of two desirable mechanisms, which could potentially be more effective in depressed patients with comorbid anxiety and fewer sexual adverse effects than the SSRIs.<sup>100</sup> The anxiolytic effects are probably mediated by the partial agonist

at the 5HT<sub>1A</sub> receptors,<sup>100</sup> similar to buspirone, which is FDA-approved to manage generalized anxiety disorder. **However, older adults may be more sensitive to the adverse effects of this antidepressant than younger adults, especially those mediated by increased serotonin activity, including GI upset and hyponatremia.** The only information of a clinical trial with vilazodone in the elderly population comes from the ClinicalTrials.gov website, showing a pilot 12-week double-blind study comparing the efficacy and tolerability of vilazodone to paroxetine for the treatment of geriatric depression. The study appears to be ongoing, and the only results posted for this study in the study completers are the adverse effects. Moreover, the study shows GI symptoms, dizziness, concentration difficulties, and increased dream activity in 12% and sedation in 4% of the patients in the vilazodone group versus GI symptoms in 17% and sedation, increased dream activity, and dizziness in 10% of the patients in the paroxetine group.

## Multimodal Antidepressants (e.g., Vortioxetine)

Although RCTs have not shown geriatric-specific problems that would limit the usefulness of vortioxetine in the elderly, elderly patients are more likely to have hyponatremia with vortioxetine, which may require caution for patients receiving vortioxetine. Thus, similar to SSRIs and SNRIs, the package insert for vortioxetine has included a caution for hyponatremia. Consequently, clinicians need to be extremely cautious about combining any of these antidepressants with medications that lower sodium levels (e.g., thiazide diuretics, carbamazepine, and oxcarbazepine).<sup>44</sup> **Nevertheless, based on a comprehensive meta-analysis of 12 RCTs, vortioxetine was the only antidepressant that improved performance on *digit symbol substitution test* (DSST).**<sup>101</sup> DSST is a polyfacetorial cognitive measure which is primarily utilized to assess the cognitive domains of psychomotor speed, attention, and working memory, frequently impaired in depressed patients.<sup>102</sup> The procognitive effects of vortioxetine appear to be separate from its antidepressant effects.<sup>103</sup> However, future studies are needed to confirm if vortioxetine offers cognitive benefits beyond its antidepressant effects in older adults with depression-associated cognitive dysfunction.



## Augmentation Strategies for Treatment-Resistant Depression in Older Adults

Remission is only achieved in about one-third of all older patients who are treated with an antidepressant.<sup>14</sup> Consequently, two out of three patients need additional treatment, making TRDOA a common and costly problem. Most studies describe TRDOA as nonresponsive to one adequate antidepressant trial. Information on some commonly used augmentation strategies in older adults will be briefly reviewed in the following sections.

### Lithium:

Lithium augmentation, with an overall response rate of 42%, is the only treatment that has good evidence for effectively treating older patients.<sup>104</sup> Most studies define a decrease of 50% or more on a depression rating scale as a response. Lithium is effective for augmenting antidepressant treatment in older adults with major depression in a single open RCT with a two-year follow-up with tremor as the main side effect, which did not significantly increase the number of dropouts.<sup>105</sup>

### Thyroid Hormones T3 (Triiodothyronine) and T4 (Levothyroxine):

Hypothyroidism is among the most frequent chronic diseases in the elderly, and supplemental thyroid hormones are among the most commonly prescribed agents in the general population. Regarding free T3 levels, most studies have demonstrated an age-dependent decline, while free T4 levels remain relatively unchanged.<sup>106,107</sup>

**No controlled augmentation trials exist with either T3 or T4 in elderly depressed patients, unlike younger subjects.** However, the management of hypothyroidism in older adults is generally based on the presence or absence of hypothyroidism symptoms, TSH levels, and age range.<sup>108,109</sup> However, a detailed discussion of thyroid supplementation in the geriatric population is beyond the scope of this review. Unlike younger adults, even short-term thyroid supplementation may result in excessive thyroid activity in older adults worsening preexisting hypertension, tachycardia, and diabetes.<sup>110</sup> In addition, subclinical hyperthyroidism has been associated with osteoporosis, especially in postmenopausal women,<sup>111,112</sup> and atrial arrhythmias.<sup>113</sup> Thus, older adults with depression

receiving thyroid supplementation require more frequent and closer monitoring for clinical evidence of hyperthyroidism than younger adults.<sup>108,109</sup>

### Second-Generation Antipsychotic Medications:

The most widely used augmentation strategy for treatment-resistant depression in clinical practice today is the use of *second-generation antipsychotic medications* (SGAMs). Several SGAMs are approved for this indication based on studies in mixed-age patients, including quetiapine, aripiprazole, and brexpiprazole and olanzapine-fluoxetine combination pill. This is not unexpected because the 5HT<sub>2A</sub> blockade is a common feature of all SGAMs, which has been associated with antidepressant response. Specific studies in TRDOA are few. In a double-blind RCT of aripiprazole (maximum, 15 mg/day) versus placebo augmentation of venlafaxine XR (range, 150–300 mg/day) in older adults aged ≥60, 12 weeks of sustained remission was noted in almost 50% of the participants in the intervention group.<sup>114</sup> Akathisia was the most common adverse effect in the aripiprazole group, consistent with its known adverse effect profile. **However, aripiprazole is less likely to produce extrapyramidal symptoms<sup>115</sup> other than akathisia because it is a partial agonist for dopamine-2 (D2) receptors.** The commonly observed akathisia with aripiprazole may be mediated by the nondopaminergic mechanism because akathisia usually does not respond to anticholinergic medications, unlike other EPS.<sup>116</sup> This view is consistent with the lack of hyperprolactinemia reported with aripiprazole, which is of clinical significance in older adults who are at an increased risk for osteoporosis due to hyperprolactinemia. Aripiprazole has been reported to reduce increased prolactin levels in younger patients.<sup>117,118</sup>

Risperidone, ziprasidone, and cariprazine also have data supporting adjunctive use but are not yet FDA-approved for the treatment of MDD.<sup>119,120,121</sup> A meta-analysis of RCT indicates that all SGAMs are similarly effective augmentation agents in MDD.<sup>120</sup> In general, risperidone and aripiprazole in standard doses were more beneficial than placebo in improving quality of life and functioning. Further, and unexpectedly, risperidone was better tolerated than the others despite its potent D2 receptor blockade.<sup>122</sup> Common adverse effects reported in augmentation studies included akathisia with

ariprazole, cariprazine, and ziprasidone; sedation with quetiapine and risperidone; weight gain with olanzapine; somnolence with ziprasidone; headache, sedation, and dry mouth with risperidone; and insomnia and nausea with cariprazine. The risk for tardive dyskinesia may be associated with all antipsychotic medications and thus should be discussed with each patient, regardless of age.<sup>123</sup>

### Stimulants:

The use of methylphenidate in older adults with major depressive disorder appears to be safe and effective based on a randomized placebo-controlled RCT of augmentation of citalopram with methylphenidate in geriatric major depressive disorder.<sup>124</sup> On the one hand, the mean dose of citalopram was 32 mg (range, 20–60 mg) in this study, which is higher than the recommended dose for patients aged >60. On the other hand, the mean dose of methylphenidate was 16 mg (range, 5–40 mg). Improvement in depression severity and the clinical global impression was most prominent in the citalopram plus methylphenidate group compared with either alone, and it occurred at a faster rate in the first 4 weeks of the trial.

### Ketamine:

**Adjunctive intravenous ketamine is effective in younger adults with treatment-resistant depression,<sup>125</sup> and studies are underway to evaluate its role in TRDOA.<sup>126</sup>** However, in the Janssen study to evaluate the efficacy, safety, and tolerability of intranasal esketamine plus an oral antidepressant in elderly subjects with treatment-resistant depression, results failed to show any significant benefit for the antidepressant esketamine over the antidepressant placebo groups.<sup>127</sup> Results from the ongoing ketamine and esketamine trials may help determine the utility of esketamine augmentation in TRDOA.

### Neuromodulation Strategies:

*Electroconvulsive therapy* (ECT) remains the gold standard in managing TRDOA due to its more effective and faster onset of antidepressant response especially in older subjects with severe suicidality, even if newer neuromodulation tools such as *repetitive transcranial magnetic stimulation* (rTMS) have been increasingly used to manage TRDOA with better tolerability and safety compared with antidepressants. The best evidence supporting ECT use in TRDOA is from the Prolonging Remission in Depressed

Elderly<sup>128</sup> study. Phase I of the study showed that the right unilateral ultrabrief pulse ECT along with venlafaxine was found to be a rapidly-acting, highly effective, and well-tolerated treatment for depressed older patients.<sup>129</sup> The average ECT treatments were about seven, and the remission and the response rates were about 62% and 70%, respectively, with a low dropout rate. The 24-week phase II of this study revealed that maintenance ECT in addition to medications (lithium and venlafaxine) was more effective and as safe as maintenance medications without ECT after an acute response to ECT.<sup>130</sup> A comprehensive review of ECT studies in the treatment of TRDOA concluded that the right unilateral ultrabrief ECT was as effective as the brief-pulse ECT during acute and maintenance treatment with fewer adverse effects.<sup>131</sup>

rTMS is a relatively easier, more tolerable and cost-effective procedure than ECT because data on efficacy for other neuromodulation strategies, such as rTMS, have generally been lower<sup>132</sup> than those reported for ECT. Many advantages of rTMS are due to a localized electrical stimulation with less significant cognitive effects and a lack of drug interactions, as well as problems associated with decreased drug disposition in the elderly. Multiple studies have now supported the safe and effective use of rTMS in depressed elderly subjects,<sup>133-136</sup> which may be the reason that rTMS is more frequently used for TRDOA. Reduction in functional hemispheric asymmetry and increased cerebral white matter disease limiting the use of rTMS in older adults<sup>137,138</sup> are some of the earlier concerns with cortical atrophy being addressed in ongoing research. One example of such efforts is the FDA approval of an H-shaped coil to apply deep rTMS to access deeper brain structures for better efficacy in elderly subjects.<sup>139,140</sup> The H-coil delivers *theta-burst stimulation* (TBS), which may have similar efficacy as the high-frequency stimulation but with shorter durations at a lower intensity. The latest study with innovative use of TBS is the Stanford Accelerated Intelligent Neuromodulation Therapy for TRDOA, which employed accelerated, high dose, intermittent TBS with precision MRI-guided targeting of a left prefrontal circuit closely associated with depression.<sup>141</sup> This study produced an impressive remission rate of 86.4% (19 out of 22 participants) without any negative cognitive effects. Though it was an open-label study in a small sample, it opens up avenues for future RCTs with this exciting neuromodulation tool.

However, no data in older adults with MDD currently exists to support the use of other neuromodulation modalities (e.g., vagus nerve stimulation, transcranial direct current stimulation, deep-brain stimulation, or magnetic seizure therapy).<sup>132</sup>

## TRDOA and Comorbid Cognitive Dysfunction

Cognitive symptoms are frequently observed in depressed older adults because about 35% of older adults with depression, but without dementia have been found to have executive dysfunction on cognitive assessment.<sup>142</sup> Cognitive and depressive symptoms appear to be linearly correlated in a temporal relationship in depressed elderly subjects.<sup>143</sup> The temporal relationship with the onset of depressive and cognitive symptoms is important and should not be confused with a new onset of depressive symptoms in patients with preexisting dementia. In one study, sertraline treatment resulted in only a modest response in overall cognitive symptoms, and the only significant improvement was observed in attention and executive function but only in patients with improved depressive symptoms.<sup>144</sup> Cognitive symptoms, regardless of their severity, are typically reversible (labeled as pseudodementia) and may often convert into irreversible dementia.<sup>145</sup> Other studies have also found depression with executive dysfunction syndrome as not only a predictor of poor treatment response but also a risk factor for progression to dementia.<sup>146</sup> Antidepressant treatment, in general, does not appear to reduce the progression to *minimal cognitive impairment* (MCI) or dementia in the long term as reported by a large meta-analysis although long-term SSRI treatment may delay the progression to dementia in short-term responders by about 3 years.<sup>147,148</sup> The presence or absence of depressive pseudodementia did not appear to affect the antidepressant response.

Different types of executive functions exist, and not all executive functions predict antidepressant response. A 12-week randomized controlled study<sup>149</sup> showed that older adults who failed to respond to venlafaxine monotherapy (300 mg/day) were randomly assigned to either venlafaxine augmentation with aripiprazole (2–15 mg/day) or placebo for another 12 weeks. Higher remission rates were only observed in the adjunctive aripiprazole group with a better pretreatment performance on set

shifting (assessed with Trail Making Test). Consequently, response inhibition assessed by the Stroop Color–Word Interference Task did not predict remission. However, high anxiety at baseline predicted a lower remission rate but not a response rate in both the aripiprazole and placebo groups.

Although memantine augmentation of antidepressant therapy does not improve depression in mixed-age<sup>150</sup> or older populations,<sup>151</sup> adjunctive treatment with memantine has been found to improve depressive and cognitive symptoms in older adults. In an open-label study, concomitant treatment with escitalopram and memantine was associated with improvements in depression and cognition and a low rate of conversion to dementia.<sup>152</sup> Although a follow-up RCT with 6-month treatment with escitalopram with or without memantine augmentation did not show any difference in antidepressant response, the escitalopram–memantine combination had a greater improvement in delayed recall, executive functioning, and global performance after a 60-month naturalistic follow-up period.<sup>153</sup>

The data on antidepressant augmentation with cholinesterase inhibitors is mixed. A randomized control pilot study showed that donepezil augmentation of antidepressant therapy was effective in improving memory for the 12-week duration of the trial as well as the 8-month open extension phase. However, similar to memantine, noncognitive benefits were not observed.<sup>154</sup> A post hoc analysis of this study revealed that improvement in odor identification may be a predictor of clinical improvement from cholinesterase inhibitors in older adults with depression and cognitive impairment.<sup>155</sup> However, a double-blind RCT showed that an increase in depressive symptoms was reported in the antidepressant plus donepezil group with MCI despite temporary global cognitive improvement.<sup>156</sup> In another RCT, no difference in dementia conversion rates or cognitive symptoms was found between add-on donepezil (5–10 mg daily) and add-on placebo group to the continuing antidepressant treatment for 62 weeks.<sup>157</sup> **On the contrary, the donepezil add-on group was associated with more adverse effects than the placebo add-on group.**<sup>157</sup> **These mixed results suggest that the combination of donepezil may not be as useful as memantine in older adults with cognitive deficits.** However, more research is warranted to examine the utility of antidepressant augmentation

with other cholinesterase inhibitors (e.g., rivastigmine and galantamine).

Finally, a newer antidepressant, vortioxetine, is the first drug to be approved by the FDA for its positive effects on psychomotor speed, attention, and working memory in patients with major depression.<sup>158</sup> Though vortioxetine has not been studied in older adults, the procognitive effects of vortioxetine in the adult population may be translatable to the geriatric patients with major depression.

## Conclusion

The newer classes of antidepressants have provided additional options to manage geriatric depression. In general, SNRIs have similar safety, tolerability, and efficacy profile as SSRIs with the notable exception of higher risk for cardiovascular effects with SNRIs. SARIs provide a conceptual transition from the serotonin and/or norepinephrine reuptake pump blockade to block specific serotonin receptors to avoid some adverse effects. This profile could have been useful in elderly subjects intolerant to SSRIs or SNRIs if initiation of SARIs was not associated with significant sedation and dizziness. The only member of the norepinephrine and dopamine reuptake inhibitors class, bupropion, is not considered as the first monotherapy option in depressed older adults due to increased risk for seizures. However, it has been frequently used as an augmentation strategy across all age

groups. Mirtazapine, unlike bupropion, is also the only representative form of noradrenergic  $\alpha_2$  and selective serotonin antagonist class of antidepressants, but it is one of the most frequently used antidepressants in nursing homes primarily due to its sedative and appetite-stimulating effects. Although clinical data are lacking with SPARIs (i.e., vilazodone), no contraindications exist in general for its use in geriatric depression if the serotonergic adverse effects are monitored closely. Vortioxetine, the single member of the multimodal antidepressants class, is the only antidepressant to show procognitive effects in the younger population, which may provide a useful treatment option for cognitively impaired patients if replicated in older adults. Aripiprazole and probably low-dose risperidone are the best pieces of evidence for augmentation strategies. However, the growing interest for ketamine augmentation is rising despite a negative study with recently approved intranasal esketamine in older adults with major depression. The antidementia drug, memantine, appears to be more effective for older adults with cognitive impairment than anticholinesterases (e.g., donepezil). Evidence supporting newer neuromodulation techniques, especially rTMS, is significantly growing with the use of innovative approaches to optimize its antidepressant response without compromising tolerability in the geriatric population. However, ECT remains the last resort to manage treatment-refractory depression across all age groups. ■

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## Multiple-Choice Questions

**73. Which of the following statements is true regarding antidepressants?**

- A. Citalopram does not cause arrhythmia and can be safely used in the geriatric population.
- B. Fluoxetine causes discontinuation symptoms in the elderly.
- C. Vilazodone is least likely to cause GI adverse effects in older adults.
- D. Venlafaxine is associated with one of the highest risks for suicide.

**74. Which statement about serotonin antagonist and reuptake inhibitors (trazodone and nefazodone) is true in older adults?**

- A. This class of medication is associated with more anxiety symptoms.
- B. They are more likely to result in cognitive dysfunction.
- C. They have higher risk for sedation and dizziness.
- D. They do not block serotonin transporters.

**75. Which one of the following statements is true?**

- A. Venlafaxine is the least serotonergic serotonin–norepinephrine reuptake inhibitors.
- B. Duloxetine has higher risk for hypertension and tachycardia for older adults.
- C. Levomilnacipran is the least noradrenergic serotonin–norepinephrine reuptake inhibitors.
- D. Desvenlafaxine is more serotonergic than its parent compound, venlafaxine.

**76. Which of the following statements is true about antidepressant augmentation strategies?**

- A. Thyroid augmentation is formally studied in elderly depression.
- B. Bupropion is safer than mirtazapine in older adults with hyponatremia.
- C. Antidepressant augmentation with memantine has more evidence for efficacy than with donepezil augmentation in older adults.
- D. Aripiprazole has higher risk for extrapyramidal symptoms in elderly patients.

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# Best Practices in Continuing Medical Education

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## A Review of Psychopharmacotherapy for Geriatric Depression

By Mujeeb U. Shad, MD, MSCS

ID#: L003460/61

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

Geriatric depression is the most common psychiatric disorder with a significant effect on the quality of life and a high cost burden. A higher prevalence of medical and substance use comorbidities complicated by polypharmacy further exposes this highly vulnerable population. Not only might the diagnosis of depression be masked by medical comorbidities, but the treatment of depression may also be quite challenging primarily due to age-related changes in underlying biology and drug disposition. These challenges may account for why treatment resistance is frequently observed in this patient population, which may not be adequately addressed by evidence-based treatment options currently available. An evidence-based approach and mechanism of action-based understanding of antidepressant psychopharmacology may enhance safe and effective pharmacotherapy for geriatric depression.

#### Key Point 1: Background

Geriatric depression is one of the most common psychiatric disorders that not only diminishes the quality of life of depressed elderly but also that of their families. A combination of evidence- and mechanism-based antidepressant psychopharmacology may help address the age-related vulnerabilities, comorbidities, and frequent polypharmacy in this population.

ment of geriatric depression primarily due to their undesirable adverse effects which can be fatal in older adults. SSRIs remain the most frequently prescribed antidepressants among all age groups, including geriatric depression, primarily due to their safety and relative selectivity for serotonergic receptors even after almost three decades of their first use.

#### Key Point 2: Medication Selection for Geriatric Patients

Except for selective-serotonin reuptake inhibitors, none of the earlier classes of antidepressants (tertiary amine tricyclic antidepressants, secondary amine tricyclic antidepressants, monoamine oxidase inhibitors) discussed are the first-line treat-

#### Key Point 3: Newer Classes of Antidepressants

The newer classes of antidepressants have provided additional options to manage geriatric depression. In general, serotonin-norepinephrine reuptake inhibitors have similar safety, tolerability, and efficacy profile as SSRIs with the notable exception of higher risk for cardiovascular effects with

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**SNRIs.** Serotonin antagonist and reuptake inhibitors provide a conceptual transition from the serotonin and/or norepinephrine reuptake pump blockade to block specific serotonin receptors to avoid some adverse effects.

**Key Point 4: Augmentation Strategies to Treating Depression in Geriatric Patients**

Aripiprazole and probably low-dose risperidone are the best pieces of evidence

for augmentation strategies. Evidence supporting newer neuromodulation techniques, especially repetitive transcranial magnetic stimulation, is significantly growing with the use of innovative approaches to optimize its antidepressant response without compromising tolerability in the geriatric population. However, electroconvulsive therapy remains the last resort to manage treatment-refractory depression across all age groups.

**Professional Development Series**

# Psychiatric Consultations from an Oncology Perspective: Medical Students' Clerkship Experience at a Comprehensive Cancer Center

Smita Saraykar, MD, MPH; Asim A. Shah, MD; Anis Rashid, MD

*This continuing medical education lesson was developed free of commercial support.*

**KEY WORDS:** Medical students • Clerkship • Psychiatric oncology • Evaluation

**LEARNING OBJECTIVES:** After completing this lesson, clinicians and other readers will be able to (1) view the unique experience of medical students going through psychiatric oncology clerkship, (2) delineate medical students' learning curve on the six competency domains outlined by the Accreditation Council of Graduate Medical Education, (3) acknowledge the strength of the program, and (4) understand students' concerns and suggestions for improving their learning processes.

**LESSON ABSTRACT:** The goals of this lesson are to highlight the unique features of a psychiatric oncology clerkship. Medical students from Baylor College of Medicine and the University of Texas Health Science Center at Houston who underwent three to four weeks of psychiatry clerkship rotation at the University of Texas MD Anderson Cancer Center from January 2007 to September 2014 were evaluated. Students' learning experiences in terms of objectives met during the rotation, concerns regarding the clerkship, and suggestions for improvement are described in this report. Overall, the trainees self-reported being very satisfied with their clerkship experiences. **They reported developing skills in core competencies—including patient care, medical knowledge, communication skills, bedside manners, professionalism, and practice-based learning.** Students also had the unique experience of managing patients with cancer who have mental illnesses. Half of the trainees did not report any concerns about their clerkship; the other half expressed concerns, which included a busy service and the need for psychotherapy and psychopharmacology training. Suggestions for improvement included increasing the length of the rotation and adding an outpatient rotation.

**COMPETENCY AREAS:** This lesson describes the unique role of psychiatric oncology clerkship as experienced by medical students. **Medical students can see not only the common psychiatric challenges faced by cancer patients but also a wide variety of mental health issues, varying from delirium to drug withdrawal, altered body image concerns, and so on. This clerkship prepares the students to understand psychiatric illnesses in medically ill patients, even if they choose any other medical specialty in their future career.**

## Introduction

Psychiatric oncology clerkships provide medical students with the specialized knowledge and clinical experiences needed to diagnose and manage psychiatric illnesses in patients with cancer successfully. Also, studies examining medical students' experiences have indicated that psychiatry clerkships encourage students to choose psychiatry as a career, positively influence and reinforce students' perceptions of psychiatry, and improve their attention to the psychosocial aspects of patient care regardless of their specialty.<sup>1,2</sup>

The Liaison Committee on Medical Education requires medical schools to base their clerkship programs on the six competency domains required by the **Accreditation Council for Graduate Medical Education and demonstrate medical students' achievement of these competencies—namely, patient care, medical knowledge, communication skills, bedside manners, professionalism, and practice-based learning.**<sup>3</sup>

The effectiveness of the educational methods employed in these clerkships is most often measured by surveys administered at the end of the clinical rotation. Factors influencing evaluations of a clerkship include the students' personalities, the teaching methods used, the organization of the clerkship, and the quality of the supervision and learning activities.<sup>4,5</sup>

Thus far, there are no reports in the literature regarding the experiences of medical students and residents who have undergone psychiatric oncology clerkships in a comprehensive cancer center. This preliminary report of evaluation forms from a psychiatric oncology clerkship rotation at the University of Texas MD Anderson Cancer Center fills this knowledge gap and highlights the unique features of psychiatric oncology clerkships.

## Methods:

The study was approved by MD Anderson's Institutional Review Board. A clerkship evaluation form was developed by the senior author and administered by the clerkship coordinator. This form consisted of three items that asked the students to (1) list the objectives they accomplished as a result of the clerkship, (2) share their concerns, and (3) suggest improvements for the clerkship program. The responses were open-ended. .

The data were placed into three categories that corresponded with the survey questions: (1) objectives met, (2)

concerns, and (3) suggestions for improvement. Concerns and suggestions were lumped into one category due to considerable overlap. Sample sizes and percentages were noted for each category. Lastly, a qualitative assessment of data collected from the clerkship evaluation forms was conducted.

## Setting:

Medical students (second-, third-, and fourth-year) from the University of Texas Medical School at Houston and Baylor College of Medicine in Houston, Texas, undergoing clerkship rotations at MD Anderson Cancer Center's Department of Psychiatry for three to four weeks were enrolled in the study. The clerkship evaluation form was administered to the medical students on their last day of the rotation. The responses were recorded and analyzed.

## Objectives Met:

Between January 2007 and September 2014, 174 students who underwent this rotation provided a completed clerkship evaluation form and were included in the initial report. The total number of students in the first cohort who completed psychiatry clerkships at MD Anderson from January 2007 through September 2014 was 332. Of these, 214 students (91 from Baylor College of Medicine and 123 from the University of Texas Medical School) returned their evaluation forms. Forty forms were incomplete and were not included in the analyses, so the final sample included 174 respondents.

Overall, the medical students were very satisfied with their clerkship experiences. They reported that they developed skills in core competencies such as patient care, medical knowledge, communication skills/bedside manners, professionalism, and practice-based learning. Individual core competency-based results are described below.

## Patient Care

One hundred forty-seven (85%) of the 174 students reported that they had developed skills needed for the diagnosis, evaluation, and management of psychiatric ailments in patients with cancer. In addition, 68 (39%) students reported that they had acquired the skills needed to conduct a psychiatric interview in a timely and comprehensive fashion. One student said, *I learned how to conduct a psychiatric interview for various*

psychiatric illnesses. *I observed different patient care styles and began the process of developing my own.* Of interest, 59 (34%) students reported learning other aspects of psychiatric care. Specifically, another student stated, *I learned about psychopharmacology and psychotherapy.* The students also felt that they benefited from the high volume of patients at our center, as reflected in yet another student's comments: *I was able to see a wide range of patients, which helped me with patient evaluation and management plans.*

### Medical Knowledge

Out of the total sample, 96 (55%) students reported learning about the most common psychiatric conditions in patients with cancer, while 15 (10%) reported learning about other important topics such as drug-drug interactions, akathisia, and the management of patients with suicidal behaviors. Thirty (17%) students reported learning case presentation skills, 15 (10%) reported improved note-writing skills, 9 (5%) reported feeling comfortable with the evaluation of a patient with psychiatric illness, and 5 (3%) reported being able to identify when to consult psychiatry. A fourth-year medical student stated, *By the end of the rotation, I was able to obtain a complete and thorough psychiatric history, perform a mental status examination, and formulate a reasonable differential diagnosis of a psychiatric illness. I gained a good appreciation of the complexity and importance of psychological issues—including coping mechanisms, spirituality, and socioeconomic issues. I became familiar with basic psychotropic medications, dose indications, and side effects while learning to deal with end-of-life and palliative care (challenges). I also learned about psychotherapies, such as supportive psychotherapy and motivational interviewing.*

### Communication Skills/Bedside Manners

Ten (6%) students reported that the rotation enhanced their knowledge of the appropriate communication skills and bedside manners to use when interacting with patients with complex medical issues. For example, one student said, *I learned how to communicate with patients coming from a wide variety of racial/ethnic, religious, cultural, and socioeconomic backgrounds.* Students also felt they were able to engage well with patients with physical and mental

illnesses. A second-year medical student expressed, *I became comfortable with talking to patients suffering from multiple and severe life stressors.* Medical students also felt they were exposed to various interviewing, assessment, and organizational techniques, as noted by one of the students: *I learned the art of giving a well-organized presentation and writing a progress note.*

### Professionalism

While others may have learned to demonstrate a commitment to carrying out professional responsibilities, only one (0.5%) student reported developing skills to work effectively on a team: *I learned how to communicate with patients, caregivers, and healthcare team members.* He felt being a part of the team and felt appreciated from both personal and professional perspectives.

### Practice-Based Learning

Students were able to identify strengths in their knowledge and experience. Sixteen percent of students mentioned that they appreciated the opportunity to receive formal and non-formal training in psychiatric issues in an oncology setting. One of the students stated the following: *The teaching helped me consolidate important information and gave me valuable clinical pearls.*

### Concerns and Suggestions for Improvement

Half of the students (50%) reported no concerns in their evaluation forms. **Among those that did report concerns, 8 (5%) students emphasized the need to increase the length of the clerkship, 10 (6%) felt that the service was too busy, 7 (4%) struggled with prescribing the correct medication doses, 10 (6%) expressed the need for more training on psychotherapy, and 10 (6%) wanted more transparent information on grading policies.**

Seventy percent of the students provided suggestions for improvement. Among those who provided suggestions for improvement, 8 (5%) wanted to receive clear expectations, 10 (6%) wanted an outline grading policy, and 42 (25%) wanted a thorough orientation at the beginning of the rotation, which would lead to a smoother transition. Some other suggestions for improvement included adding an outpatient clinic rotation, a pediatric rotation, and more didactic teaching.



## Discussion

Our study indicates that the medical students who underwent the psychiatric oncology clerkship acquired ACGME competencies, appreciated the opportunity to learn about psychiatric illnesses in patients with cancer, and felt that the rotation prepared them for their future practice of medicine. Our report adds to the current literature on this topic and is the first report to evaluate a psychiatry clerkship in a cancer center. A psychiatry clerkship plays a dual role in medical education. For future physicians who are not planning careers in psychiatry, it serves as the core psychiatric clinical experience. For those who intend to pursue a career in psychiatry, it helps with the mastery of core psychiatry principles. Studies evaluating psychiatry clerkships have reported that psychiatric clerkship serves as an essential psychiatric experience for all physicians irrespective of their future specialty choice. Medical students find the skills learned during their psychiatry clerkships essential to their future practice of medicine.<sup>1</sup>

The clerkship experience is particularly important in modifying medical students' attitudes to mental illness.<sup>3</sup> Psychiatry clerkship positively impacts students' attitudes toward psychiatry but does not necessarily increase their interest in psychiatry as a career option.<sup>7</sup> Similar findings were reported in yet another study,<sup>8</sup> which did not see a difference in change in attitudes or career intentions among fourth-year medical students who completed an eight-week psychiatry attachment. Teaching psychiatry can get the students rid of their negative attitudes, but it is not enough to encourage them to pursue psychiatry as a career.<sup>9</sup> Since the impact of clerkship on students' attitudes toward psychiatry is unclear, developing more sophisticated studies to fully evaluate the impact of clerkship and to correctly determine the factors positively or negatively influencing students' attitudes and career choice was suggested by Balon.<sup>10</sup>

The goal of MD Anderson's psychiatric oncology clerkship program was similar to other clerkship programs—to provide students with general psychiatry experience but in a specialized setting. **A major strength of MD Anderson's psychiatric oncology clerkship program is that it exposes students to a unique patient population and helps them to develop a specialized skill set that cannot be obtained in a general psychiatry rotation.** For example, medical students learn to manage

delirium. Students learn to manage challenging cases of agitation while helping the intensive care unit team to wean patients off ventilators and manage doses of neuroleptics. They learn to differentiate between functional and organic anxiety in medically ill patients. In addition, students learn how to manage cases of alcohol and drug withdrawal and the importance of drug interactions while multiple drugs are on board.

Most importantly, this clerkship helped students to acquire the skills needed to practice psychiatry. They benefited from the high volume of patients at our center, and the clerkship increased their comfort level in working with patients who have psychiatric issues along with coexisting medical conditions. This experience will allow them to become more effective physicians. While many of these students may not choose psychiatry as their profession, they will work with patients with psychiatric conditions at some point in their careers. These skills will serve them well as future physicians.

The largest limitations of this study are its small sample size and the fact that the clerkship evaluation form was not designed for quantitative data collection, as it allowed only open-ended, semi-structured responses. Due to the nature of the form, students provided feedback only on areas that they felt were important to them. The fact that students were not required to comment on their progress regarding the ACGME competencies explains why some of the percentages given in this study were so small and indicates that the data from the evaluations may inaccurately reflect student achievement. The evaluation form has now been redesigned to incorporate quantifiable measures, and specific questions for key competency areas and the resultant data will be reported in future studies. Another factor that has limited our study is that it was done at a single center that has a specialized psychiatry oncology clinic, which limits the generalizability of our findings. Similar studies should be repeated at other cancer centers for the reliability of results.

The students' interest in receiving more formal teaching and psychotherapy training is worth noting. Faculty are responsible for taking care of a large number of critically ill patients and are under pressure to remain clinically efficient while supervising and educating medical students. Although these challenges are difficult to address in the ever-changing and competitive field



of medicine, modifying and restructuring the clerkship program would enhance medical students' learning experience and directly impact patient care by producing empathetic doctors. One possible modification would be to provide dedicated faculty with some protected time to teach and discuss cases seen in the hospital, as this seems to be the best way to learn any psychiatric or medical illness. Individualized supervision, seminars and lectures, teaching rounds, and timely feedback would further enhance the quality of the clerkship program.

## Conclusion

Psychiatry clerkships offer the only opportunity to receive formal clinical experience in dealing with psychiatric

conditions for medical students who do not choose psychiatry as their career in the future. **By exposing students to a wide variety of mental health issues and treatment considerations specific to patients with cancer, such as the selection of appropriate psychotropic medications and the employment of stress management therapies, these clerkships enhance students' learning experience and give them specialized knowledge and skills that may not be obtainable through a general psychiatry clerkship.** Students pursuing a career in psychiatry will find the experience gained during their psychiatric oncology clerkships useful in their future careers, while students practicing other areas of medicine will be able to apply their training in communicating empathetically and effectively with their patients to any specialty. ■

## About the Faculty

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### Declarations

Ethics approval: This study was approved by the University of Texas MD Anderson Cancer Center's Institutional Review Board.

Consent for publication: All the authors consent to publication.

Availability of data and materials: The clerkship forms are with the senior author, AR, and are safely stored in a locked cabinet within the Department of Psychiatry at MD Anderson Cancer Center. The de-identified data are stored as a password-protected Excel file on an MD Anderson computer and are secured by an institutional firewall. The data cannot be shared since they are the property of MD Anderson.

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Author contributions: SS entered and interpreted data, drafted the article, and approved the final version of the manuscript. AR came up with the idea for the manuscript, collected data, revised the article, and approved the final version of the manuscript.

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## Multiple-Choice Questions

**77. What are the six correct competency domains accredited by ACGME?**

- A. Patient care, medical knowledge, communication skills, bedside manners, professionalism, and practice-based learning.
- B. Patient care, teamwork, communication skills, bedside manners, professionalism, and practice-based learning.
- C. Patient care, medical knowledge, the maintenance of a high patient volume, bedside manners, professionalism, and practice-based learning.
- D. Patient care, medical knowledge, communication skills, bedside manners, professionalism, and infomatics.

**78. Which of the following is the major strength of the psycho-oncology clerkship?**

- A. The psychiatric oncology clerkship exposes medical students to a wide variety of mental health disorders in medically ill patients.
- B. Education and teaching activities during the rotation.
- C. Teamwork.
- D. Grading policies.



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# Best Practices in Continuing Medical Education

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## Psychiatric Consultations from an Oncology Perspective: Medical Students' Clerkship Experience at a Comprehensive Cancer Center

By Smita Saraykar, MD, MPH; Asim A. Shah, MD; Anis Rashid, MD

ID#: L003462

**This valuable take-home reference translates research and theory that are presented in the accompanying continuing medical-education lesson into a systematic review of the lesson's key points for easy assimilation into your armamentarium of knowledge and daily practice.**

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### CME Lesson Overview

This lesson aims to describe the unique features of psychiatric oncology clerkship as experienced by medical students. This clerkship exposes medical students to various psychiatric disorders in medically ill patients, helps them understand the psychological aspects of medical care, and trains them to manage these disorders in vulnerable patients. It is important to note that this clerkship experience plays a major role in removing the negative perception toward psychiatric disorders and preparing medical students to be empathic clinicians in the future, especially if they choose any other specialty as their future career.

#### Key Point 1: Liaison Committee Requirement for Trainees

The Liaison Committee on medical education requires that medical students develop core competencies in six areas during their training, including patient care, communication skills, bedside manners, medical knowledge, and professionalism practice-based learning.

#### Key Point 2: Psychiatric Disorders in Medically Ill Patients

Psychiatric-oncology clerkship helps medical students develop core competencies required to be effective clinicians in the future and exposes them to a wide variety of psychiatric disorders in medically ill patients.

#### Key Point 3: Specialized Care for Cancer Patients

This clerkship exposes students to a unique experience of managing certain psychiatric disorders not seen in other psychiatric rotations, such as delirium.

#### Key Point 4: Understanding the Psychosocial Aspect of Patient Care

The clerkship trains students to understand patients' psychological and social challenges during any prolonged illness and its treatment, especially for students who do not choose psychiatry as their future career. They learn to communicate empathetically and effectively with their patients.

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