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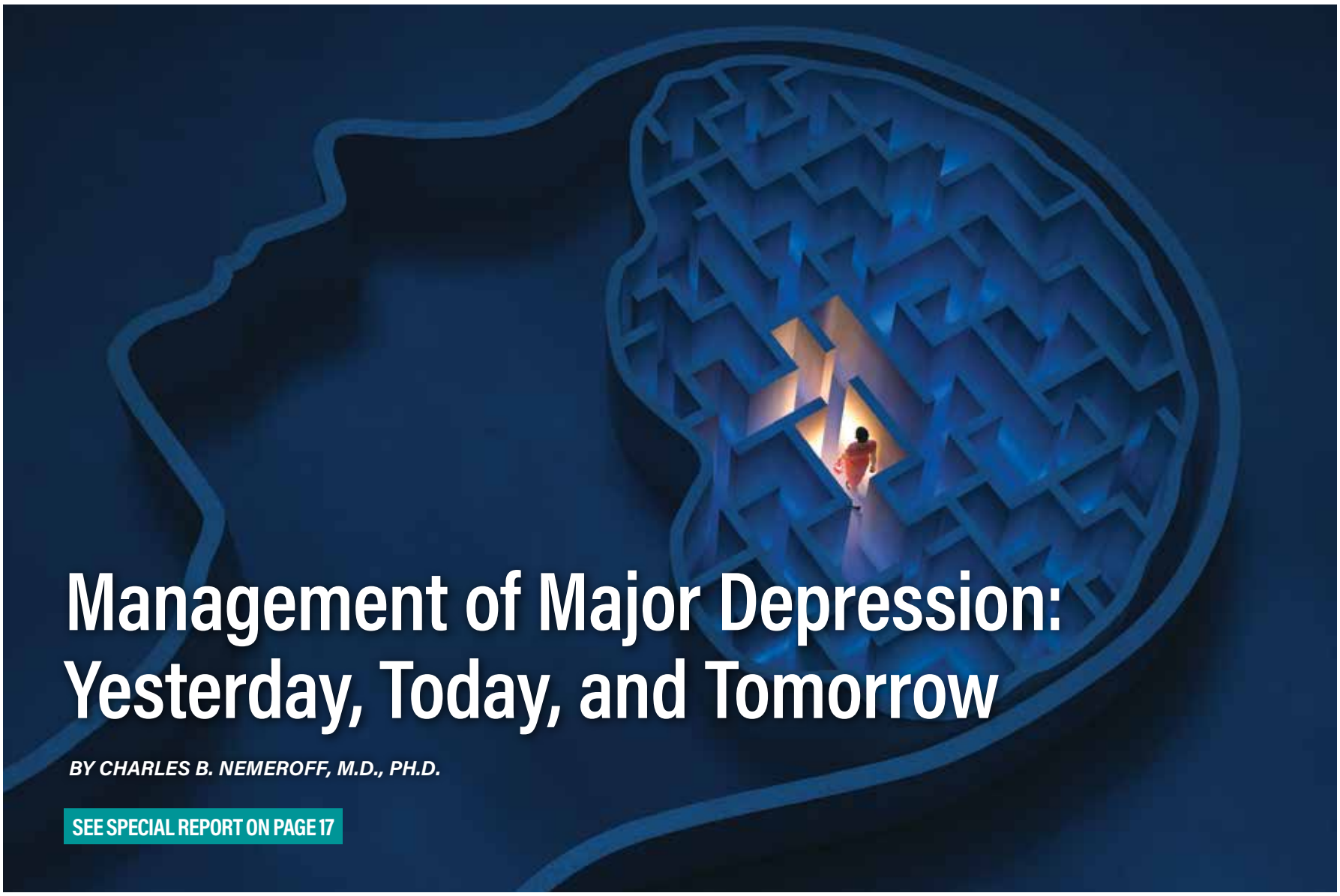

# Management of Major Depression: Yesterday, Today, and Tomorrow

BY CHARLES B. NEMEROFF, M.D., PH.D.

SEE SPECIAL REPORT ON PAGE 17

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# Class Action Grants Appeal Rights for Insurance Repayments

*Insurers claw back $1 billion a year from clinicians in repayment demands. A new class action settlement with UnitedHealthcare requires rights of notice and appeal.* **BY LINDA M. RICHMOND**

The settlement of a class action lawsuit brought by some 50,000 physicians over UnitedHealthcare's repayment demands sends a strong message to insurers and confers important and often overlooked rights to out-of-network physicians and other providers, according to a lawyer who worked on the case.

The lawsuit alleged that repayment demands sent to out-of-network providers failed to provide meaningful opportunities to challenge, obtain detailed plan information, or appeal them, as required by the federal law that governs private employer benefit plans, the Employee Retirement Income Security Act of 1974 (ERISA). The settlement covers any out-of-network clinician who submitted a claim to UnitedHealthcare and received a demand for repayment after January 2005.

D. Brian Hufford, J.D., who is an expert in ERISA law and partner with Zuckerman Spaeder LLP and represented clinicians in this case, told *Psychiatric News* that it is a widespread and lucrative practice for payors to perform postpayment audits and demand repayment of claims, also known as "takebacks" or "clawbacks," from providers, both in network and

*see* **Class Action** *on page 7*

PERIODICALS: TIME SENSITIVE MATERIALS

## APA's 2022 Election Season Begins

*See pages 12 and 13*

This issue contains the names of the candidates in APA's 2022 election, general information about the election, and the election guidelines. Please note that the guidelines have been changed for the 2022 and 2023 elections as part of a pilot test to create a level playing field for all candidates and ensure that candidates reflect the diversity of APA's membership.

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AMERICAN PSYCHIATRIC ASSOCIATION

FROM THE PRESIDENT

# Why We Must Confront Discrimination in Psychiatry

***BY VIVIAN B. PENDER, M.D.***

Discrimination is one of the most destructive social determinants of mental health. Discrimination and its associated social exclusion can be based on race, ethnicity, nationality, gender, age, disability, or other perceived vulnerability. Ubiquitous and pervasive, it can be overt or implicit—but in all circumstances, it is exploitative and immoral. It occurs in psychiatric training, clinical practice settings, academic departments, research arenas, and administrative policies. It can be found in virtually all areas of medicine. It is based on a common relationship paradigm of the strong versus the weak, reflecting its relevance to power and authority. Such a culture of exclusion and exploitation originally evolved in a world of medicine populated overwhelmingly by privileged White men.

Such exploitation and exclusion are clearly based on race and gender but can be based on virtually any kind of difference. The Association of American Medical Colleges (AAMC) published a detailed chart of chairs of psychiatry divided into categories such as race and gender (2015). They reported that only 10% were White women, and none were women of color. *The Lancet* in 2020 reported that whereas 46% of all physicians in medicine are now women, the number of tenured women is only 12%.

Another example is the physical and mental abuse of medical students, traditionally and ironically accepted as an integral part of medical training. Since 1978, the AAMC Graduation Questionnaire has been administered yearly to graduating medical students to provide feedback to medical schools to improve student experience. Although in 2020 satisfaction with medical school education was generally high, about 40% of respondents reported experiencing abusive behavior; the questionnaire listed 16 types, including hazing, public humiliation, derogatory remarks, bullying, intimidation, harassment, retaliation, and discrimination based on gender, race, sexual identity, sexual orientation, physical appearance, or other personal traits or beliefs. (See https://www.aamc.org/media/46851/download.)

Medical lore has enshrined the concept of "see one-do one-teach one." And thus it comes as no surprise that attitudes learned from medical school experiences can carry over into the ways that practicing physicians might approach patients. This can result in tacit discrimination against patients with mental illness, for example. This can also result in institutionalized stigma: Structural policies of private organizations and government that tend to impose limitations on people with mental illness. Examples include lower funding for research or fewer mental health services relative to other health care. On May 6, the *New England Journal of Medicine* published a distressing and compelling article written by psychiatrists Eric Rafla-Yuan, M.D., Divya K. Chhabra, M.D., and Michael O. Mensah, M.D., M.P.H., about the deaths and failure of U.S. mental health emergency services related to discrimination. (See https://www.nejm.org/doi/full/10.1056/NEJMms2035710.)

What characterizes these several examples is at best a thoughtlessness that belies prejudice and at worst a purposeful intent to maintain or increase power regardless of the harm inflicted.

*see* **From the President** *on page 6*

## IN THIS ISSUE






## DEPARTMENTS

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# Women Physicians Pay High Price—Again

*Women physicians have significantly higher rates of infertility, pregnancy loss, and pregnancy complications than women in the general population.* **BY MAUREEN SAYRES VAN NIEL, M.D.**

Two recent *New York Times* articles on health documented the increased incidence of infertility, pregnancy loss, and pregnancy complications among studied groups of women physicians. Here is a small sample of the recent papers on this topic.

A study of 327 women physicians, published in October 2016 in the *Journal of Women's Health*, found that 24% (more than twice the rate of general population) had been diagnosed with infertility at a mean age of 33.7 years. Among those with infertility, 29.3% reported diminished ovarian reserve, and 21.3% never conceived. Faced with this infertility, many respondents would have tried to conceive earlier, chosen a different specialty, or pursued oocyte cryopreservation.

Maureen Sayres Van Niel, M.D., is the immediate past president of the APA Caucus of Women Psychiatrists. She is a reproductive psychiatrist and private consultant in Cambridge, Mass.

A study posted July 28 in *JAMA Surgery* surveyed 692 female surgeons and 158 nonphysician female partners of male surgeons, who were used as controls. Female surgeons had fewer children and delayed childbearing. Nearly 25% of women surgeons had infertility necessitating in vitro fertilization. The survey also found that 42% of women surgeons had experienced a pregnancy loss, more than twice the rate of the general population, following which most of them had taken no time off. Female surgeons had significantly higher rates of major pregnancy complications such as perinatal depression, hypertensive and placental disease, and intrauterine growth restriction. More than half (56%) of the pregnant women surgeons surveyed worked more than 60 hours a week, and those working 12 or more hours a week in the operating room (OR) during the last trimester had a higher complication rate. A woman surgeon featured in one of the *Times* articles had a small stroke after developing severe preeclampsia at 34 weeks after working long hours in the OR.

A January 2015 study in the *Journal of Obstetrics and Gynaecology Canada* of 3,767 medical and surgical residents found that residents have higher rates of pregnancy loss and pregnancy complications than the general population and that the rate of pregnancy complications was five times higher for those working more than 8 hours a week in the OR.

These are sobering findings despite the fact that we do not yet have a prospective, randomized, controlled study that would provide more accurate data. Women physicians can likely anticipate double the infertility and pregnancy loss of other women and will have significantly more pregnancy complications, especially when they work long hours. Authors of the articles cited have proposed solutions to these problems that include providing residents and medical students with more education on infertility and cryopreservation, offering built-in support for women who undergo a pregnancy loss, and anticipating that the problem will likely self-correct because the percentage of female medical students has now surpassed men, giving women more agency in the system.

One cannot help but think when reading this: Have we in medicine lost our minds? Have the institutions of medicine become so intransigent that they would rather see their women physicians suffer infertility, pregnancy complications, and loss than recognize the fact that, for example, women surgeons who are in their third trimester should not be required to stand in surgery for more than 12 hours a week—period? And why can't residency programs that train future heart transplant surgeons solve the logistics of creating a residency system with built-in redundancy to accommodate the predictable number of women who will become pregnant during residency?

The same women physicians who have already possibly endured unequal pay and sexual harassment and who have hidden in bathrooms to pump their breast milk to conform to present expectations are now suffering painful intrusions into their ability to get pregnant, carry their baby to term, and have a pregnancy freer of complications. Academic medicine has not autocorrected over the years to accommodate the beautiful biology of so many of its contributing members. If we had not already reached the limit, we have reached it now. We don't need small adjustments to the current system; we need a wholesale change. Medical institutions, all physicians, and especially we as psychiatrists must rise up immediately to enact solutions to this intolerable reality. **PN**

**Links to the articles cited in this article are posted in its online version at https://psychnews.psychiatryonline.org/doi/10.1176/appi.pn.2021.11.32.**

## From the President

*continued from page 5*

A shift in attitude is required, from one of indifference or malintent to one of acknowledging our role in maintaining an environment that weakens people. In psychiatry, if we do not have empathy and compassion for our students, trainees, and patients, then we are not acting with professional integrity. Progress will continue to apply only to some people, and too many will be left out. However, if we embrace the idea that there are enough resources for everyone—money, power, prestige—then everyone can benefit.

No amount of mentoring students or helping patients to manage the harm they endure by discrimination will reduce the self-inflicted psychological injury that many psychiatrists ironically experience. If the main task of psychiatry is to diagnose and treat individuals suffering from a mental illness, then an inclusive, diverse, and unbiased approach must be employed, one that does not discriminate and fail to take into account the social determinants of mental health.

As long as we remain complicit with systems that conflict with our moral compass, we will all suffer moral injury and associated burnout. The COVID-19 pandemic has enabled, perhaps even forced, many people to re-examine their options and what they are willing to tolerate. I am hopeful that a more diverse cohort of medical students will emerge who will exercise their idealism and social awareness to correct previous cultures based on discrimination and social exclusion and demand a more enlightened house of medicine, beginning with psychiatry. **PN**

# UBH to Reimburse Beneficiaries, Pay Penalties


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*A Department of Labor investigation found that United Behavioral Health reduced rates for mental health professionals, overcharged beneficiaries for services, and subjected them to utilization review and denials of care.* ***BY MARK MORAN***

United Behavioral Health (UBH)/UnitedHealthcare Insurance Co. will pay $13.6 million to beneficiaries and $2,084,249 in penalties related to investigations and a lawsuit brought against UBH by the U.S. Department of Labor (DOL) and the office of the New York State Attorney General.

An investigation by DOL's Employee Benefits Security Administration found that since 2013, United had reduced reimbursement rates for out-of-network mental health services provided by psychologists, thereby overcharging participants for those services. The managed care company especially flagged mental health patients for utilization review, resulting in many denials of payment for those services.

United's actions violated the Mental Health Parity and Addiction Equity Act of 2008, which prohibits health plans governed by the Employee Retirement Income Security Act (ERISA) from imposing treatment limitations on mental health and substance use disorder benefits that are more restrictive than the treatment limitations they impose on medical and surgical benefits.

Investigators also found United failed to disclose sufficient information about these practices to plans and their participants and beneficiaries. In the settlement, United agreed to cease the violations, improve its disclosures to plan participants, and commit to future compliance.

"Protecting access to mental health and substance use disorder treatment is a priority for the Department of Labor—and something I believe in strongly as a person in long-term recovery," said U.S. Secretary of Labor Marty Walsh in a statement. "This settlement provides compensation for many people who were denied full benefits and equitable treatment. We appreciate [New York] Attorney General Letitia James and her office's partnership in investigating, identifying, and remedying these violations."

In a statement, James said United's violations were especially egregious in light of the great need for treatment during the opioid epidemic and the COVID-19 pandemic.

"In the shadow of the most devastating year for overdose deaths and in the face of growing mental health concerns due to the pandemic, access to this care is more critical than ever before," she said. "United's denial of these vital services was both unlawful and dangerous—putting millions in harm's way during the darkest of times. There must be no barrier for New Yorkers seeking health care of any kind, and I will always fight to protect and expand it. I thank Secretary Walsh for his partnership on this important matter." **PN**

**Information about the DOL lawsuit is posted at https://www.dol.gov/newsroom/releases/ebsa/ebsa20210812.**

## Class Action

*continued from page 1*

out of network. Industrywide, insurers are estimated to claw back more than $1 billion a year from providers in repayment demands.

Hufford estimated that UnitedHealthcare issues 1.6 million repayment demands a year. For out-of-network providers who don't repay the money, UnitedHealthcare typically subtracts the funds from subsequent payments to the provider, even from unrelated claims. Takebacks can be very disruptive and difficult to dispute because unlike the initial claims, physicians are often given no rationale for them, and there is no way to check their accuracy.

The class action didn't seek the repayment of any money, but rather sought to require UnitedHealthcare to provide out-of-network clinicians with specific notice and appeals rights under ERISA in connection with past and future repayment demands. These include the specific reason for the adverse determination, reference to the specific plan provisions upon which the determination is based, and a description of the plan's review procedures and applicable time limits.

For the class action, one particular repayment demand was designated to serve as the basis for all of the claims. Integrated Orthopedics Inc., a Chicago-based supplier of postsurgical supplies, was paid $849.16 by UnitedHealthcare for care provided to a patient. The insurer's computerized audit correctly flagged the patient as not having received the required preauthorization. However, instead of applying a 10% payment as provided for under the patient's plan, United clawed back the entire $849.16.

UnitedHealthcare allegedly ignored or denied requests for more information, an explanation of its reasoning, and copies of the governing plan documents. After a lawsuit was filed, UnitedHealthcare eventually agreed to withdraw its repayment demand.

The settlement of *Integrated Orthopedics Inc. v. UnitedHealth Group, et. al.,* stipulates that for the claims in question and for new claims going forward, repayment demands must treat out-of-network providers as "Authorized Representatives" under ERISA and grant them ERISA due protections, so long as providers furnish United with an Authorized Representative form completed by the patient. UnitedHealthcare denied any wrongdoing in the settlement.

Going forward, ERISA should provide substantial protection for out-of-network clinicians billing commercial insurance plans on behalf of their patients, Hufford said. "For physicians who exercise their right to appeal a repayment demand, United must now defer taking further steps to recover alleged overpayments until the appeals process has been completed."

Gittings Photography

D. Brian Hufford, J.D., advises out-of-network providers to obtain Authorized Representative forms from patients to retain important rights of appeal in case insurers demand repayment.

However, Hufford advises clinicians to obtain proper authorization by ensuring that all intake forms designate them as an Authorized Representative. This allows them to pursue appeals or take appropriate legal actions, as necessary, on behalf of their patients. "The insurer may still refuse to cooperate with the provider, but this will substantially strengthen the ability of the provider to push back against these types of repayment demands." Authorized Representative designations can also be obtained by the provider from the patient after a repayment demand, he said.

The settlement specifically involves out-of-network providers, but Hufford said, "We would encourage all providers to take full advantage of the appeal rights they are given under their contracts. However, it is more difficult for in-network providers to push back, because they have entered into agreements that allow such audits and repayment demands."

Other insurers might also fall in line with this ruling. "It is unclear that this settlement will impact other insurers, but the decisions in the case strongly support our view that ERISA should govern repayment demands like this and that physicians should be entitled to due-process protections. We obtained certification of a nationwide class of out-of-network providers who were subjected to repayment demands by United. That should send a strong message to all insurers engaged in such conduct," he said. **PN**

**The website for the class action is http://unitederisarightsclassaction.com.**

# SMI Adviser to Offer Virtual Learning Collaboratives

*SMI Adviser offers free CME/CE-certified education, expert consultations, and resources to help frontline clinicians and staff provide evidence-based care to individuals who have serious mental illness.* **BY MARK MORAN**

SMI Adviser, APA's Clinical Support System for Serious Mental Illness, will offer 10 free virtual learning collaboratives beginning in February 2022. These 12-week courses provide in-depth information on specific topics related to caring for patients with serious mental illness (SMI). Each course is guided by experts in SMI.

SMI Adviser was funded in July 2018 by a five-year, $14.2 million grant from the Substance Abuse and Mental Health Services Administration (SAMHSA). It offers free CME/CE-certified education, expert consultations, and resources to help frontline clinicians and staff—including physicians, nurses, psychologists, social workers, counselors, and peer recovery specialists—provide evidence-based care to individuals who have SMI, including those living with schizophrenia, bipolar disorder, or major depressive disorder.

The virtual learning collaboratives that launch in the spring include the following:

- Getting Started Building Your Clozapine Practice
- Protocol-Driven System to Manage Efficacy and Side Effects of Clozapine
- Getting Started with Telehealth for Serious Mental Illness
- Getting More From Telehealth: Increasing Engagement and Supporting Remote Diagnostics and Interventions
- Motivational Interviewing for People With Serious Mental Illness
- Implementing Tools for Symptom and Functional Assessment of Individuals With SMI
- Building and Using a Comprehensive Psychiatric Mental Health Nursing Assessment
- Treating the Whole Patient: Addressing the Physical Health Needs of Populations With SMI

These learning collaboratives are an ideal opportunity to build skills using an intensive, real-world, evidence-based approach. Clinicians can consult with faculty experts and get real-time feedback during virtual office hours, participate in group calls with colleagues, complete skills-based assignments, and share ideas on interactive discussion boards. The time invested in these courses helps translate skills directly from concept into actionable care for individuals with SMI.

SMI Adviser offers a wealth of information in addition to its virtual learning collaboratives. It is free and accessible via https://smiadviser.org and a smartphone app dowloadable from https://smiadviser.org/getapp. This allows clinicians to easily obtain consultation from experts, access tools

*see* **SMI Adviser** *on page 11*

## APA'S GOVERNMENT, POLICY, AND ADVOCACY UPDATE

### Surprise Billing Rules Yield to Insurers, Draw Ire From Physicians

Physician organizations, including APA, are concerned about the way the Biden administration is implementing the No Surprises Act. The law is set to take effect January 1 and aims to protect patients from unexpected bills that arise when out-of-network clinicians provide emergency or other services at an in-network facility.

The problem of surprise billing has gotten worse in the past decade because health plans have narrowed their networks of clinicians, APA asserted in comments (http://apapsy.ch/billing) filed in September with the Centers for Medicare and Medicaid Services (CMS) on the law's Part 1 proposed rule (CMS-9909-IFC). APA expressed concern that the law could have unintended results: By increasing financial stress for inpatient psychiatric units, it could hasten the loss of beds when demand is rising, and there is a growing shortage of psychiatrists.

In its comments, APA urged the following:

- A requirement that insurers create adequate networks of clinicians to treat mental and substance use disorders—in accordance with the Mental Health Parity and Addiction Equity Act.
- A requirement that insurers streamline the approval process for joining a network panel to no more than 30 days.

According to the Part 2 interim final rule (RIN 1210-AB00) that CMS issued in September, in the event of a surprise medical bill, the amount of the bill will be determined by the insurance plan's median in-network rates for a similar service.

The AMA criticized the rule for disregarding the insurance industry's role in creating the problem of surprise billing at the expense of independent physician practices. It urged the Biden administration to delay implementation and re-evaluate the rule.

### APA: Medicare Patients Need Telehealth, Audio-Only Care Access

APA urged the Biden administration to reconsider a proposed rule (CMS-1751-P) (https://www.govinfo.gov/content/pkg/FR-2021-07-23/pdf/2021-14973.pdf) that would require clinicians to see Medicare patients for an in-person appointment to be eligible for any telehealth encounter.

The changes that CMS put in place during the pandemic "showed the potential and benefits of virtual care in meeting treatment needs, including reduced no-show rates for appointments, increased continuity of care, and increased patient satisfaction," APA wrote in formal comments (http://apapsy.ch/telehealth-rule) submitted to CMS in September. However, the proposed requirement for an in-person appointment either initially or for subsequent visits for Medicare enrollees could dilute the benefits of easily accessed telehealth and erect barriers to care.

APA also recommended that CMS continue to allow audio-only telehealth services for Medicare enrollees on a permanent basis. Putting restrictions on audio-only care will disproportionately affect individuals who are low-income; elderly; or are without transportation, reliable access to broadband, or personal electronic devices.

### Coalition States Mississippi Abortion Law Harms Doctor-Patient Relationship

APA joined a coalition of 25 health care organizations urging the U.S. Supreme Court to overturn Mississippi's ban on abortion after 15 weeks of pregnancy for nearly all patients, according to an amicus brief (http://apapsy.ch/Mississippi-law) filed in September in the case *Dobbs v. Jackson Women's Health Organization*.

The brief asserts that the state law grossly interferes in the patient-clinician relationship and is fundamentally at odds with scientific evidence, medical ethics, and the provision of safe and essential health care. The organizations further argue that the law would have a disproportionate impact on rural and low-income individuals and those from communities of color.

Mississippi's law was blocked by lower courts from taking effect, but the U.S. Supreme Court will hear the case starting December 1. The case is a direct challenge to *Roe v. Wade,* testing whether a law that bans abortion previability is unconstitutional. (Twelve states, including Mississippi, have abortion trigger laws on the books that will automatically ban abortion in the first and second trimester if *Roe v. Wade* is overturned.)

Meanwhile as of press time, a near-total abortion ban in Texas will continue to be enforced, pending an expected appeal to the Supreme Court. A panel of judges from the U.S. Court of Appeals for the Fifth Circuit sided against a Justice Department request to lift the ban. APA, as part of a coalition of leading medical societies, had urged the Fifth Circuit in an amicus brief to uphold a lower court ruling temporarily halting the abortion ban, which gave providers a 48-hour reprieve from the ban.

ON MENTAL HEALTH, PEOPLE, AND PLACES

# Peace Cranes in a Sanctuary

***BY EZRA E. H. GRIFFITH, M.D.***

Ezra E. H. Griffith, M.D., is professor emeritus of psychiatry and African American Studies at Yale University.

Whenever I am away from home on Sunday, I find it rejuvenating to attend a church service as a visitor. I enjoy observing the rituals and listening to a new preacher. I take note of the level of the music ministry and the lay members' participation in their faith group. Most recently, I took the one-mile stroll from my lodging to St. John's Scottish Episcopal Church in downtown Edinburgh. I decided to visit this branch of Protestantism because I had already attended a service at a Church of Scotland, with its philosophy and rituals closer to those of John Knox and the Calvinist Reformers. One glance at the day's service program and my eyes landed on the claim that St. John's "seeks to be an open community, walking in the way of Jesus, engaging with an ever-changing world, and living a faith that is timeless yet contemporary, thoughtful, and compassionate." This declaration of modernity was in striking contrast with the greying mass of stone that characterized the external appearance of the building. The seeming contradiction would come up in my conversation after the service with the associate rector, the Rev. Rosie Addis.

Everyone followed the public health rules and wore a mask. The choristers took off theirs while fulfilling their duties, as did the clergy when leading the prayers, preaching, and reading the liturgical texts. Clergy and congregation had found an operational middle ground, a way of functioning while wearing masks and respecting distance. No collection plate was circulated during the service. A member explained that the new method, forced by COVID-19, was for someone to stand at the church door after the service, with the collection plate in hand. I learned that the new method is called "retiral collection."

Brigitte Griffith with permission of the Rev. Rosie Addis

A mobile of cranes floats above the sanctuary in St. John's Scottish Episcopal Church in Edinburgh.

It is hard to explain the Sunday morning peacefulness of an urban church, built almost 200 years ago. With the organ in the hands of an aficionado and the choir chanting the psalm expertly, the 16th-century motet by William Byrd was performed elegantly. The sacred sounds were bouncing lightly off the church walls accompanied by the sun's rays dancing on the mobiles hanging from the ceiling and light fixtures around

*see* **Cranes** *on page 11*

# Stanford Initiative Engages Media About Mental Health, Suicide


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*This is the second in a series of articles on media reporting and suicide. The author provides examples of how media—including entertainment venues—can promote positive messages about mental health.*

***BY VICTOR SCHWARTZ, M.D.***


Media Reporting and Suicide

Throughout my professional life, in roles such as medical director of New York University's student mental health services and chief medical officer of The Jed Foundation (JED), I have been profoundly aware that media can do much to shape how society and individuals understand mental illness and mental health care.

Our Media and Mental Health Initiative based at Stanford University's Department of Psychiatry and Behavioral Sciences has the potential to improve media narratives around mental health and head off harmful storytelling. A notable concern is media coverage of suicides, which can raise or lower the risk of subsequent suicides in communities.

The initiative, led by Steven Adelsheim, M.D., a clinical professor and director of the Stanford Center for Youth Mental Health and Wellbeing, aims to promote public education about mental health and suicide through proactive, sustained engagement on best practices with content producers in the news media and entertainment industry and among social media platforms and users.

Working at NYU during the September 11 attack on the World Trade Center in Lower Manhattan, I keenly appreciated the importance of effective communication. NYU had several thousand students displaced by the attack, and the campus was left in both physical and emotional turmoil for weeks after this tragedy. While in the first days after the attack, our phone and IT systems were not functional, we managed the practical/physical needs of the campus with written notes and messengers and successfully communicated clearly and regularly to contain the anxiety and confusion that ensued.

Victor Schwartz, M.D., is a clinical associate professor of psychiatry at NYU School of Medicine, CEO of Mind Strategies Advising, and a core member of the Stanford Media and Mental Health Initiative.

During NYU's 2003-2004 academic year, I was confronted with the challenge of providing clinical and administrative guidance through a suicide cluster on campus. I realized that the reporting by the college newspaper and local media had a strong impact on the emotional tone on campus. Again, clear and balanced communication—enough information to allay fear, confusion, and gossip but not so much as to feel triggering or promote identification with the decedents—felt essential.

At that time, I began to learn about prior research regarding the impact of reporting on suicide contagion risk and had the opportunity to consult with and learn from leaders in this field including Madelyn Gould, Herb Hendin, and Mort Silverman.

At JED, a nonprofit devoted to suicide prevention and mental health promotion in teens and young adults, I had the opportunity to advise news organizations, social media platforms, films, and TV shows on best practices in mental health storytelling. I have had the honor to advise Sheila Nevins (formerly president of HBO Documentary Films and currently director of MTV Documentary Films) on her excellent recent film, "Each and Every Day," focused on young people who have experienced suicide attempts or suicidal ideation. I also served as adviser to the recent Oprah/Prince Harry/Apple TV series, "The Me You Can't See," a wonderful series examining mental health around the world.

Another member of the Stanford initiative's development team is Scott MacLeod, who is a longtime correspondent and bureau chief for *TIME* magazine. He and his wife, Susan Hack, also a journalist, founded The Sophie Fund, a nonprofit mental health advocacy organization in Ithaca, N.Y., after the suicide of their 23-year-old daughter Sophie in 2016.

MacLeod believes that the media must play a life-changing role in educating the public about mental health and mental health care and that improved understanding about mental health among journalists, as well as filmmakers, social media platforms, content producers, and other media practitioners, can preempt damaging narratives.

In addition to engaging media practitioners, the Stanford initiative also plans training programs for psychiatrists to improve their communications skills when talking to reporters and media outlets. It is essential that mental health professionals understand the role they too can and must play in guiding responsible media portrayals.

A 2014 paper in the *Proceedings of the National Academy of Sciences (PNAS)* found experimental evidence that social media could profoundly change people's mood and risk for suicide through "emotional contagion." All forms of media have the power to make a transformational impact on our health, mental health, and well-being. Media narratives that align with evidence-informed guidelines break down prejudice and discrimination surrounding mental health challenges/suicide and encourage help-seeking behavior. Conversely, media narratives that do not adhere to evidence-informed guidelines often trigger negative reactions in people experiencing mental health disorders and may inspire dangerous imitative behaviors, potentially increase the risk of others dying by suicide, and perpetuate mental health discrimination.

While safe suicide reporting guidelines have been published by leading organizations to educate journalists in best practices, there has not been sustained outreach to provide education and real-time guidance to journalists and other media content producers. It is our hope that through the Stanford initiative, the mental health community can actively and constructively engage the media and make a difference in people's lives. **PN**

**More information about the Stanford Media and Mental Health Initiative is posted at https://med.stanford.edu/psychiatry/special-initiatives/mediamh.html. Information about the film "Each and Every Day" is posted at https://www.mtv.com/movies/elnypx/each-and-every-day. The *PNAS* article is posted at https://www.pnas.org/content/111/24/8788.full.**

# A Psychiatrist to Doctors Is Witness To Impact of Stigma on Physicians

*Michael F. Myers, M.D., has complemented his educational and clinical work with advocacy for nondiscriminatory policies toward physicians with a history of mental illness.* **BY MARK MORAN**

Adam was a 23-year-old third year medical student in the final week of his psychiatry clerkship. At the end of the day, he approached a teacher. Looking pale and frightened, he said to the instructor, "Got a few minutes?"

"Sure, what's going on?" The instructor was Michael F. Myers, M.D., who also happened to be the director of medical school education in psychiatry at the institution where Adam was training.

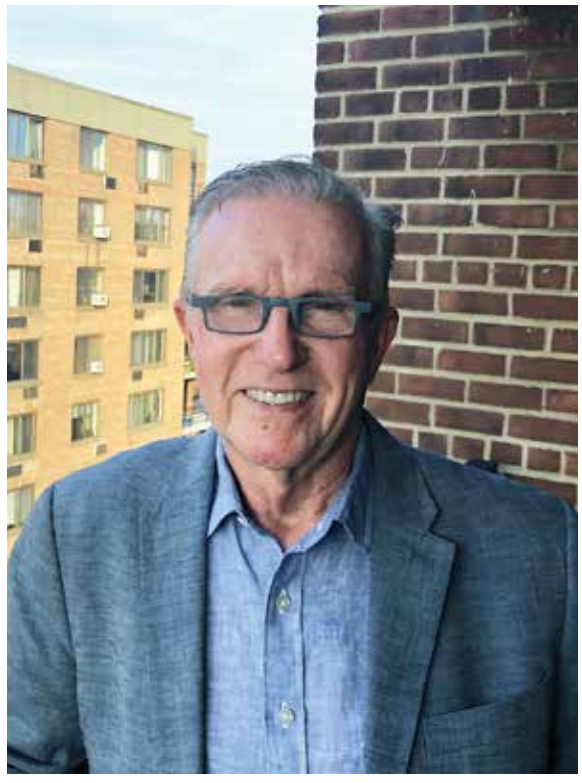
Adam began talking, and Myers—switching hats from educator to diagnostician—quickly realized that the student was severely depressed. Adam spoke of feeling like a failure, feeling "old." His grades were dropping, and he was withdrawing socially. He confided that, 10 days previously, he had loaded his father's shotgun in his car in case he "needed it."

Recognizing that Adam was at risk of suicide, Myers had him hospitalized. Following discharge, Myers began seeing Adam for weekly and later biweekly psychotherapy and medication management for about eight months.

That was 38 years ago. Throughout the following years—through educational and career advancement and career and personal changes and upheavals for both men—they remained in contact. Adam, who earned a medical degree and became a highly skilled physician, returned as a patient in 1991, again in 1999, and one more time in 2008.

"He had come in and out of my life over the years, and we grew older together," Myers told *Psychiatric News*. "I was a very young psychiatrist—in my third year of practice—when he approached me, and he was a medical student. Now he is retired."

In the intervening years, Myers, who is a clinical professor of psychiatry at SUNY Downstate Medical Center, built a career in education and had a half-time private practice in which he made a specialty of treating physicians—a psychiatric physician to other physicians. For him, the story of Adam is emblematic, because it runs counter to perceptions about physicians held by the public and, importantly, by physicians themselves.



Michael F. Myers, M.D., has had a unique practice as a psychiatrist to doctors. "It's very gratifying work. You can help so many people who are in turn helping others get well."

As a doctor's doctor, Myers has spent years listening to accounts of his physician patients who have felt shunned or judged by colleagues and the institutional rules of medicine because they are experiencing a mental illness or substance use disorder. Stigma, magnified by an unforgiving professional culture, courses like a poison through their stories.

"There is still a lingering mythology that if a medical student or resident becomes ill, he or she may not return and may not have been cut out for medicine," Myers told *Psychiatric News*. "It simply isn't true. Throughout all the years and the periods when his depression returned, Adam advanced in his specialty and was and is a strong, functioning individual."

### Helping Others Who Help Others

Early in his life, Myers came to know the force of stigma when he lived with and saw up close—at age 12—his

*see* **Stigma** *on page 14*

## SMI Adviser

*continued from page 8*

that support care, and earn CME/CE credits. SMI Adviser's online education catalog includes more than 200 webinars and interactive modules on a wide range of subjects on SMI—among them, the interface between SMI and the criminal justice system, the use of telepsychiatry for treating patients with SMI, engagement of patients and families in treatment planning, strategies for successful use of clozapine, use of psychiatric advance directives, and chronic physical health management for individuals with SMI.

Last year SMI Adviser released My Mental Health Crisis Plan (https://smiadviser.org/mymhcp), a mobile app that includes a step-by-step guide for people with SMI to create a psychiatric advance directive (PAD) and share their treatment preferences in advance of a mental health crisis. A PAD is a legal document that details an individual's treatment preferences in the event they are unable to make decisions due to worsening illness.

SMI Adviser also operates two Centers of Excellence (CoEs) to promote best practices in psychopharmacology—the Clozapine Center of Excellence (www.smiadviser.org/clozapine) and Long-Acting Injectable Center of Excellence (www.smiadviser.org/lai). Each is dedicated to providing free CME/CE-certified education, consultations, resources, and other evidence-based tools.

The CoEs host a community listserv and monthly virtual forums for moderated peer-to-peer discussions on trending topics on either clozapine or long-acting injectable medications. Clinicians can engage with colleagues and share challenges and questions on the month's trending topic. Virtual forums are held from 4 p.m. to 4:45 p.m. ET on the first Wednesday of every month. Those interested in participating may sign up to receive email invitations at the Clozapine Center of Excellence or Long-Acting Injectable Center of Excellence.

APA CEO and Medical Director Saul Levin, M.D., M.P.A., said that SMI Adviser breaks new ground in using technology to bring expert advice on SMI to clinicians who need it.

"I urge our members and mental health professionals to visit the SMI Adviser website and download the app and explore this remarkable resource," he said. "It's a huge step in realizing the vision of the SAMHSA grant to bring customized, evidence-based information to those caring for patients with SMI." **PN**

## Cranes

*continued from page 9*

the church. The photograph on page 9 shows an example of the extensive mobile made of thousands of peace cranes handcrafted from origami paper. I learned the cranes were part of an exhibition by artist Janis Hart intended to transform St. John's Church into a bird sanctuary for peace. The idea was to provoke viewers into thoughts about the victims of the 1945 bombing of Hiroshima. That is complemented by the church's work for inclusion of LGBTQ people in the life of the church and in society.

The Rev. Addis explained the mission of this urban faith group, first by helping me understand better the morning's sermon. It was about EFM, which stands for "Education for Ministry" or "Exploring Faith Ministry." She pointed out that this movement is not intended for the education of clergy. It is to help church members explore religious matters and facilitate their theological reflection about what God is asking them to do in service to others. Hence, the mission's orientation toward peace, abolition of nuclear weapons, and fellowship with nondominant groups such as Blacks, other minorities, and the LGBTQ community. Rev. Addis has also determined her pathway toward serving a unique group. She is an expert in British Sign Language and directs a monthly service for what she calls the "Messy Church." This meeting is for those suffering the indignities and problems related to hearing disabilities.

Several elements in the service collectively framed an ambience of togetherness and concern for others. The play area to one side of the sanctuary welcomed children. The tables and chairs at the rear invited attendees to socialize and enjoy tea and cake at the conclusion of the service. These ideas about caring for others, or for one another, reinforced the aesthetic and moral impact of the multicolored paper cranes fluttering in the air currents above us. The reminder of what we should do for neighbors was powerful. **PN**

# Candidates Announced for APA's 2022 Election

*Candidates must follow new campaign rules that are meant to level the playing field for all candidates.* **BY CATHERINE F. BROWN**

There are 15 candidates vying for national and Area office in APA's 2022 election. Below are their names and the offices for which they are running.

The campaigning rules that candidates must follow are different from those for previous elections. In December 2020, the Board of Trustees voted to launch a two-year pilot campaign plan for candidates to start with the 2022 election. Under the new rules, all campaigning is prohibited except through APA-managed activities and other activities as the APA Elections Committee may permit.

The changes are meant to level the playing field for all candidates and ensure that APA's leadership reflects the diversity of the APA membership and thus includes candidates who are from minority and underrepresented groups. The new process was recommended by the APA Presidential Task Force to Address Structural Racism Throughout Psychiatry, appointed by then President Jeffrey Geller, M.D., M.P.H.

These are the approved APA-managed campaign activities:

- Live "Meet the Candidates" town halls will be held during the campaigning period (see box at right). These one-hour sessions will be open to all APA members. Members may submit questions before the town halls at https://survey.alchemer.com/s3/6566652/Meet-the-Candidate-Town-Hall-Q-A or during the town halls. Sessions will be recorded and posted on the APA election website for viewing by members who are unable to participate in the live sessions.
- A "special edition" APA election newsletter of candidates' platforms will be emailed to all voting members on December 1.
- *Psychiatric News* will publish the names and photos of the candidates and election details in its December issue.
- APA's election website (psychiatry.org/election) will be expanded to serve as a centralized location for all election and candidate-related information. Information includes candidates' biographical statements and photographs. The site will go live in early December.

As the election guidelines on the facing page indicate, no other forms of campaigning are permitted, such as letters, phone calls, emails, and messages on APA listservs by or on behalf of candidates.

Sanctions for violations are included in the new guidelines.

All voting will be by electronic ballot. Beginning January 3, ballots will be emailed to all eligible voting members with a valid address on file with APA; they may also go to psychiatry.org/election and use their member login information to access their electronic ballot.


Paper ballots will be mailed only to eligible voting members who request them by contacting the APA Election Office through January 10 at election@psych.org.

The deadline for online voting is Monday, January 31, at 11:59 p.m. ET. Also, paper ballots must be postmarked by that deadline.

If you have any questions, contact the APA Election Office at election@psych.org. **PN**

## Candidates in APA's 2022 Election

Below are the names of the candidates and the offices for which they are running. The slate was approved by the Board of Trustees last month.

**President-Elect**
Petros Levounis, M.D., M.A.
James B. Potash, M.D., M.P.H.

**Treasurer**
C. Freeman, M.D., M.B.A.
Richard F. Summers, M.D.

**Trustee-at-Large**
Samuel O. Okpaku, M.D., Ph.D.
Michele Reid, M.D.

**Area 3 Trustee**
Kenneth M. Certa, M.D.
Geetha Jayaram, M.B.B.S., M.B.A.
Mark S. Komrad, M.D.

**Area 6 Trustee**
Mary Ann Schaepper, M.D., M.Ed.
Shannon Suo, M.D.
Barbara Yates Weissman, M.D.

**Resident-Fellow Member Trustee-Elect**
Faiz Kidwai, D.O., M.P.H.
Mary-Anne Hennen, M.D.
Seth L. Daly Stennis, M.D.

## Schedule for 'Meet the Candidates' Town Halls

APA members will have an opportunity to hear directly from the candidates and ask questions in a series of virtual town halls next month. Below is the schedule:

- President-elect, treasurer, and trustee-at-large: December 13
- Area 3 trustee (elected by Area 3 members): December 14
- Area 6 trustee (elected by Area 6 members): December 15
- Resident-fellow member (RFM) trustee-elect (elected by RFMs): December 16

The town halls will be moderated by the chair and members of the Elections Committee. Candidate presentations of five to seven minutes will be followed by a question-and-answer session that includes questions from the committee and APA members; members may submit questions in advance at https://survey.alchemer.com/s3/6566652/Meet-the-Candidate-Town-Hall-Q-A or during the town halls. To attend the town halls, please RSVP by visiting the APA election website at psychiatry.org/election. A registration link will be emailed to you in early December.

For members who can't attend the town halls, they will be archived on the APA election website.

# Election Guidelines: Know the Rules

*Based on guidelines approved as amended by the Board of Trustees in December 2020.*

## A. OVERVIEW

The intent of the guidelines is to encourage fair and open campaigning by APA members on a level playing field by (1) specifying permitted and prohibited election related activities, (2) fostering opportunities for candidates to educate their colleagues about the issues, (3) informing voters about candidate experiences and views, (4) keeping costs down, and (5) maintaining dignified and courteous conduct appropriate to the image of a profession.

All APA members are expected to abide by the APA election guidelines in APA elections, including in their capacity as officers and members of other organizations. APA requests that other organizations adhere to the intent of the campaign guidelines and provide fair and equitable coverage of opposing candidates.

The Elections Committee investigates any potential violation by a candidate or supporter of which it becomes aware and reports violations to the Board of Trustees. The procedures used by the Elections Committee to investigate and report campaign violations are in Chapter 2 of the Operations Manual.

## B. CAMPAIGNING

Campaigning is defined as any attempt to influence a potential voter's vote. Campaigning includes mentioning one's candidacy or making any statement that might be interpreted as a position statement reflecting what actions the candidate would take if elected. It does not include appearances made as part of one's normal work activities. Permitted campaign activities are specified in this document. All other activities are prohibited.

Approved APA-organized campaign activities may include the following:

- "Meet-the-Candidates" live town hall/webinar
- Special APA Election Edition, published during campaign period
- *Psychiatric News* December election issue
- APA election website (psychiatry.org/election)

### 1. Resources

- Use of APA, Area Council/State Association, or District Branch resources or personnel is generally prohibited, except for any Election Committee–approved communication of candidate statements to members.
- APA, Area Council/State Association, or District Branch funds, services, stationery, or staff may not be used to endorse, support, or promote any candidate.
- Permitted APA resources are the APA Election website (psychiatry.org/election) and platform used for campaigning on live Town Hall/Webinar and election publications. All other resources are prohibited.

### 2. Campaign Communications

Permitted forms of campaigning include the following; all others are prohibited.

**a. APA Website**
APA will include information on all candidates (photos, biographies, and statements provided for the ballot booklet) and on the election itself (campaign guidelines, ballot mailing and return dates, etc.) on its website. This election information can be accessed through the election logo and linked to other information as appropriate.

**b. Private Discussion**
Private election-related communication with individual colleagues is permitted.

**c. District Branch/State Association Campaigning: Newsletters**
District Branch or State Association newsletters may announce as news items, without endorsement, two types of announcements:

- A news item that requires equal representation of all candidates for an APA office, and/or
- A limited 150-words per candidate news item describing the candidacy for an APA office of local member(s) affiliated with that District Branch or State Association.

Editorial endorsement of candidates is prohibited, as are letters to the Editor in support of (or opposition to) candidates. Newsletters may print other statements or materials by or about a candidate only if they give equal opportunity to opposing candidates. Newsletters may not be distributed beyond the usual newsletter distribution.

**d. Introduction at Professional Presentations**
A candidate's candidacy may be mentioned when the candidate is introduced for the purpose of giving a professional presentation, provided that the candidate is not endorsed. Candidates are to inform the hosts/speakers of the events that an endorsement or any statement of an endorsement is not permitted.

There are no restrictions on professional presentations, defined as events where no campaigning occurs and a candidate participates in the dissemination of information through any medium. Running for office should not inhibit or prohibit candidates from conducting their usual professional business.

**e. Endorsement**
Endorsement by organizations is prohibited. Candidates may submit a list of individual endorsements to be included on the candidates' APA Election Website.

- Supporters may not campaign on behalf of the candidates.
- Candidates may not coordinate campaign activities. Campaign committees (entities that can make statements or take other actions on behalf of the candidate) are not allowed.
- Candidates are responsible for calling attention to the guidelines or sending a copy of the guidelines located on the APA Election website to any members whom they ask for endorsement.
- Members of the Board of Trustees, Nominating, Elections, and Tellers committees are not permitted to endorse or support a candidacy.

**f. Use of Candidate Position Titles**
The use of candidate position titles, for example, candidate for APA president-elect, through electronic or written communication is prohibited.

## C. ADDITIONAL ELECTION ACTIVITY

Election-related activity that is not permitted under the APA election guidelines includes (but is not limited to) letters, calls, email communications, texts, instant messages, and other communications to multiple recipients not originated by APA (except as approved by the Elections Committee), advertisements in print or other media, election websites, distribution of "campaign" items, or swag, and publication of position papers except through APA. A candidate is not permitted to use (or direct someone else to use) the APA Member Directory to generate mass communications in any medium.

It is a violation of the APA election guidelines for candidates to participate in webcasts or panel discussions, issue press releases, respond to surveys, or allow publication of interviews relating to the election unless approved in advance by the Elections Committee.

It is also impermissible for a nominee to engage in a debate over social media channels about the election, the candidate's qualifications, or particular issues relating to the election.

Any request of additional election activity, for example, surveys, questionnaires, debate, interview requests, etc., requires advance approval by the Elections Committee.

## D. ENFORCEMENT OF GUIDELINES

If a candidate engages in election activity inconsistent with the APA election guidelines, the committee will take appropriate action to address the violation with the candidate, including (but not limited to) addressing the violation with the candidate, requiring the candidate to withdraw with Board approval, or any other appropriate action(s) as determined by the Elections Committee.

The Elections Committee is charged with enforcing the APA election guidelines as set forth in conjunction with the Board of Trustees. This document outlines the principles that will guide enforcement of the guidelines.

In considering appropriate enforcement of the guidelines, the Elections Committee will be guided by the following goals:

- To sustain the high professional reputation of the APA
- To maintain the integrity and goals of the guidelines
- To be fair to all candidates
- To not reward candidates who violate the guidelines.
- To ensure enforcement of action is appropriate to the violation

## E. ELECTION PRINCIPLES

**The EQUITY OF ACCESS AND ECONOMIC PRINCIPLE**
The electorate and the candidates should have access to each other as set forth and approved by the Elections Committee. The committee and APA should utilize the most economic means of conducting the election campaign in terms of time and money.

**The FAIRNESS PRINCIPLE (ensuring equity)**
Every qualified member should have equal opportunity to run for leadership positions in the APA. (This addresses the problem of the power and privilege of incumbents, which pose handicaps to challengers or outsiders. Equal opportunity addresses the issue of finances and expense problems.)

**The COLLEGIALITY PRINCIPLE**
An atmosphere of collegiality should be promoted among candidates and among members, fostering the fellowship spirit, a more open communication and exercise of professionalism that would ensure focus on issues and fair play. Candidates who do not adhere to this principle, as determined by the Elections Committee, may be referred to the Board for removal from candidacy or their votes nullified.

**The MEMBERSHIP ENGAGEMENT PRINCIPLE**
The election process should arouse members' interest in and knowledge of APA affairs and foster optimum ballot returns. Well-informed members will likely be involved voters.

# How to Handle Online Harassment, Cyberstalking by Patients

*Don't hesitate to take action if a patient engages in harassing online behavior.* **BY ALLISON M. FUNICELLI, M.P.A., C.C.L.A., A.R.M.**

Several studies have concluded that as many as 75% of workplace assaults and violent attacks occur in health care settings. Furthermore, as many as 20% of physicians surveyed reported being the victim of at least one instance of stalking or harassment by a patient.

Unfortunately, predicting who may exhibit this type of behavior is difficult. In addition, the internet allows perpetrators to harass their victims, such as health care professionals, more frequently, easily, and anonymously than ever before. Both male and female physicians report stalking events with almost the same frequency. Mental illness and fear are two of the top reasons cited as why patients act out against their health care professionals. Transference is another potential cause for cyberstalking and harassing behavior; a patient may redirect some of his/her feelings for others onto the psychiatrist, enhancing their need to interact with his/her psychiatrist in unhealthy ways.

Online harassment is defined as using online media (such as social media platforms, websites, apps, emails, and text) to cause emotional distress to an intended victim. Cyberstalking is the repeated use of electronic communications to harass or frighten someone, for example, by sending threatening emails.

APA has a resource document that addresses stalking, intrusive behaviors, and related phenomena by patients (see link below). It provides key information related to personal safety, prevention, and intervention. Depending on the level of threat, psychiatrists may need to seek personal counseling to deal with the stress of being harassed or intimidated by a patient and determine if the patient requires hospitalization or transfer of care to another psychiatrist. Moreover, consider if there is a duty to warn others who may be in danger. It may be important to inform staff members if there is a credible threat to their safety as well.

- Maintain clear boundaries with patients. Do not accept friend requests on social media platforms.

- Maintain professionalism to avoid blurred lines in the doctor/patient relationship.

- Report threatening behavior to law enforcement; consider filing a civil protection order for stalking behavior.

- Provide the minimum necessary information to law enforcement/court to comply with the Health Insurance Portability and Accountability Act (HIPAA).

- Document the details of the event both in the patient's medical record and in your personal records.

- Block the telephone number of the harasser and/or change your personal telephone number if necessary.

- Contact patients through HIPAA-compliant privacy apps or a patient portal that encrypts your telephone number and email address.

- Use separate cell phone numbers and email addresses for work and personal use.

- Dismiss the patient from the practice if necessary. Follow proper termination procedures.

- Consider safety precautions such as panic buttons installed in the office, protective barriers where possible (patient session rooms, waiting areas, private staff areas), and other security measures.

- Consult your risk management professional or practice attorney for guidance. **PN**

Allison M. Funicelli, M.P.A., C.C.L.A., A.R.M., is a risk management consultant in the Risk Management Group of AWAC Services Company, a member company of Allied World. Risk management services are provided as an exclusive benefit to insureds of the APA-endorsed American Professional Agency Inc. liability insurance program.

**APA's "Resource Document on Stalking, Intrusive Behaviors, and Related Phenomena by Patients" is posted at http://apapsy.ch/Intrusive_Behaviors.**



## Stigma

*continued from page 11*

mother's alcoholism and the family secrecy that surrounded it. "She was a woman with an alcohol problem in the 1940s and '50s—when the shame associated with that was far greater than it is today," Myers said. "It took me a while before I could mature enough to realize how much my mother was struggling with it in those days—raising five kids, a husband who was a workaholic. She gave up her own career—she had been a legal secretary—to embark on motherhood."

Later, in medical school, Myers was confronted with another stark example of the silence that shrouds mental and emotional distress—this time in the medical community he was joining—when his first-year roommate, a fellow medical student, died by suicide.

Myers felt obligated to announce the tragedy to his peers and recalls the shocked silence from his first-year class. After a period of silence, Myers recalled, the professor—evidently at a loss for how to respond—said, "OK, … let's return to the Kreb's cycle."

"At the time, I don't think I realized how really indicative this was of the stigma that gripped our society around suicide," Myers told *Psychiatric News*. "I felt I had this obligation to make this announcement to my class. The silence was deafening."

Funeral plans for his roommate were kept under wraps, as if he had died an embarrasing death, died of some shame. "It was as if he had never existed," Myers said. "If he had died of cancer or in a car crash, the funeral would not have been so secretive and private."

In a book self-published last year, *Becoming a Doctor's Doctor: A Memoir,* Myers shares the story of his mother, his medical school roommate, Adam, and dozens of physician patients he has treated over the years—physicians with mental illness and/or substance use disorders and physicians with HIV/AIDS.

It is a chronicle of a remarkable journey of a psychiatrist who has devoted his private practice entirely to the treatment of other physicians. Myers has complemented his educational and clinical work with advocacy for nondiscriminatory policies toward physicians with a history of mental illness.

He was a consultant on "After a Suicide: A Toolkit for Physician Residency/Fellowship Programs," developed by the American Foundation for Suicide Prevention.

For years, Myers regularly presented at APA Annual Meetings about medical student and physician health and mental health with the late Leah Dickstein, M.D., a colleague and friend who had devoted a private practice to treating medical students. "Leah and I would get excited when two or three residents or early career psychiatrists would attend and say they just saw their first physician patient," Myers said.

Together they advised psychiatrists to remember that their physician patients were struggling individuals, no different from other patients, who happened to share the same profession. When possible and with the patient's consent, they urged psychiatrists to interview family members who could provide a more comprehensive appraisal of the patient. And they emphasized that many physician patients need and welcome psychotherapy.

In the years since Myers began practicing as a doctor to doctors, the culture of medicine around treatment of physician mental illness and substance use disorders has dramatically improved. But stigma persists, and Myers said that there is a great need for psychiatrists to "be there" for their colleagues.

There is also a great reward in helping physicians recover from mental illness or substance use disorders. "I grew up in the era of what was called 'professional courtesy'—the idea that as fellow professionals, we look after our own," he said. "It's very gratifying work. You can help so many people who are in turn helping others get well." **PN**

**"After a Suicide: A Toolkit for Physician Residency/Fellowship Programs" is posted at https://www.acgme.org/portals/0/pdfs/13287_afsp_after_suicide_clinician_toolkit_final_2.pdf.**

# Lifelong Learning Has Never Been More Important—or Easier

*New technologies and older established educational tools have combined with the demands of the COVID-19 pandemic to make lifelong learning easier than ever before.* **BY JOEL YAGER, M.D.**

Although lifelong learning has always been one of medicine's central mantras, it has never seemed as pertinent or as easy to accomplish as it is today.

The rate of change with which new scientific information and innovative technological, biomedical, and psychosocial applications related to psychiatric practice continue to emerge is astounding and constantly accelerating. If anything, some changes have been pushed to hyperspeed by novel demands of the COVID-19 pandemic. At the same time, access to useful information has mushroomed.

Thankfully, after completing residency and fellowship training, few psychiatrists assume that they can put away their books and journals and simply cruise along on what they have already learned. In fact, most novice practitioners feel shaky and insecure about their competence and seek ways to continue to get advice, consultation, and reassurance.

By midcareer, however, practitioners may start to feel comfortably set in their ways, confident in what they're doing. They may start to sense that journal articles and professional talks peppered with unintelligible PowerPoints aren't all that helpful. Older practitioners might even feel tired and jaded—that efforts to keep up are beyond them and that they can simply keep doing what they've been doing for years and years. Clinicians who feel that they've seen it all, know enough, and can simply go through the same routines over and over can become bored and burned out. Some may be so burned out that "lifelong learning" becomes one more burden.

Clearly, getting too comfortable and set in one's ways can sometimes be bad for patients and bad for practitioners. While "same old, same old" ways of practicing might result in optimum care for certain patients treated by expert clinicians, in other instances practicing by rote might result in patients' receiving suboptimal care.

Joel Yager, M.D., is a professor of psychiatry at the University of Colorado.

But, properly done, lifelong learning should feel like a fun quest, not a chore. It should help satisfy one's perpetual curiosity itch. Lifelong learning should be an "I want to," not a "should." Lifelong learning should be personally meaningful to your professional activities, not performed as an obligation or prescribed by bureaucracies.

Happily, most psychiatrists are naturally curious. Day to day, such curiosity is most easily activated in practice settings. Regardless of your years of experience, just about every patient or administrative encounter should present challenges or evoke questions capable of stimulating "learning issues" suitable for "just-in-time learning." These are topics you don't know enough about but definitely want to know about before your next encounter with these individuals. The practical urgencies and demands of these issues fire up your attention to ease learning. By keeping a running list of your learning issues, you always have something important to look up during spare moments. What about all those technical terms you've heard about but really don't understand?

Accessing resources to help answer these questions is simpler today than ever before. First, traditional methods apply. For quick answers to highly specific problems, clinicians usually reach out to respected and knowledgeable "go to" peers, mentors, and former teachers by email, telephone, or video. For more detailed information, they turn to standard, authoritative texts such as those from APA Publishing; APA's practice guidelines; and online texts such as UpToDate, Medscape, or even Wikipedia. Increasingly, clinicians turn to Google Scholar and PubMed.

When clinicians belong to health care systems whose libraries subscribe to publishers' bundled journal subscriptions, they can usually access full texts of the most current research and review articles. (If you or your

*see* **Lifelong Learning** *on page 37*

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# Visual Diagnostics Become More Accessible

*With powerful cameras widely available in phones and tablets, eye-based tools to screen for such disorders as autism and dementia may soon become part of routine practice.* **BY NICK ZAGORSKI**

"The eyes are a window to the soul," the saying goes. From a clinical perspective, the eyes—via the optic nerve—are also a key conduit into the brain. For decades, researchers in psychiatry have been trying to understand this eye-brain connection, with the goal of developing objective, optical diagnostic tests. Experts say that such tests could be particularly useful for disorders that may hinder a person's insight, such as schizophrenia, autism, and dementia.

One promising area involves tracking someone's gaze; many studies have scientifically validated the use of eye-tracking to detect psychiatric conditions, but until recently financial and technical hurdles have kept such tools from being widely implemented. Now, as phones and tablets with powerful processors and high-quality cameras become widely available, obtaining a an eye-tracking test may be as simple as downloading an app.

Geraldine Dawson, Ph.D., the director of Duke University's Center for Autism and Brain Development, has been leading one effort to bring eye-tracking technology to routine pediatric care.

"It has been well established that children with autism pay attention to the world differently; they tend to focus on the nonsocial elements of a scene," Dawson said. "Tracking a child's gaze can be a direct way to screen for autism."

Technology companies such as Tobii have developed tools that use infrared light to precisely track children's eye gaze, but these devices are expensive and must be calibrated before every use.

Dawson and Guillermo Sapiro, Ph.D., the James B. Duke Distinguished Professor of Electrical and Computer Engineering at Duke University, set out to create a low-cost eye-tracking app. They created software that tracks the gaze of children as they watch a series of brief videos (each 60 seconds or less). The app uses the cameras available on tablets and phones to track both eye and facial movements of the children as they watch the short videos, which include a conversation between people, people engaged in an activity (for instance, blowing bubbles), and static toys. Children can watch the videos from the comfort of their caregiver's lap during a routine well-child visit.

A report on the app, published in the August issue of *JAMA Pediatrics*, described how the eye-tracking app was able to predict which children (aged 16 to 38 months) would be subsequently diagnosed with autism with about 90% accuracy. Dawson noted that the app picked up on previously studied phenomena in children with autism, including their preference for social versus nonsocial stimuli and differences in gaze patterns. For example, she said, "We found that toddlers with autism had less ability to coordinate their gaze with the flow of a conversation."

Dawson noted that current clinical checklists used in autism screening are generally reliable but rely on parental reports of children between the ages of 1 and 3 years and rely on identifying behaviors considered typical from a White, European-American perspective. Her clinical work with the eye-tracking app has involved hundreds of diverse families in the Durham, N.C., area and thus far works equally well regardless of the child's sex or racial/ethnic background. Among other projects, her team is testing how well the app works in infants under 12 months as well as children over 3 years.

## Eyes May Offer Clues About Dementia

Visual tests may also aid in detecting people with early stage dementia. "Accurate, early identification of dementia is such a pressing need, yet clinicians have been using the same tools for over 50 years," noted Chris Kalafatis, M.D., a consultant psychiatrist at the South London and Maudsley NHS Foundation Trust.

As with autism checklists, cognitive tests used to identify people with dementia are prone to bias when given to people of different educational or cultural backgrounds (for example, someone with less formal education may underperform on a word-based test even in the absence of dementia). Cognitive tests also suffer from a practice effect when given repeatedly—people get better with repetition.

A few years back at Cambridge University, neuroscience graduate student Seyed-Mahdi Khaligh-Razavi made an interesting discovery. In visual recognition tests, the brain produced completely different electrical signals when individuals were shown images of animals as opposed to other images. That difference reflects one of the oldest evolutionary jobs of the human brain—the ability to recognize other animals quickly and undertake the appropriate flight or fight response. What's more, he found that a person's speed of animal recognition got slower with age or cognitive impairment.

Khaligh-Razavi, along with Cambridge colleague Sina Habibi, Ph.D., and Kalafatis, formed the start-up Cognetivity and developed a five-minute online test known as the Cognetivity Integrated Cognitive Assessment (CognICA). As part of the test, which can be given on any tablet, people are shown a series of black-and-white images for one-tenth of a second. Individuals must then identify whether the image they saw was an animal or not as quickly as possible.

Based on an individual's response relative to their age, the CognICA algorithm calculates the individual's overall cognitive health. Habibi noted that because the brain circuit involved in animal recognition passes through multiple brain regions, the algorithm can identify cognitive problems even when only one or two regions of the brain are affected.

Pilot studies found that the CognICA could identify cognitive impairment in 88% of adults with early stage Alzheimer's disease and that CognICA reliability was not influenced by the participants' years of education. These studies led to regulatory approval of CognICA in the United Kingdom, and the company is deploying their tool in multiple clinics across the country. Cognetivity is also preparing to submit paperwork to the Food and Drug Administration to clear their diagnostic as a medical device in the United States.

"We have seen perhaps the most interest from primary care doctors, since this test can close a critical service gap," Kalafatis said. "It's hard to regularly follow up with people who screen positive for pre-dementia because the volume is too high and the tools are lacking; the ICA can be used at home, so patients can send in results on their own and physicians can focus on those who are declining more rapidly."

Dawson said she also sees a future where parents will use eye-tracking apps to monitor their children and provide real-time updates to their physician. "These tools can be used even after a diagnosis is made, for example to track a child's progress with a prescribed therapy," she said.

"The COVID pandemic has been an inflection point for digital technologies," Kalafatis said. "Both patients and providers have taken a greater interest in virtual and online care." With this new desire to adopt digital technologies, Kalafatis added, "we may finally bring the field of cognitive assessment into the 21st century."

Dawson's study was funded by the NIH Autism Centers of Excellence Award, with additional support from the National Institute of Mental Health and other groups. **PN**

**"Computational Methods to Measure Patterns of Gaze in Toddlers With Autism Spectrum Disorder" is posted at https://jamanetwork.com/journals/jamapediatrics/fullarticle/2779395. "Validity and Cultural Generalisability of a 5-Minute AI-Based, Computerised Cognitive Assessment in Mild Cognitive Impairment and Alzheimer's Dementia" is posted at https://www.frontiersin.org/articles/10.3389/fpsyt.2021.706695/full.**

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PSYCHIATRIC NEWS
*Special Report*

# Management of Major Depression: Yesterday, Today, and Tomorrow

*There are a large number of evidence-based treatments for depression, but for now we are still relying on trial-and-error approaches. This article discusses available treatments and guide you through the decision-making process.* **BY CHARLES B. NEMEROFF, M.D., PH.D.**

Charles B. Nemeroff, M.D., Ph.D., is the Matthew P. Nemeroff Professor and Chair of the Department of Psychiatry and Behavioral Sciences at the University of Texas at Austin Dell Medical School. He is president of the Anxiety and Depression Association of America. He is the co-editor of *The American Psychiatric Association Publishing Textbook of Mood Disorders, Second Edition.* APA members may pre-order the book at a discount at https://www.appi.org/American_Psychiatric_Association_Publishing_Textbook_of_Mood_Disorders_Second_Edition.

*The pain is unrelenting, and what makes the condition intolerable is the foreknowledge that no remedy will come—not in a day, an hour, a month, or a minute. If there is mild relief, one knows that it is only temporary; more pain will follow. It is hopelessness even more than pain that crushes the soul. So the decision-making of daily life involves not as its normal affairs, shifting from one annoying situation to another less annoying—or from discomfort to relative comfort, or from boredom to activity—but moving from pain to pain. One does not abandon, even briefly, one's bed of nails, but is attached to it wherever one goes.*

*—William Styron, Darkness Visible: A Memoir of Madness*

Major depression is one of the most often encountered syndromes in psychiatric practices and, indeed, in general medicine. Lifetime prevalence rates in the United States of 11% to 13% in men and 21% in women confirm the ubiquitous nature of this disorder. It is truly a killer—both due to the high rate of suicide in the depressed population (suicide is still in the top 10 causes of death in the United States) and the marked increased vulnerability of depressed patients to severe medical comorbidities including cardiovascular disease, stroke, diabetes, and certain forms of cancer. Taken together, these findings surely account for the reduced life span of patients with depression.

All medical students and psychiatry residents are well versed in the *DSM*-5 diagnostic criteria for major depression, and space constraints preclude repeating them here. However, it is worth noting that additional symptoms not contained in the *DSM*-5 diagnostic criteria may be helpful to consider including diurnal mood variation and unexplained crying spells. This author, however, believes that the pathognomonic symptom of major depression is anhedonia, in a similar way that pathological worry is the single most cardinal and important symptom of generalized anxiety disorder.

In terms of the diagnostic process as the necessary precursor to any discussion of treatment, three points are important. First, assessment for medical disorders or medications that are associated with depression such as hypothyroidism and glucocor-

*continued on next page*

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ticol treatment, respectively, to name a few, is essential. Occult hypothyroidism is the leading medical disorder associated with causing depression, and there is evidence that patients with a TSH > 3.5 IU/ml (not the 5.0 IU/ml cutoff described by most laboratories) already have incipient thyroid disease and do not respond well to antidepressants. Men with low levels of testosterone also frequently display the cardinal symptoms of depression and respond to testosterone supplementations, often not requiring antidepressant treatment. More importantly, there is evidence that men with low testosterone concentrations do not respond to antidepressant treatments.

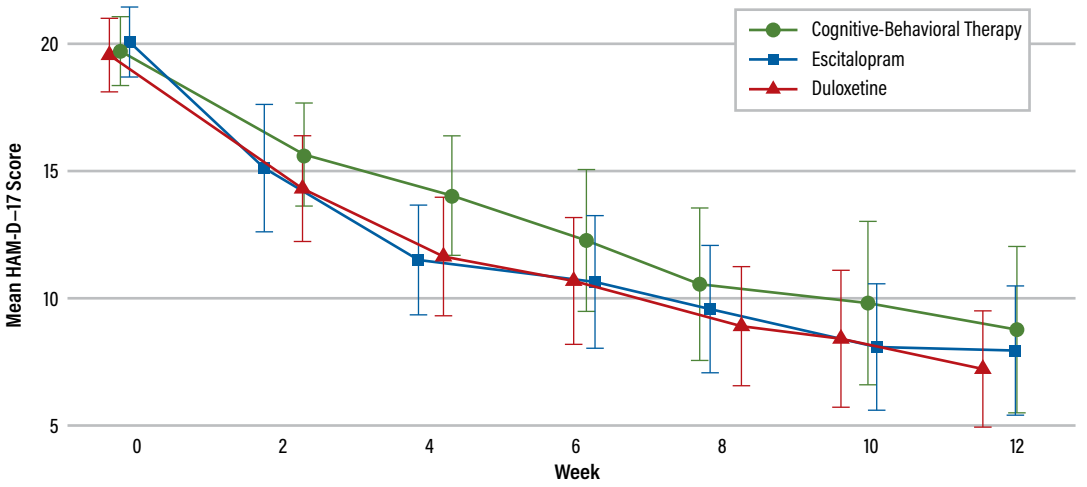
Second, psychiatric comorbidity is more the rule than the exception in patients with major depression, and these comorbidities must be formally diagnosed and considered in the development of a treatment strategy. The most common include anxiety disorders (generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, and social anxiety disorder) and posttraumatic stress disorder.

Third, delineating the subtypes of major depression is of great importance, as it too will impact optimal treatment decisions. The most pressing is, of course, major depression with psychotic features, which requires a treatment regimen completely distinct from that for nonpsychotic depression. Other subtypes of depression, more notably atypical depression, also suggest particular treatment algorithms.

Space constraints preclude any discussion of pathophysiology of depression here, an area I reviewed in considerable detail in the August 2020 issue of the *American Journal of Psychiatry* (see https://ajp.psychiatryonline.org/doi/full/10.1176/appi.ajp.2020.20060845). Suffice it to say that in spite of several decades of research, the underlying pathogenesis of major depression remains painfully obscure and, as such, does not guide treatment in any clinically useful way. This is perhaps best exemplified by the repeated failure of commercially available pharmacogenomic tests to predict response to one or another antidepressant in controlled trials despite claims to the contrary, a position now rigorously supported by the Food and Drug Administration.

It is important to note the consequences of inadequately treating major depression. It is now very well documented that persistent syndromal depression is associated with increasing treatment resistance, risk of suicide, risk of increased substance and alcohol abuse, vulnerability to several major medical disorders, and poor treatment out-

**Figure 1. Modeled Change in the Mean Hamilton Depression Rating Scale (HAM-D) Score by Week[a]**




[a] Error bars represent 95% confidence intervals.

Source: Dunlop B, et al. Effects of Patient Preferences on Outcomes in the Predictors of Remission in Depression to Individual and Combined Treatments (PReDICT) Study. *American Journal of Psychiatry*; March 24, 2017

**"Psychiatric comorbidity is more the rule than the exception in patients with major depression, and these comorbidities must be formally diagnosed and considered in the development of a treatment strategy."**

**Table 1. FDA-Approved Antidepressants**

| Drug | Putative Mechanisms of Action |
|---|---|
| Fluoxetine | SSRI |
| Sertraline | SSRI; blocks DA reuptake at high doses |
| Paroxetine | SSRI; blocks NE reuptake at high doses |
| Fluvoxamine* | SSRI |
| Escitalopram | SSRI |
| Citalopram | SSRI |
| Vortioxetine | SSRI; 5-$HT_{1A}$ agonist |
| Vilazodone | SSRI; 5-$HT_{1A}$ partial agonist |
| Venlafaxine | SNRI |
| Duloxetine | SNRI |
| Levomilnacipran | SNRI |
| Bupropion | Unknown |
| Nortriptyline | TCA; primarily NE reuptake inhibitor |
| Imipramine | TCA; NE and 5-HT reuptake inhibitor |
| Amitriptyline | TCA; NE and 5-HT reuptake inhibitor |
| Maprotiline | Tetracyclic primarily NE reuptake inhibitor; no longer available in the U.S. |
| Clomipramine* | TCA; primarily 5-HT but also NE reuptake inhibitor |
| Protriptyline | TCA; primarily NE reuptake inhibitor |
| Desipramine | TCA; primarily NE reuptake inhibitor |
| Trimipramine | TCA; NE and 5-HT reuptake inhibitor |
| Phenelzine | MAOI |
| Tranylcypromine | MAOI |
| Isocarboxazid | MAOI |
| Selegiline Transdermal | MAOI |
| Mirtazapine | NASSA=alpha-2 antagonist; 5-$HT_2$ and 5-$HT_3$ antagonist |
| Esketamine | NMDA antagonist, MU opiate agonist |

*Approved for OCD

**Figure 2. Diabetes**

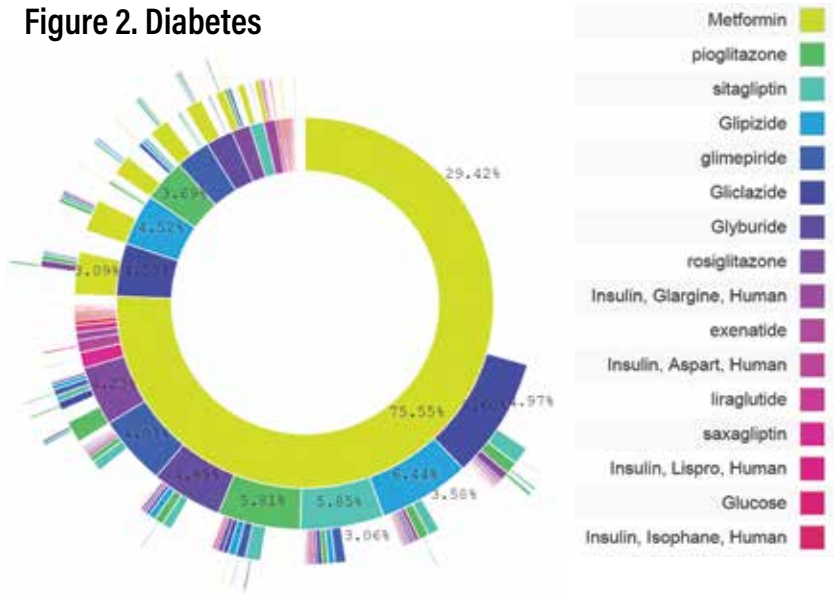
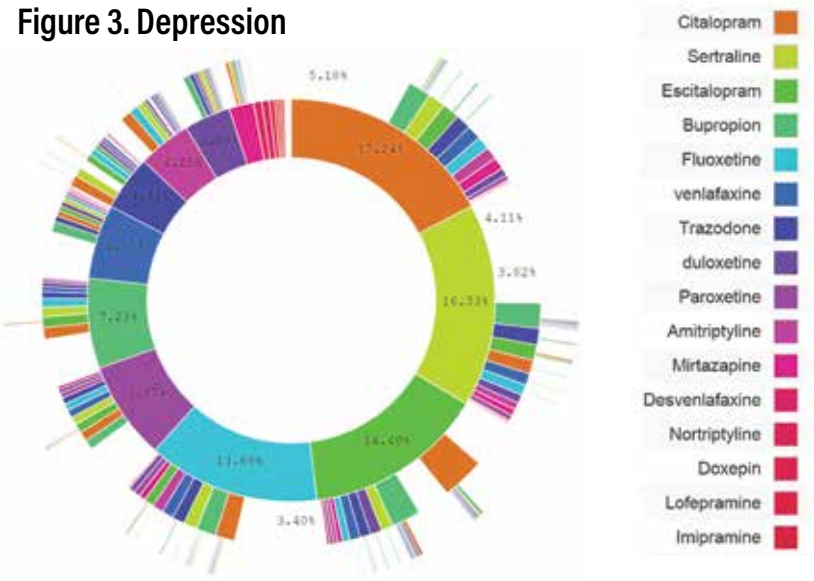



**Figure 3. Depression**




In each diagram, the inner circle shows the first relevant medication that the patient took, the second circle shows the second medication, and so forth.
Source: Hripcsak G, et al., Characterizing Treatment Pathways at Scale Using the OHDSI Network. *PNAS*; July 5, 2016

**"A great many patients, perhaps the majority, do not respond to evidence-based monotherapy including antidepressants or psychotherapy."**

comes. In view of these data, it is imperative to treat depression aggressively as you would any potentially lethal disorder.

## Evidence-Based Treatment of Major Depression

Large-scale treatment studies ranging from the STAR*D study composed of a broad range of depressed patients to the PReDicT study of never-treated depressed patients revealed, using the Hamilton Depression Rating Scale (HAM-D), remission rates of 28% and 50%, respectively (see Figure 1). This suggests that a great many patients, perhaps the majority, do not respond to evidence-based monotherapy including antidepressants or psychotherapy. (STAR*D stands for Sequenced Treatment Alternatives to Relieve Depression; PReDicT stands for Predicting Response to Depression Treatment.)

Evidence-based treatments for major depression can be divided into several categories: Antidepressants, psychotherapies, and nonpharmacological somatic treatments. These last two include cognitive-behavior therapy (CBT), interpersonal psychotherapy (IPT), electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), and vagal nerve stimulation (VNS). The aforementioned antidepressants and neuromodulation modalities are FDA approved. In addition, there are a number of FDA-approved augmentation strategies—atypical antipsychotics that have been demonstrated in randomized, controlled trials to convert antidepressant nonresponders and partial responders to responders. There is also evidence that several non-FDA-approved treatments are also effective in this regard. Table 1 on the facing page summarizes the FDA-approved treatments of major depression.

Figures 2 and 3 illustrate the conundrum of treating depression compared with treating another common complex disorder, diabetes. Figure 2 reveals prescription data on the treatment of type 2 diabetes. Metformin is the clear first choice of treatment. Figure 3, in contrast, shows similar data for treatment of depression—there is no clear choice as there are no data indicating that any one antidepressant is superior in efficacy and/or has a most favorable side-effect profile. This leads to an almost purely trial-and-error approach to selection of treatment. In Table 2, the other treatment modalities are briefly discussed, followed by augmentation and combination therapies and finally novel approaches in various stages of development in Table 3 (see next page).

*continued on next page*

**Table 2. Augmentation Strategies**

| Drug | Mechanisms of Action |
|---|---|
| **Data of efficacy available** | |
| Olanzapine* | 5-$HT_2$/$D_2$ antagonist |
| Aripiprazole* | 5-$HT_{1A}$/$D_2$ partial agonist |
| Brexpiprazole* | 5-$HT_{1A}$/$D_2$ partial agonist |
| Risperidone | 5-$HT_2$/$D_2$ |
| Ziprasidone | 5-$HT_2$/$D_2$ |
| Quetiapine* | 5-$HT_2$/$D_2$ |
| **Few or no data available on efficacy** | |
| Lurasidone | $D_2$/5-$HT_{2A}$ antagonist; 5-$HT_7$ antagonist |
| Lumateperone | $D_2$/5-$HT_{2A}$ antagonist; $D_1$ antagonist and 5-HT reuptake inhibitor |
| Cariprazine | $D_2$ and $D_3$ partial agonist; 5-$HT_2$/5-$HT_{2B}$ antagonist |
| Asenapine | 5-$HT_{2A}$/$D_2$ |
| Paliperidone | 5-$HT_{2A}$/$D_2$ |
| Clozapine | 5-$HT_{2A}$/$D_2$ +unknown mechanism of action |
| Ketamine | NMDA antagonist |
| Esketamine* | MU Opiate agonist |

*FDA Approved

**Table 3. Neuromodulation Treatment of Major Depression**

| |
|---|
| Electroconvulsive therapy (ECT)* |
| Repetitive transcranial magnetic stimulation (rTMS)* |
| Vagal nerve stimulation (VNS)* |
| Deep brain stimulation |

*FDA Approved

*continued from previous page*

What is a busy clinician to do?

Once a comprehensive diagnostic evaluation is completed and a diagnosis of major depression is established and underlying medical disorders have been ruled out, clinicians are faced with the first treatment decision. They should obtain a dimensional measure of depression severity such as the Beck Depression Inventory and obtain this assessment at each patient visit. This treatment decision is ideally made not solely by clinicians but by the clinician-patient dyad. Clinicians should present the menu of evidence-based treatments ranging from antidepressants to psychotherapy to neuromodulation. An important factor is family history—if a patient's first-degree blood relative has suffered with depression and responded to a particular antidepressant, some evidence suggests that this agent should be a first choice for that patient.

As noted above, psychiatric comorbidities should also play an important role in decision-making, as should depression subtype. As an example, the place of monoamine oxidase inhibitors (MAOIs) in the treatment algorithm is higher in patients with atypical depression. Psychotic depression requires the use of not only an antidepressant but an atypical antipsychotic as well, unless ECT is chosen.

## Factors to Consider Regarding Treatment Choice

With these exceptions, there is little to guide clinicians on treatment choice. Patient preference is clearly important and will drive much decision-making as to initial treatment direction, that is, antidepressants versus psychotherapy versus neuromodulation. As noted above, the available data from randomized trials do not support the use of commercially available pharmacogenomics testing to predict antidepressant response.

In terms of antidepressant treatment strategy, clinicians should initially choose an antidepressant within a class with the most favorable side-effect profile and few, if any, drug-drug interactions. This, of course, eliminates tricyclic antidepressants (TCAs) and MAOIs as first-line agents, as well as older selective serotonin reuptake inhibitors (SSRIs) such as paroxetine, fluoxetine, and fluvoxamine. Most clinicians would opt for escitalopram or citalopram although a case could be made for sertraline, fluoxetine (in children and adolescents), or vortioxetine. If there are major concerns about sexual dysfunction with SSRIs, buproprion is a reasonable first choice. Although a few studies that sought to determine whether beginning treatment with two antidepressants of different classes would result in a higher rate of treatment response had mixed results, what is clear is that the combination of two antidepressants at subtherapeutic doses is not effective.

Although no antidepressant can make the claim of being more effective than any other, there is evidence that the selective norepinephrine reuptake inhibitor (SNRI) venlafaxine has an advantage in remission rates over SSRIs as a group.

In general, the data suggest that patients who exhibit less than a 30% improvement after three weeks on antidepressant monotherapy are unlikely to respond to that dose. In the absence of side effects, the dose can certainly be increased, for example, sertraline from 50 mg to 100 mg. Moreover, in clinical practice, we have seen many patients who respond only to inordinately high doses of antidepressants, for example, sertraline 300 mg to 400 mg, venlafaxine XR 600 mg, and escitalopram 40 mg.

## Suggested Next Steps if Failure Occurs

Once the antidepressant monotherapy trial is considered a treatment failure—the patient has not attained remission after an adequate trial of six to eight weeks at an adequate dose—the clinician and patient must make a crucial decision: to switch to another therapy (antidepressant, psychotherapy, or neuromodulation) or to maintain the current antidepressant and add a second agent (an antidepressant of another class or an augmentation agent such as an atypical antipsychotic, lithium, T3, or pramipexole). Again, if the initial antidepressant has not resulted in any substantial improvement in symptoms, the patient should be switched to another antidepressant of a different class, for example, from an SSRI to an SNRI, TCA, MAOI, or one of the atypical antidepressants (mirtazapine or bupropion). In contrast, if the patient has experienced considerable improvement, say 40% to 50%, then an augmentation or combination therapy should be initiated.

Similar to the dearth of information on predictors of response to individual antidepressants, there is little information to guide the clinician on next best steps. There is evidence for the addition of CBT to the antidepressant regiment, as well as TMS and a host of medication strategies, the latter summarized in Table 2. Space constraints preclude a comprehensive discussion

"In terms of antidepressant treatment strategy, clinicians should initially choose an antidepressant within a class with the most favorable side-effect profile and few, if any, drug-drug interactions."

**Table 4. Medications in the Pipeline**

| Treatment | Mechanism |
|---|---|
| Dextromethorphan and Bupropion | NMDA antagonist + FDA-approved antidepressant |
| Zuranolone | Positive allosteric modulator of the $GABA_A$ receptor |
| Psilocybin | 5-$HT_2$ agonist |
| Other psychedelics | 5-$HT_2$ agonist |
| Ezogabine | KCNQ2/3 channel opener |
| Minocycline | Anti-inflammatory |
| TNF-α antagonists | Anti-inflammatory |
| IL-6 antagonists | Anti-inflammatory |
| Nitrous oxide | Unknown |
| Kappa opiate antagonists | Kappa opiate antagonist |
| R-ketamine and modified ketamine preparations | NMDA receptor antagonists, opiate agonists |
| Stanford Accelerated Theta-Burst TMS | DLPC target |

other than to illustrate the few agents approved by the FDA to convert antidepressant nonresponders to responders. It is important to note that the magnitude of the beneficial effect of antipsychotic drug-induced augmentation is relatively meager. As an example, a study by Michael Thase, M.D., and colleagues in the September 2015 *Journal of Clinical Psychiatry* on the use of brexpiprazole as an adjunct to antidepressant treatments found that the groups treated with brexpiprazole attained only modest levels of remission compared with placebo. The good news is that there are many augmentation and combination strategies from which to choose, including lithium, tri-iodothyronine, and pramipexole, as well as combinations of antidepressants. Recently the literature on ketamine and esketamine was comprehensively reviewed by Roger McIntyre, M.D., and colleagues in an article posted March 17 in the *American Journal of Psychiatry*. Although much remains unknown about the long-term consequences of these drugs and clear abuse liability, it does ameliorate severe depression, even if transiently, in some patients.

## Looking to the Future

A remarkable resurgence in the development of new antidepressants is underway after a lull of several years. Table 4 on the facing page summarizes some of these new candidates that are in various stages of development.

All of the treatments listed in Table 4 have at least one randomized, controlled clinical trial demonstrating efficacy in depression, mostly in treatment-resistant patients. Nonetheless, much additional work needs to be done before one or more of these treatments receive FDA approval. One obvious issue of great importance is the inability to "blind" treatment with some of these agents, most notably psychedelics and ketamine-related agents. The striking data from the Stanford group that the mu opiate antagonist naltrexone completely abolishes the antidepressant effects of IV ketamine suggest that the drug is acting as an antidepressant by either increasing endogenous opiates or acting as a mu opiate agonist. The difficult issue of the increasing placebo response in depression trials is a major obstacle in drug development and the use of electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) as well as machine-learning methods to predict placebo response would be a major advance.

Writing a few words about advances in neuromodulation strategies to treat depression is pertinent. In an open study posted in the *American Journal of Psychiatry* on April 7, 2020, Eleanor J. Cole, Ph.D., and colleagues reported that high-dose, accelerated theta burst TMS administered more precisely with a neuronavigator 5 minutes per hour for 10 hours on five consecutive days produced remarkably high remission rates in refractory depression, and there is now reportedly a completed sham-controlled, double-blind trial that confirms and extends these findings.

In summary, unlike the situation in the treatment of schizophrenia in which nonresponsive patients fundamentally have one treatment modality—clozapine, there are a large number of evidence-based treatments for depression. In terms of antidepressant treatment strategy, clinicians should initially choose an antidepressant within a class with the most favorable side-effect profile and few, if any, drug-drug interactions. **PN**

*Dr. Nemeroff's disclosure statement appears in the online version of this article at https://psychnews.psychiatryonline.org/doi/10.1176/appi.pn.2021.11.14.*

**"The good news is that there are many augmentation and combination strategies from which to choose, including lithium, tri-iodothyronine, and pramipexole, as well as combinations of antidepressants."**

## Additional Resources

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# Building Resilience in Our Children For the Aftereffects of COVID-19

*Children and adolescents have the capacity to become resilient and adaptive when we give them the opportunities and resources to do so, but half to two-thirds of those needing mental health services may not have access to them.* ***BY VICTOR G. CARRION, M.D.***

Victor G. Carrion, M.D., is the John A. Turner, M.D. Chair of Child and Adolescent Psychiatry, professor and vice chair of the Department of Psychiatry and Behavioral Sciences, and director of the Early Life Stress and Resilience Program at Stanford University.

It has been over a year since the World Health Organization confirmed that we were all living through a global pandemic. Since then, many of us have experienced tragedy, loss, and sustained threat and continue to do so. At times, we are navigating these stressors with uncertainty, limited guidance, and national divisions. Measures necessary to maintain our physical safety have caused isolation. Although technology has helped us maintain a sense of connectedness, its limitations prevent it from sparing us from the full impact of aloneness on our emotional life. Compounding the effects of the isolation that the pandemic has inflicted are additional ravages to our mental and physical well-being in the form of unemployment, academic interruption, and the loss of loved ones.

If ever there was a time to prioritize the building blocks of resilience, it is now. Our profession strives to provide resources to strengthen support systems, alleviate burdens, and help those most vulnerable. We have guided our patients in building new coping mechanisms, utilizing technology to engage in therapy, and identifying resources as we were developing these skills for ourselves. We aim to build resilience as individuals face what was once an acute stressor that has become chronic.

In truth, we know very little about what constitutes resilience. However, an accurate and humbling acceptance of our developing understanding of resilience can inform our aspirations and target our approach. Resilience is a physics term; it literally means that the spring bounces back to its original form. In our clinical circles, we use the term to refer to the return to prior function and, in a very narrow fashion, to describe the absence of symptomatology or dysfunction.

This clinical definition is limited because it does not reflect the possibility of biological and psychological factors that may be bringing the individual closer to a threshold of symptom expression and altered function. In other words, it is below this threshold where the truly resilient live, but also those whose allostatic loads (the cumulative burden of chronic stress and life events) have increased in a clinically unnoticeable manner. Identifying the factors associated with resilience will allow us to better assess the impact of stressors on an individual.

Some of the variables that play a role in resilience center on the individual and others in the individual's environment. The presence of a robust support system, a dependable relationship, perseverance, optimism, and a sense of humor all come into play. It is essential to assess these as we evaluate how our patients will bounce back. The possibility for adaptation, bouncing back to an even better stance, should also be a goal.

Contrary to popular belief, children and adolescents are not resilient simply by virtue of being young. The opposite is true. They are, in fact, more vulnerable. This is why we take care of them. Developmental dynamics during a period of active neuronal and physiological development may place youth at higher risk. Children and adolescents do have the capacity to become resilient and adaptive when we give them the opportunities and resources to do so. But it is of concern that half to two-thirds of those need-

*see* **Children** *on page 39*

VIEWPOINTS

# Psychiatrists Can Help Support 'New Normal' at Schools

***BY ANTHONY NG, M.D.***

The return to in-person school for most children in the United States this fall marked an exciting time for teachers and other staff, students, and families—reunited after what, for many, was more than a year of connection only over a computer screen. As COVID-19 continues to impact communities across the country, however, school staff, teachers, parents, and youth have faced numerous challenges. I believe that psychiatrists have a tremendous role to play in supporting teachers, students, and parents in our communities as they navigate mask mandates, classroom quarantines, and more this school year. One way that psychiatrists can offer this support is by testifying before school boards about the importance of measures aimed at minimizing school disruptions and maintaining a routine for children this school year.

Anthony Ng, M.D., is the medical director of community services and director of neuromodulation services at Northern Light Acadia Hospital in Bangor, Maine. He is also a member of the APA Committee on the Psychiatric Dimensions of Disaster and the Council on Communications.

It is well documented that children have been affected adversely by the pandemic. Social isolation from lockdowns, home schooling, and even hybrid learning has taken a toll on kids, as has the fear of being infected by COVID-19, having a relative or friend infected, and/or experiencing other family hardships related to the pandemic (such as a parent losing a job and loss of housing). Many students have repeatedly stated that they are willing to practice safety measures to reduce the spread of COVID-19 and any related school disruptions so that they might have as normal a school life as possible.

Current guidance from the Centers for Disease Control and Prevention (CDC) recommends universal masking to help mitigate the significant risk of COVID-19 transmission in schools. Additionally, mandatory masking can reduce bullying of those who wear or do not wear a mask in an optional masking scenario. The decision to mandate student and staff masking versus allowing parents the option to choose on behalf of their children has for the most part rested with local communities and school districts. The debates regarding mask mandates in schools have been extremely emotionally charged, with some arguing for optional masking based on such misinformation as COVID-19 not being as severe as the experts have reported, COVID-19 not being harmful to kids,

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# Transdiagnostic Approach May Benefit Patients With Sleep, Mood Disorders


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*A transdiagnostic approach could help clinicians more easily treat patients with diverse psychiatric disorders, especially in low-resource routine practice settings.* ***BY LYNNE LAMBERG***

Focusing on commonalities across mental illnesses can hasten the application of advances made in one disorder to others, Allison G. Harvey, Ph.D., said at the 2021 virtual annual meeting of the Associated Professional Sleep Societies.

Comorbidity among mental illnesses is the norm, not the exception, said Harvey, a professor of psychology and director of the Golden Bear Sleep and Mood Research Clinic at the University of California, Berkeley.

Sleep and circadian disturbances commonly accompany mental illnesses, which affect 27% of the U.S. population each year, said Harvey. She received the Sleep Research Society's 2021 Distinguished Scientist Award at the meeting for her career contributions to sleep and circadian science.

People with bipolar disorder, for example, typically alternate between mania and depression. Sleep disturbance is the most common prodrome of mania and the sixth most common prodrome of depression. Sleep loss is highly correlated with daily manic symptoms and negative affect, Harvey said.

Sleep and circadian disturbances contribute to interepisode dysfunction and foster difficulty regulating mood, she said, adding, "This vicious bidirectional cycle may confer a vulnerability to relapse."

Harvey's group found variability in sleep and wake times of about three hours over the week in their secondary analysis of data from 2,024 individuals diagnosed with bipolar disorder enrolled in a federally funded treatment study. These patients experienced a shift comparable to flying coast to coast across the United States and back again every week, Harvey said.

People with bipolar disorder often had not only insomnia but also hypersomnia, short sleep, irregular bed and wake times, nightmares, nocturnal panic attacks, posttraumatic stress disorder, and/or long sleep inertia (long-lasting fogginess after awakening). The same problems affect people with anxiety, schizophrenia, and other mental illnesses, Harvey said, but often get little attention.

Research on specific mental disorders has advanced the understanding of their etiology and persistence, as well as the ability to treat them, Harvey said. Hundreds of treatments for mental illnesses now exist, she said.

This abundance puts a burden on clinicians in routine practice settings, such as community mental health centers, she said, as it requires them to learn multiple disorder-focused protocols with common theoretical underpinnings. There would be a substantial cost advantage to training psychiatrists and other health professionals in one treatment tactic they could adapt to treat patients with multiple sleep and circadian disorders and diverse mental illnesses. Harvey and colleagues call this transdiagnostic approach for sleep and circadian disorders TranS-C.

Harvey's group received a grant from the National Institute of Mental Health for a pilot study using cognitive-behavioral therapy for insomnia (CBT-I) adapted for patients with both bipolar disorder and sleep or circadian disorders, including insomnia, hypersomnia, and delayed sleep phase disorder. The participants, all adults, continued to receive treatment as usual, that is, mood stabilizing medications prescribed by a psychiatrist.

The researchers randomized patients to receive eight sessions of either the CBT-I modification (n=30) or psychoeducation (n=28). Patients in the CBT-I group learned, for example, why they should be exposed to light at certain times of day and avoid it at others, why and how to regularize daily schedules, how to get going in the morning, and how to reduce sleep-related worries. Those in the psychoeducation group received information on sleep, stress, mood, diet, yoga, meditation, and other health topics, but they were not asked to change their behavior or given instruction in any techniques.

While sleep improved in both groups, it improved more in patients receiving CBT-I. At six-month follow-up, patients who had received CBT-I showed greater improvement in mood than those in the control group. They had lower relapse rates and spent fewer days in manic or hypomanic episodes.

This and further studies suggest psychiatrists can apply TranS-C principles successfully in outpatient settings, including community mental health centers, to help patients with different mental illnesses, Harvey told *Psychiatric News*. **PN**

**"Implementing a Transdiagnostic Sleep and Circadian Intervention in a Community Mental Health Setting: A Qualitative Process Evaluation With Community Stakeholders" is posted at https://doi.org/10.1016/j.psychres.2020.113443.**

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and COVID-19 being a politically driven disease; others have argued masks should be optional in schools because they believe that wearing a mask is emotionally damaging to children and view mask mandates as an infringement of personal liberty.

Rather than focusing on differing views on strategies to prevent the spread of COVID-19 in the schools, psychiatrists can help teachers and parents to recognize where they are unified: ensuring children have as normal an academic year as possible during a pandemic. Psychiatrists, for example, can assist school boards in crafting risk communication messages about COVID-19 and advocate for good public health measures, including supporting efforts by school boards to develop COVID-19 medical advisory committees to provide guidance on COVID-19 mitigation measures.

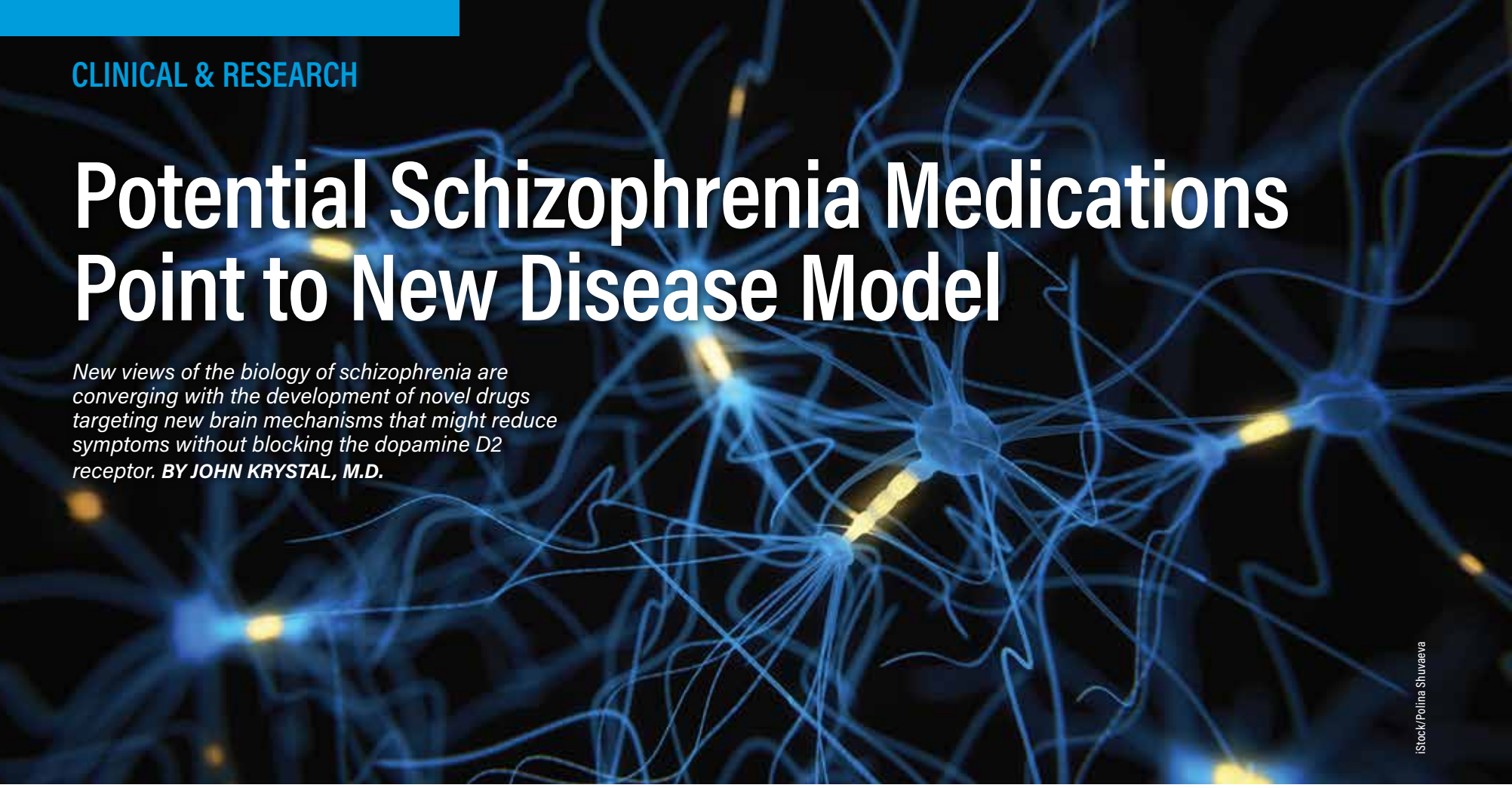
Instead of focusing on the limitations of masks and other measures to prevent the spread of COVID-19 in schools, psychiatrists can work with parents and teachers on ways they might foster awareness in students about how such measures empower students to be part of the solution to reducing the spread of COVID-19 and promote their mental health by keeping them in school.

Despite efforts to mitigate the spread of COVID-19 in schools, there have been and will continue to be positive cases in the classroom. The way in which school districts support their teachers and students who are suddenly quarantined due to possible exposure and must return to virtual learning environments will be key to mitigating the adverse effects of a disrupted school year. Psychiatrists can help to educate schools on the importance of parents and teachers of quarantined students working collaboratively to ensure the children's learning and routine be as minimally disrupted as possible. This can include trying to maintain the same schedule as if the child is going to school; having the child wear school clothes to virtual school; and substituting missing routines with other learning activities, including reading and creative learning through pre-identified educational programs. Using social media to connect with other parents in similar situations, sharing learning tools, and providing support can also be helpful.

COVID-19 remains a significant threat, and schools have become one of the front lines in the public health response to the virus. Many school districts, school staff, teachers, and parents have done an excellent job at protecting our students. Maintaining school activities is important for all children, especially those with special needs, as it provides structure and support. We must continue to promote ways to further those efforts to ensure our children are safe and learning disruptions are minimized. By masking and other measures, communities and students can choose not to live in fear but with determination to fight the spread of COVID-19 and end this pandemic. **PN**

# Potential Schizophrenia Medications Point to New Disease Model

*New views of the biology of schizophrenia are converging with the development of novel drugs targeting new brain mechanisms that might reduce symptoms without blocking the dopamine D2 receptor.* ***BY JOHN KRYSTAL, M.D.***



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Despite progress in the treatment of schizophrenia, it remains one of the leading causes of disability worldwide.

The limited efficacy of antipsychotic treatments contributes to the burden of schizophrenia. A large meta-analysis found that only 23% of patients participating in clinical trials of schizophrenia had a good response, as defined by a 50% or greater reduction in symptoms on the Brief Psychiatric Rating Scale/Positive and Negative Symptom Score (BPRS/PANSS), and this was only approximately 10% better than the response rate on placebo.

Since the discovery of the antipsychotic effects of chlorpromazine, all medications approved by the Food and Drug Administration for the treatment of symptoms of schizophrenia have blocked the actions of dopamine at D2 receptors. This makes sense, as increased dopamine release in the antero-dorsal "associative" striatum associated with schizophrenia contributes to psychotic symptoms. Occupancy of these D2 receptors by D2 receptor antagonists normalizes their level of dopaminergic stimulation.

However, the extent to which schizophrenia symptoms are attributable to dopamine hyperactivity varies across patients, and many other mechanisms are implicated in the biology of schizophrenia that may not be addressed by blockade of D2 receptors.

This is an exciting moment in schizophrenia research—new views of the biology of schizophrenia are converging with novel drugs targeting new brain mechanisms that might treat symptoms without blocking the D2 receptor. This article will begin by reviewing these promising new medications and then suggesting a general neurodevelopmental framework that supports the exploration of these novel treatment mechanisms.

John Krystal, M.D., is the Robert L. McNeil Jr. Professor of Translational Research, a professor of psychiatry and of neuroscience, and co-director of the Yale Center for Clinical Investigation. He is also chair of the Department of Psychiatry and chief of psychiatry at Yale-New Haven Hospital and director of the Clinical Neuroscience Division at the VA National Center for PTSD.
Contributing to this article were Alan Anticevic, Ph.D., John D. Murray, Ph.D., Deepak Cyril D'Souza, M.D., Mohini Ranganathan, M.D., and Naomi Driesen, Ph.D.

## Targeting Glutamate

Several medications currently or previously under development target glutamate synaptic deficits that may be the earliest primary drivers of pathophysiology in schizophrenia. The mechanisms reviewed below include inhibition of the glycine transporter-1 (GlyT1), stimulation of metabotropic glutamate receptor-2 (mGluR2), stimulation of muscarinic M4 receptors, and stimulation of trace amine-associated receptor 1 (TAAR1). As will be reviewed below, stimulation of mGluR2, M4, and TAAR1 receptors share the ability to reduce striatal dopamine release and cortico-striatal glutamate release via mechanisms summarized in Figure 1.

There has been extensive testing of strategies to enhance the stimulation of the glycine co-agonist site of the N-methyl-D-aspartate (NMDA) glutamate receptor. Studies have evaluated amino acid agonists (glycine, D-serine, D-alanine), a modified amino acid partial agonist (D-cycloserine), blocking the uptake of glycine (GlyT1), blocking the uptake of D-serine (ASCT1), and inhibiting the enzyme that metabolizes D-serine (D-amino acid oxidase, DAO). Overall, these substances have either not been adequately evaluated or they have not consistently produced sufficient clinical improvement to result in FDA-approved clinical indications.

One promising recent finding, though, suggested that GlyT1 inhibitors might reduce neuroplasticity deficits associated with schizophrenia. Although a Roche GlyT inhibitor, bitopertin, failed to show efficacy in phase 3 trials after generating promising results in phase 2, a recent study with the GlyT1 inhibitor BI425809 did find promising effects on cognitive deficits. This 12-week study (n=509, approximately 85 patients per group) reported dose-related performance improvements on the Matric Consensus Cognitive Battery, particularly improvements in processing speed as measured by the Trail-Making Task, but no significant changes in symptoms. They also suggested that improvements were greater in patients who were not taking benzodiazepines. However, GlyT1 inhibitor studies have yet to be conducted in prodromal or early course patients, groups for which an illness phase-related model would predict benefit. The only data to date come from a promising open-label study of glycine showing reductions in symptoms in patients with prodromal symptoms in ultra-high-risk patients.

Arguably the first novel medication tested to show efficacy in reducing psychosis in schizophrenia without blocking D2 receptors was the metabotropic glutamate receptor 2/3 (mGlur2/3) agonist LY2140023, a prodrug of LY404039. mGluR2 receptors serve both as inhibitory auto- and heteroreceptors for glutamate, where mGluR2 agonists inhibit glutamate release in the cortex and in the striatum, and where these drugs secondarily inhibit dopamine release (see Figure 1B). After an initial positive study as monotherapy for schizophrenia, subsequent studies did not show efficacy. However, a secondary analysis found that LY21340023 was helpful early in the course of illness, when cortical functional hyperconnectivity predominates, and was ineffective or even worsened symptoms in chronic illness, when functional connectivity deficits associated with synaptic losses might be exacerbated by mGluR2/3 agonism. Thus, while mGluR2/3 agonists may not have general efficacy for symptoms of schizophrenia, it may some day play a treatment role within a precision medicine strategy.

Promising results from two recent phase 2 clinical trials identified two innovative strategies for treating schizophrenia symptoms without blocking D2 receptors: stimulation of muscarinic M1/M4 receptors and agonism of TAAR1. There has been longstanding interest in the therapeutic role of M4 receptor agonism after clozapine, its metabolite desmethylclozapine, and xanomeline. All were shown to exhibit M4 agonist or partial agonist activity. While the therapeutic effects of clozapine are well known, a pilot study of xanomeline and more recently a larger study of xanomeline-tropsium (n=90, placebo n=92) combining xanomeline and a peripheral muscarinic receptor antagonist intended to improve

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# High-Dose Buprenorphine in the ED Effective for OUD

*Patients with opioid use disorder who come to the emergency department often do not want to wait several days for buprenorphine to provide relief from their cravings. Doses higher than the standard induction of 8 mg to 12 mg may offer them a safe option.* ***BY TERRI D'ARRIGO***

Offering buprenorphine to patients who come to the emergency department (ED) with opioid use disorder (OUD) is more common than it was several years ago, but the existing treatment guidelines by the Department of Health and Human Services were developed for treatment in office-based practices, not the ED. The guidelines limit the maximum sublingual dose during the first 24 hours of treatment to 8 to 12 mg, which means it may take two to three days to achieve therapeutic levels of the medication. Yet many people with OUD who come to the ED are in crisis and need treatment that works faster than that.

"They are looking for an effect that they can feel quickly and are not necessarily going to trust a lengthy process whereby the benefits of the medication are felt days later," said Andrew A. Herring, M.D., an attending emergency physician and the associate director of research at Highland Hospital-Alameda Health System in Oakland, Calif. He is an assistant clinical professor at the University of California, San Francisco. "There is a very high risk that these patients will return to using opioids immediately after leaving the emergency department, so you want to achieve a blockade dose as quickly as possible to prevent overdose."

**Higher doses of buprenorphine should be considered only in patients who are generally healthy aside from their OUD. —Andrew A. Herring, M.D.**

Herring, the medical director of the hospital's substance use disorder treatment program, is the lead author of a study in *JAMA Network Open* that suggests that using higher doses of buprenorphine—doses greater than 12 mg—during induction is safe and well-tolerated in patients with OUD.

"When we looked at the evidence, there was no clear reason for the guidelines to require three days to achieve a therapeutic dose," Herring told *Psychiatric News*, adding that although the guidelines recommend lower doses, using higher doses is not unheard of, especially for patients whose OUD is severe.

Herring and his colleagues reviewed the records of 391 patients with OUD who were treated with buprenorphine at Highland Hospital in 2018. Some of the patients had multiple visits to the ED, bringing the total number of cases in the study to 579. Higher doses of buprenorphine were given to patients

*see* **Buprenorphine** *on page 38*

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xanomeline tolerability (trospium) showed evidence of efficacy for positive and negative symptoms. A TAAR1 and 5HT1A agonist, SEP-363856, also showed efficacy as monotherapy for both positive and negative symptoms associated with schizophrenia in a large phase 2 trial of SEP-363856 (n=125, placebo n=120).

These novel antipsychotic medications have been hypothesized to produce clinical improvement through both dopaminergic and glutamatergic mechanisms (see Figure 1B). For example, both M4 agonists and TAAR1 agonists are reported to reduce dopamine release. As has been reviewed, M4 agonists appear to reduce dopamine release by stimulating M4 receptors located on dopamine-1 receptor-bearing medium spiny neurons (MSN) in the striatum that are postsynaptic to dopamine projections. M4 receptor stimulation in these MSNs causes the release of endocannabinoids, particularly 2-AG. 2-AG then back diffuses across the synapse to stimulate CB2 cannabinoid receptors and suppress dopamine release. M4 receptors are also located on several other cellular elements in the striatum including cholinergic interneurons and glutamatergic axon terminals of neurons projecting from the cortex and thalamus.

TAAR1 agonism inhibits striatal dopamine release through several mechanisms. TAAR1 can co-localize with dopamine D2 receptors, form D2-TAAR1 heterodimers, and facilitate D2 autoreceptor inhibition of dopamine release. TAAR1 facilitation of D2 receptor function also triggers endocannabinoid release from MSNs and stimulation of cannabinoid CB1 receptors on cortical projections to the striatum, inhibiting glutamate release. Also, TAAR1 is present in layer V pyramidal neurons in the prefrontal cortex (PFC), where it may affect the balance of AMPA and NMDA glutamate receptor signaling and buffer stress related effects on PFC function.

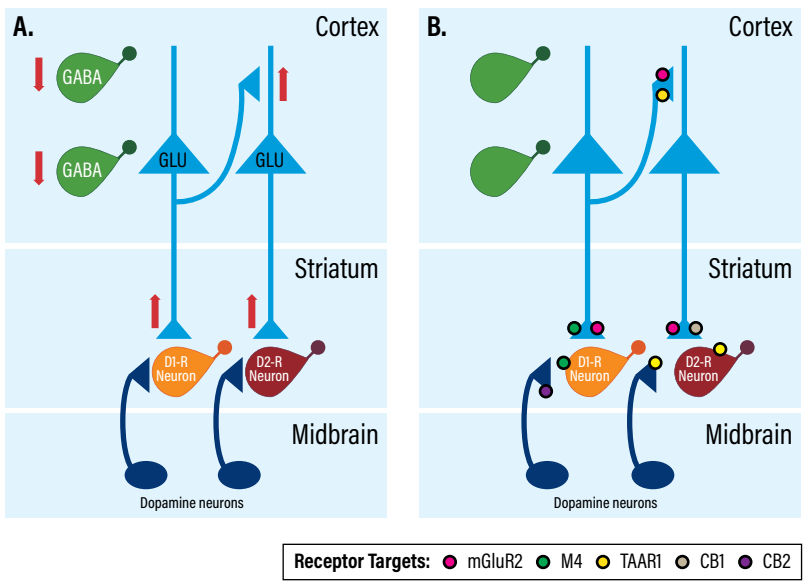


**Figure 1.** This figure provides a simplified schematic about the relationship between cortical network disinhibition and novel pharmacologic approaches to schizophrenia treatment that do not directly target the dopamine D2 receptor. **Figure A** highlights that deficits in GABA inhibition of glutamate-releasing pyramidal neurons may produce excessive functional connectivity within the cortex ("noisy cortical communication") and excessive cortical drive to dopamine D1 receptor- and dopamine D2 receptor-expressing striatal medium spiny neurons as well as dopaminergic terminals in the associative anterior dorsal striatum. **Figure B** presents a selected view of the targets for the novel pharmacotherapies (mGluR2, M4 receptor, TAAR1 receptor). It highlights loci where these drugs might reduce glutamate release in the cortex or glutamate and dopamine release in the striatum. It also illustrates that M4 receptor agonist inhibition of dopamine release is dependent upon local release of endocannabinoids by D1 receptor-expressing medium spiny neurons and stimulation of cannabinoid-2 (CB2) receptors on dopamine nerve terminals. Also, that TAAR1 inhibition of glutamate release in the striatum is dependent upon stimulation of endocannabinoid release by D2 receptor-expressing neurons and stimulation of CB1 receptors on glutamate nerve terminals. References are provided in the text.

## Targeting Medications to Illness Stages

The three new medications that reduce psychosis without blocking dopamine D2 receptors are all believed to reduce the release of dopamine and glutamate in cortico-striatal circuits (see Figure 1B). This constitutes a striking mechanistic convergence at the circuit level. We previously suggested that the neurobiology of schizophrenia evolves over the lifespan of the individual and that medications might be developed that targeted particular illness phases.

This model suggests that glutamate synaptic deficits are present prenatally and that they compromise the development and maintenance of GABA interneurons. During adolescence, the resulting deficits in GABA signaling disinhibit cortical networks, giving rise to cortical functional hyperconnectivity, noisy cortical information processing, less precise cortical representations of information, and hyperactivity of cortical projections to the striatum, contributing to the dorsal striatal dopaminergic hyperactivity that is associated with psychosis (see Figure 1A). We posit that in chronic schizophrenia, the network disinhibition triggers a homeostatic downregulation of glutamate synaptic structure and function that exacerbates the impact of programmed synaptic elimination and other mechanisms through which synaptic elimination might be accelerated in schizophrenia, such as enhanced expression of complement C4A.

Implicit in this model is that, across development, the pathology of schizophrenia not only progresses but it becomes more complex; this makes it more difficult to treat the full spectrum of schizophrenia symptoms with single agents. The key therapeutic implication of this model, which hypothesizes both progressive and increasingly complex pathophysiology, is that a given treatment is likely to have its greatest impact at the earliest phase of illness

*see* **Medications** *on page 39*

# To Minimize Medication Withdrawal, Taper Slowly

*After experiencing withdrawal symptoms while trying to wean himself off antidepressants, one doctor began questioning if traditional tapering protocols have it right.* **BY NICK ZAGORSKI**

A few years back, Mark Horowitz, M.D., wondered if the fatigue, memory, and concentration issues he had started to experience were due to his antidepressant therapy. He decided to wean off his medication, and as a doctor with psychiatric training, Horowitz decided he was comfortable handling the medication taper on his own. He knew the clinical consensus was that antidepressants could be tapered to zero over a period of about four weeks with minimal risk. To be extra cautious, Horowitz decided to taper his medication over four months. During this process, however, he became blindsided by insomnia, dizziness, anxiety, and panic attacks so severe and persistent that he had to go back to his original antidepressant dose.

After these symptoms subsided, Horowitz, who was then finishing his Ph.D. in neurobiology at the Institute of Psychiatry at King's College London, became determined to find a better tapering strategy that minimizes both withdrawal symptoms and the risk of relapse.

"There is an urgent need to develop official guidelines for how to safely taper psychotropics"—for both patients and physicians, Horowitz said.

### Rapid Discontinuation Increases Relapse Risk

As Horowitz began searching for information on how to taper antidepressants safely, he discovered that there was little scientific literature published on this subject. Some reports noted that abrupt discontinuation could lead to withdrawal symptoms, but it was generally regarded that a short tapering period would limit withdrawal effects and those that occurred would be transient. Any longer-lasting effects were simply attributed to a relapse of the patient's depressive symptoms.

Turning to online support groups for people coming off antidepressants, Horowitz found numerous testimonials by people experiencing antidepressant withdrawal symptoms for weeks or even months after tapering their medications based on the recommendations of their doctors. These online groups also included testimonials by people who reported they had avoided withdrawal symptoms by reducing their dose by tiny amounts over a year or more (some of them going as far as buying jeweller's scales so they could weigh out tiny fractions of pills).

Horowitz decided to reach out to David Taylor, Ph.D., one of his graduate school mentors. Taylor, a professor of psychopharmacology at King's College London and director of pharmacy and pathology at the Maudsley Hospital, had done some research into withdrawal following antidepressant discontinuation. Taylor's research of calls to a U.K. medication helpline in the late 1990s and early 2000s had revealed that the most frequent patient calls involved reports of severe withdrawal-like symptoms after stopping antidepressant therapy, including many instances of skin tingling or other sensory problems that were not related to depression.

Taylor and Horowitz believe that these types of symptoms arise when tapering antidepressants because traditional tapering protocols reduce the medication dose by fixed amounts (for example going down by 25% over four weeks), which is inconsistent with how psychotropic medications interact with their biological targets.

A review of pharmacological studies on antidepressant receptor binding (which all companies conduct as one of the first steps of psychiatric drug development) by the pair revealed that antidepressants can effectively bind to targets at low doses. For example, just 1 mg citalopram daily (a fraction of the typical starting dose for treating patients with depression) occupies over 20% of serotonin transporters in the brain; occupancy rises to nearly 60% at 5 mg daily and 80% at 20 mg daily (the typical starting dose of citalopram). The effect plateaus at higher levels; 40 mg of citalopram daily (the maximum recommended dose) occupies about 86% of serotonin transporters, while 60 mg daily occupies about 88% of these receptors.

In the context of tapering, this means that the first reduction of antidepressant dose will have minimal biological impact, but as the antidepressant dose gets lower, the ratio of available receptors and neurotransmitters will change more significantly; it's this chemical imbalance that can

*see* **Withdrawal** *on page 38*

### Receptor Occupancy May Help Inform Antipsychotic Tapering

Based on calculations of antipsychotic receptor binding, Horowitz and colleagues believe the following 10 steps of tapering would enable a gradual and consistent reduction of antipsychotic levels in the brain that can minimize relapse as well as withdrawal side effects.

| Steps | Risperidone (mg) | Olanzapine (mg) | Quetiapine (mg) |
|---|---|---|---|
| 1 | 4.0 | 7.5 | 300 |
| 2 | 2.5 | 5.9 | 240 |
| 3 | 1.7 | 4.6 | 200 |
| 4 | 1.2 | 3.6 | 160 |
| 5 | 0.85 | 2.7 | 120 |
| 6 | 0.60 | 2.0 | 90 |
| 7 | 0.40 | 1.4 | 65 |
| 8 | 0.25 | 0.9 | 40 |
| 9 | 0.10 | 0.4 | 20 |
| 10 | 0 | 0 | 0 |

Source: Mark Horowitz, M.D., Ph.D., et al., *Schizophrenia Bulletin*, March 23, 2021

# Healing After Moderate to Severe TBI Takes Time

*Functional status at two weeks is not necessarily an indicator of outcomes a year down the road.*
**BY TERRI D'ARRIGO**

The early weeks after a moderate to severe traumatic brain injury (TBI) can be frightening for patients and their loved ones, especially if a patient has severe impairments in function. Yet there is reason to have hope: A study in *JAMA Neurology* has found that more than half of these patients will experience major functional improvements after 12 months, suggesting that in many cases recovery is not only a matter of good care, but of time.

"Our data indicate that the degree of impairment evident during the first two weeks postinjury should not be taken as a definitive indicator of unfavorable long-term functional outcome," wrote Michael A. McCrea, Ph.D., a professor in the Department of Neurosurgery at the Medical College of Wisconsin in Milwaukee and colleagues.

The researchers analyzed data from 484 patients with moderate to severe TBI in the Transforming Research and Clinical Knowledge in TBI (TRACK-TBI) study. This prospective, multicenter observational study, conducted at 18 level 1 trauma centers in the United States, enrolled patients with TBI between February 26, 2014, and August 8, 2018. The researchers focused on patients who were at least 17 years old at enrollment and had either a moderate TBI (defined by a Glasgow Coma Scale, or GCS, score of 9 to 12) or a severe TBI (a GCS score of 3 to 8) within 24 hours of their injury. Patients were assessed in person at two weeks, six months, and 12 months or by telephone if an in-person visit was not possible. All patients were assessed at three months by telephone. If patients were too impaired to respond for themselves, their designated proxies provided responses.

At each assessment, the patients' function was evaluated using the Glasgow Outcome Scale-Extended (GOSE). Patients were asked to report functional difficulties in six major life domains (independence in the home, independence outside the home, work functioning, social/leisure

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University of New Mexico/Mary Neiberg

A great deal of change and improvement can occur during the first year after a TBI, says Davin Quinn, M.D.

# Symptoms, Impaired Function of ADHD Often Persist Beyond Childhood

*Even when their symptoms abate, people who were diagnosed with ADHD in childhood may face challenges in school or at work well into adulthood.* **BY TERRI D'ARRIGO**

The symptoms of childhood attention-deficit/hyperactivity disorder (ADHD) often persist into adolescence and adulthood and may result in negative outcomes in educational, occupational, and other key areas of functioning, a review in the *Journal of the American Academy of Child & Adolescent Psychiatry* has found.

"We need to see ADHD as a chronic illness, not an acute one. Whatever support children need, they will continue to need for a long time in order to change the direction and trajectory of their development and have better outcomes," principal investigator Lily Hechtman, M.D., told *Psychiatric News*. Hechtman is a professor of psychiatry and pediatrics and the director of research in the Division of Child Psychiatry at McGill University and Montreal Children's Hospital.

Hechtman and colleagues reviewed the results of seven prospective studies that followed children with a diagnosis of ADHD and matched control groups at regular intervals from childhood through adolescence and into adulthood. Among all studies combined, there were 1,817 people with ADHD and 1,163 without ADHD. The studies began following participants when they were anywhere between 6 and 12 years old and concluded when participants were anywhere between 22 and 40 years old.

Overall, symptoms of ADHD persisted into adolescence or adulthood in 60% to 86% of those who were diagnosed as children. All of the studies that evaluated educational functioning revealed significant and ongoing impairments among participants with ADHD compared with those without ADHD. Those with ADHD tended to have lower grades, were more likely to require tutoring or placement in special classes, and were less likely to attend or complete college.

Compared with their peers without childhood ADHD, participants with childhood ADHD had lower occupational functioning in their early 20s, were more likely to be laid off, and were more likely to have lower performance ratings from their supervisors. This remained true even when their ADHD symptoms abated as they grew into adulthood.

ADHD should be regarded as a chronic illness that requires ongoing care and support, says Lily Hechtman, M.D.

"Enduring impairments in participants with remitted ADHD symptoms raise the possibility that educational deficiencies caused by childhood ADHD symptoms have downstream effects on later educational and consequently occupational outcomes," Hechtman and colleagues wrote. "For example, childhood ADHD may interfere with the acquisition of foundational knowledge and skills that are necessary for further learning or even competent job performance."

Most of the studies found increased rates of substance use among participants with ADHD compared with those without ADHD, and some suggested that this may be especially true during adolescence. In all of the studies, conduct problems and antisocial behaviors were more common among participants who had childhood ADHD.

Hechtman said that this may be because the experiences of children with ADHD may erode their self-esteem.

"Elementary school children with ADHD often have a hard time. They're not doing well in classes because they are always getting in trouble for being disruptive. They're also challenged socially because some do not read social cues well or are impulsive and other kids don't want to play with them," Hechtman said. "When they get to high school their self-esteem is already affected and they may be drawn to a negative peer group that is into antisocial behaviors, abusing substances, and problematic sexual behavior."

She added that many adolescents stop taking their ADHD medications to try to fit in with their peers or because they want to try alcohol or other substances that they know they should not mix with their medications, which further compounds the problem.

Yet not all children who have ADHD have negative outcomes as adolescents and adults, Hechtman said.

"They may learn to adapt to some of their symptoms or they may get assistance so their symptoms are no longer impairing," she said. For example, some may hire administrative assistants who keep their schedules and workflow organized for them so they can be productive.

Hechtman, who worked on two of the studies in the review, the Montreal Study and the Multimodal Treatment Study of Children With ADHD, noted that her prior research in the Montreal Study revealed the importance of social support in attaining positive outcomes.

"For those who do well, it's often that they found someone who believed in them and encouraged them—a teacher, a coach, a parent, a romantic partner—someone who gave them the feeling that they had value and helped them do what was necessary to succeed," Hechtman said.

The review and the studies therein were funded by the Canadian Medical Research Council, the National Institute of Mental Health, and the National Institute on Drug Abuse. **PN**

**"Adult Outcome as Seen Through Controlled Prospective Follow-up Studies of Children With Attention-Deficit/Hyperactivity Disorder Followed Into Adulthood" is posted at https://www.jaacap.org/article/S0890-8567(21)00366-X/fulltext.**

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functioning, relationship problems, and other problems that affect daily life) and to report only problems that were worse than those they may have had before their TBI. Participants were also assessed using the Disability Rating Scale (DRS), which evaluates the degree of impairment in life function after TBI in four domains: consciousness (for example, eye opening, communication ability, motor response), cognitive ability (for example, to feed and groom oneself), overall level of functioning, and employability.

Overall, the 12-month mortality rate was 30.6% in the severe TBI group and 13% in the moderate TBI group.

In the moderate TBI group, 41% had a "favorable" outcome, defined by a GOSE score of greater than or equal to 4, within two weeks of their injury. Over time this increased such that 75% of patients with moderate TBI who were still in the study at 12 months had at least a favorable outcome. Among those with moderate TBI who were still in the study at 12 months, 35% achieved a good recovery as defined by a GOSE score of 7 to 8, and 19% had a complete recovery.

At two weeks 79.2% in the moderate TBI group had moderate disability or worse as defined by a DRS sore of at least 4. Among those who were still in the study at 12 months, 32% reported no disability and 15% reported only mild disability.

In the severe TBI group, 12.4% had achieved a favorable outcome within two weeks of their injury. However, over time this increased such that 52.4% who were still in the study at 12 months had at least a favorable outcome. Among those with severe TBI who were still in the study at 12 months, 22.9% achieved a good recovery and 12.5% had a complete recovery.

At two weeks, 92.9% in the severe TBI group had moderate disability or worse as measured by the DSR. Among those who were still in the study at 12 months, 19% reported no disability and 13.9% reported only mild disability.

"While a substantial proportion of patients die at high rates or incur considerable lasting disability, there is growing evidence that severe acute impairment … does not portend uniformly poor long-term functional outcomes," McCrea and colleagues wrote. "Accordingly, clinicians should be cautious about suggesting a high likelihood of permanent severe disability within the first two weeks postinjury, … and early prognostic counseling and decision-making about withdrawal of life-sustaining care should acknowledge the limitations of prognostic certainty."

"This study is an important reminder of how we need to be humble in medicine in terms of our prognostication and estimation of recovery trajectory," Davin Quinn, M.D., who was not involved in the research, told *Psychiatric News*. Quinn is a professor of psychiatry, vice chair of adult clinical services, and chief of the Division of Behavioral Health Consultation and Integration at the University of New Mexico School of Medicine in Albuquerque. "A great deal of change and improvement can happen in the first year after a TBI. The patient you see at two weeks can look very different by three months and again very different a year after the injury."

The study was funded by the National Institutes of Health, the National Institute of Neurologic Disorders and Stroke, and supported in part by the U.S. Department of Defense. Patient travel and stipend expenses were supported by One Mind. **PN**

**"Functional Outcomes Over the First Year After Moderate to Severe Traumatic Brain Injury in the Prospective, Longitudinal TRACK-TBI Study" is posted at https://jamanetwork.com/journals/jamaneurology/article-abstract/2781523.**

# Collaborative Care Expands Reach To Racial/Ethnic Minority Patients

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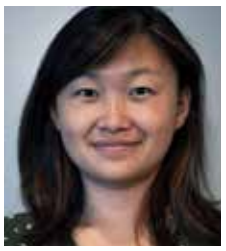
*This article is one of a series coordinated by APA's Council on Consultation-Liaison Psychiatry and the Academy of Consultation-Liaison Psychiatry.*

***BY TINA WU, M.D., JENNIFER HU, M.D., AND HSIANG HUANG, M.D., M.P.H.***

Consultation-Liaison **PSYCHIATRY**

Racial and ethnic minorities face unique challenges accessing and utilizing mental health services in the United States. These include lack of insurance, communication barriers, and perceived stigma. Even when minority patients have access to mental health care, they often receive lower quality care and have worse outcomes. The Collaborative Care Model is a well-studied health care delivery model that aims to improve mental health care access and outcomes. Key elements of this model include utilizing patient-centered team care, a population focus through the use of registries, measurement-based treatment to target, and application of evidence-based care. Consult psychiatrists have expanded their participation in collaborative care in primary care and specialty settings and, as a result, are often faced with addressing disparities in care for minority patient populations.



Tina Wu, M.D., is a PGY-4 psychiatry resident at Cambridge Health Alliance. Jennifer Hu, M.D., is a first-year child and adolescent psychiatry fellow at Duke University. She completed her adult residency at Cambridge Health Alliance. Hsiang Huang, M.D, M.P.H., is an assistant professor of psychiatry at Harvard Medical School and the director of Primary Care Behavioral Health Integration at Cambridge Health Alliance.

Evidence from our systematic review in the November-December 2020 issue of *Psychosomatics* (now the *Journal of Academy of C-L Psychiatry Systematic Review*) shows that collaborative care may be an effective intervention for treating racial/ethnic minority patients for depression in primary care. This review included 19 studies: 10 randomized, controlled trials and nine observational studies. Most studies included Latino and/or Black adults with fewer studies including Asian and Native Americans. Eleven studies included at least one cultural component (such as bilingual educational materials, culturally adapted interview protocols, or ethnically matched clinicians). Although cultural adaptations can be helpful, high fidelity to the core key elements of collaborative care was sufficient for improving depression outcomes.

## Case Study

Ms. G is a 30-year-old Spanish-speaking immigrant from Honduras with elevated symptoms of depression and anxiety based on patient self-report measures. During her assessment by her primary care physician (PCP), she reported feeling irritable and engaging in frequent verbal arguments with others, and she appeared "fairly sullen" throughout the interview. Her identified stressors included limited English proficiency, working long hours, and missing her children, who live in Honduras. Ms. G acknowledged that she has had difficulties following through on multiple prior referrals from her PCP to outpatient psychiatry and instead requested treatment from her PCP.

The PCP referred the patient to a behavioral care manager who is embedded in the primary care clinic. The care manager met with the patient, collected a clinical history, and learned that the patient had previously tried several antidepressants, specifically fluoxetine, amitriptyline, and citalopram. Two months ago, she started escitalopram to take at bedtime, though she said it worsened her already long-standing disrupted sleep.

The care manager discussed this patient (using a mental health registry) with the consult psychiatrist at their weekly case review session. The psychiatrist recommended additional psychiatric screening using validated screening scales and a diagnosis of moderate-severity major depressive disorder with insomnia. The psychiatrist recommended that the patient take the antidepressant in the morning, increasing the dose and tracking depressive symptoms using a rating scale over time. The psychiatrist also recommended that the patient keep a sleep log and for the care manager to provide cognitive-behavioral therapy for insomnia (CBT-I). Over the next few weeks, the care manager worked with the patient to practice CBT-I techniques and, as part of behavioral activation, supported her in resuming gardening, a longstanding hobby. Four weeks later, the patient experienced a significant reduction in depressive symptoms, improved sleep quality, and a closer connection to friends and family.

## Discussion

This case highlights the many obstacles minority patients face in seeking mental health care. These include language barriers, perceived stigma, and difficulty navigating the complex health care system. PCPs are often the first point of access to health care for underserved minority patients and are therefore uniquely positioned to develop relationships and foster trust. As in Ms. G's case, patients may decline to see psychiatrists and instead ask for their mental health treatment to be provided by their PCPs, whom they already trust.

The Collaborative Care Model provides access to mental health care for patients who may otherwise never present to a psychiatric clinic for treatment. This evidence-based population health approach to care amplifies the clinical impact a consult psychiatrist can have by allowing the psychiatrist to provide diagnostic clarification and management recommendations (including medication, behavioral, and social interventions) for a large number of patients, including those from racial-ethnic minority groups. **PN**

**"The Effectiveness of Collaborative Care on Depression Outcomes for Racial/Ethnic Minority Populations in Primary Care: A Systematic Review" is posted at https://www.sciencedirect.com/science/article/pii/S0033318220300608?via%3Dihub.**

# From Heretical Idea to Mainstream Psychiatry: Brain Stimulation Has Ridden a Wave

*Brain stimulation methods have progressed from unusual novelties and way-out ideas to sophisticated treatments that are now saving lives daily.* **BY MARK GEORGE, M.D.**

I live a stone's throw from the beach near Charleston, S.C., where I sometimes enjoy surfing. In the surf, I sit on my board and watch the incoming waves, selecting the one that seems best, paddling to it, and then timing my board with the wave. Once you're up, it's a rush, and you stay up as long as the wave allows and enjoy the ride.

They call this feeling "pura vida"—joyful being and gratitude. My career in brain imaging and then brain stimulation has been like riding a most remarkable wave.

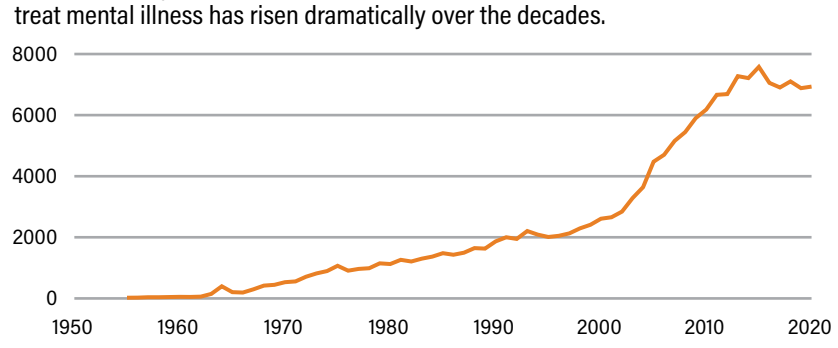
Brain imaging techniques and analysis methods have transformed our ability to understand and image the brain. I remember the day during my residency when the first MRI scanner arrived. Disappointingly, a patient with a dense hemiparalysis had a "normal" MRI scan. We had a lot more to learn. (Acute ischemic strokes were not detectable with MRI.) Now we have robotic MRIs with the ability to image structure or function as well as compare a single patient's results with thousands of other scans in the human connectome. We can map exactly what parts of the brain are involved in most activities and which cortical regions control deeper structures. PET, SPECT, and advanced EEG can reveal amazing information about our patients.

Amazing as the brain imaging advances have been, the brain stimulation methods are the most thrilling developments of my career. Brain stimulation methods have progressed from unusual novelties and way-out ideas to sophisticated treatments that are now saving lives daily. The graph below shows the number of publications a year that mention "brain stimulation." Starting with almost nothing in the year I was born—1958—about 7,000 publications a year now have the keywords "brain stimulation." More important than publications, almost every other month now the FDA approves yet another brain stimulation method for treating a severe brain disorder.

Although I and several others somehow knew that focally stimulating the brain would benefit psychiatric patients, we were a small minority. And the ideas that are now mainstream were largely considered heretical. Psychiatry had long-established traditions of talking therapies and psychopharmacology, but brain surgery and stimulation had a checkered past. Electroconvulsive therapy was and still is a life saver, but we had not yet invented the modern modifications that reduce its cognitive and other side effects.

**Publications Skyrocket on Brain Stimulation Methods**

The number of journal publications about various methods of brain stimulation to treat mental illness has risen dramatically over the decades.




Source: Mark George, M.D./Medline search

Mark George, M.D., is a Distinguished University Professor of Psychiatry, Neurology, and Radiology and holds the Layton McCurdy Endowed Chair at the Medical University of South Carolina. He is also a staff psychiatrist at the Ralph H. Johnson VA Medical Center in Charleston and oversees the TMS clinic there. He is the editor-in-chief of the journal *Brain Stimulation: Basic, Translation and Clinical Research in Neuromodulation.*

### Refining Transcranial Magnetic Stimulation

I was extremely fortunate to see one of the first transcranial magnetic stimulation (TMS) machines being used for research when I was at Queen Square Hospital in London during my first imaging fellowship. I then was able to carry out important discovery studies at my next fellowship at the National Institutes of Health (NIH) in Bethesda, Md. Over many years, we refined TMS methods and then launched a positive industry trial, and the NIH sponsored the OPT-TMS study. The FDA cleared TMS in 2008, and developments have snowballed since then. There are now at least seven TMS devices that are FDA cleared for treating depression and likely over 40 TMS manufacturers on the planet. My friend and colleague Harold Sackeim, Ph.D., recently published a landmark post-registry study of real-world outcomes of patients with treatment-resistant depression who have received TMS in the years following FDA approval. Roughly 30% of patients who have tried and failed medications reach remission, and another 30% have their symptoms at least cut in half. TMS is also FDA cleared for obsessive-compulsive disorder (OCD), anxious depression, and smoking cessation. Exciting research is refining where to place the coil on each individual based either on imaging studies, biomarkers like heart rate changes, depression symptoms, or some combination. Other researchers are reducing six weeks of therapy to a single week. We've even done TMS in zero-G, preparing for TMS and other forms of brain stimulation on interplanetary missions.

The excited surfer in me shouts, "Cowabunga!" What a wave!

Another interesting aspect of brain stimulation methods is that they are not competitive with pharmacology or talking therapy. Brain stimulation brings together psychiatry's different treatment traditions. In fact, brain stimulation methods are much more powerful when they are combined with integrated forms of therapy. The recent TMS approvals for smoking and OCD require that patients be anxiety provoked or craving during stimulation. And some medications boost the plasticity of TMS, pointing the way toward future combinational pharmacology.

*see* **Brain Stimulation** *on page 39*

## Lifelong Learning

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For ongoing education, clinicians can delve into the informative columns and articles published in *Psychiatric News* and other trade newspapers and newsletters. Even throwaway journals and the myriad psychiatrist-directed information offered by commercial education companies online contain useful information, although readers are cautioned to be on high alert for commercial spin and fake medical news where medications, devices, and other interventions are hyped and oversold. To prepare for recertification examinations and maintenance of certification requirements, clinicians often turn to APA's *FOCUS* journal and its related programs.

Psychiatrists should also indulge in the pleasures afforded by deeper dives into the literature and emerging technologies. Thanks to COVID-19, learning to practice via telehealth has become almost mandatory. Reading entire books, watching TEDMed talks, listening to podcasts, and taking formal courses (live, hands-on, asynchronously online) take time. However, these activities not only provide intellectual satisfaction but also offer practice-building and other career-building skills.

Psychiatrists have jumped into executive and online M.B.A. and certificate programs designed to increase administrative, financial, political, research, and other skill sets. Numerous free, high-quality courses are available online for those wishing to refresh or update their knowledge of all aspects of neuroscience, genetics, genomics, psychology, and much more.

Finally, the "Zoomiverse" has opened up many other opportunities. We can effortlessly Zoom across boundaries of time and space and join our best friends and colleagues to develop accessible, socially meaningful, educationally rich get-togethers. We can create journal clubs, book clubs, teaching and peer-supervising conferences, collaborative scholarly projects, and all manner of (HIPAA compliant) professional activities. And all from the comfort of our own homes.

So, what would *you* like to do with the times you routinely set aside for your ongoing education—which you do, of course. Don't you? **PN**

## Buprenorphine

*continued from page 33*

in 63.2% of cases overall and doses of 28 mg or more were given in 23.8% of cases overall.

When the researchers reviewed the vital signs recorded in the patients' records, they found no significant association between buprenorphine dose and blood pressure, respiratory rate, heart rate, and oxygen saturation. Overall, there were five cases of precipitated withdrawal—intense withdrawal symptoms brought on by the medication—but four of them occurred in patients who received a dose of 8 mg.

Herring said that while a higher dose of buprenorphine can be effective and well tolerated, it's not for everyone who comes to the ED with OUD. For example, patients with congestive heart failure would not be good candidates for a higher dose because of buprenorphine's potential sedating and respiratory effects.

"[G]ood clinicians using sound judgment should feel like they can use higher doses in people who are generally healthy [aside from their OUD]," he explained.

Patients with greater opioid dependence and tolerance are more likely to derive a benefit from a higher dose, Herring said. To determine which patients might be good candidates for a higher dose, he suggests simply asking them how often they use opioids and how much they take.

"People are usually quite credible historians regarding their own use," he said.

Herring added that higher doses of buprenorphine may be particularly useful for patients at safety-net hospitals, those that offer health care regardless of a patient's insurance status or ability to pay. Highland is one such hospital, and 22.5% of the patients in the study were homeless.

"These patients exist in a world of very pressing survival needs because of their socioeconomic status and other social determinants of care," Herring said. "Recognize that after discharge, many patients face a system that is fundamentally fragmented, and they experience it as hostile and discriminatory."

Herring explained that because using a higher dose extends buprenorphine's duration of action, it buys both the patient and health professionals several days to arrange for follow-up and continued treatment.

"There's a real role for this in making both patient and [health professional] more comfortable with discharging the patient," he said. "We can tell them, 'We know you have a lot going on, but at least right now you are safe.'"

This study was supported in part by grant funding through the National Institute on Drug Abuse. **PN**

**"High-Dose Buprenorphine Induction in the Emergency Department for Treatment of Opioid Use Disorder" is posted at https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781956.**

## Withdrawal

*continued from page 34*

lead to withdrawal symptoms that can persist until the receptors adjust to the new biological environment, Horowitz said.

Horowitz and Taylor used the available pharmacological data for antidepressants to develop an "evenly spread" tapering plan: a patient's antidepressant dose is reduced in a way to produce a consistent reduction of receptor occupancy at each interval, such as 10 reductions of 10% each. Horowitz and Taylor recommend two to four weeks between each dose reduction to see if any withdrawal or relapse symptoms emerge.

"If some symptoms develop, it indicates that the rate of reduction has been too fast," Horowitz said. "If the symptoms are severe, then the dose should be increased back to where the patient was stable; if [the symptoms] are tolerable, then maintain the current dose until symptoms subside, then proceed more cautiously for the subsequent rounds."

Near the end of the taper, some medication doses can get to miniscule amounts way below even the smallest pill doses. Horowitz noted that liquid formulations can be useful in such instances since they can be diluted.

After publishing their proposed antidepressant protocol in *The Lancet* in 2019, Horowitz and Taylor moved on to antipsychotic tapering and published those results this year. The general principles of evenly reducing receptor occupancy are the same as with antidepressants, though spread over a longer timeframe—about three to six months between dose changes instead of one to two months.

"The effects of antipsychotics on dopamine receptors can be quite persistent," Horowitz said. He noted studies have shown that some patients with psychosis still had symptoms of tardive dyskinesia—a side effect of antipsychotics—more than two years after stopping their medication.

Tapering antipsychotics could take many months or even years, but Horowitz said that he believes many patients, some of whom have been on an antipsychotic for decades, would be open to a slow taper if it meant possibly eliminating an unnecessary medication.

### More Research Needed

"I think our field has overvalued relapse prevention when treating schizophrenia," said Sandra Steingard, M.D., chief medical officer at Howard Center, a community mental health clinic in Burlington, Vt. "But relapse is just one potential harm that needs to be weighed alongside other harms that medications might cause."

"[I]f patients are insistent on stopping their treatment, we need to let them try using the safest way possible."

—William Carpenter, M.D.

Steingard, who is now retired, said she discussed the benefits and risks of antipsychotic tapering with dozens of clinically stable patients at her clinic. She found that the patients who expressed interest and began slowly tapering did not experience any worse rates of adverse outcomes such as job loss or hospitalization than those who remained on their full dose. Even several patients on clozapine—which is prescribed to people with severe and treatment-resistant psychosis—managed to significantly reduce their dose without adverse outcomes.

"Patients stop taking their medications all the time without their doctor's guidance, and that can pose serious risks," said William Carpenter, M.D., a professor of psychiatry at the University of Maryland School of Medicine and a leading expert in schizophrenia. Carpenter said that he believes Horowitz's scientifically supported protocol gives physicians a framework to discuss tapering with a degree of confidence. "We need to work with our patients; if patients are insistent on stopping their treatment, we need to let them try using the safest way possible."

Carpenter said that the antipsychotic tapering data particularly could strike a chord in a professional field that has too long seen schizophrenia as a chronic deteriorating illness. "We now know—and have stated clearly in *DSM*-5—that schizophrenia is a clinical syndrome with a wide diversity of symptoms. Different patients have different manifestations and different long-term medical needs."

Steingard acknowledged that a few patients who participated in tapering at her clinic did experience significant relapse during the process, typically before complete discontinuation from the antipsychotic. "It's not going to work for everybody, but if we could get more rigorous research, we might have a better grasp of the optimal tapering approach to minimize these risks."

Horowitz, who is a clinical research fellow in psychiatry at University College London (UCL) and the North East London NHS Foundation Trust, is involved in one such study: the Research into Antipsychotic Discontinuation and Reduction (RADAR) trial. This ongoing five-year study, funded by the U.K. National Institute of Health Research and led by Joanna Moncrieff, M.D., a professor of critical and social psychiatry at UCL, has enrolled 250 patients on maintenance antipsychotic therapy for schizophrenia and randomized half of them to gradually taper their medication over 12 months. The RADAR trial will track outcomes in these participants for two years, comparing both relapse rates and social functioning between the two groups.

In the meantime, Horowitz noted that the Royal College of Psychiatrists has adopted the antidepressant tapering protocol that he and Taylor created as their official method for tapering antidepressants. He is hopeful that this group will also adopt the pair's new antipsychotic protocol.

"I'm both a mental health professional and someone with lived experience of a mental health condition, so I know psychotropic medications are a necessity for some patients," said Horowitz. "But we should try to make sure each patient takes the lowest dose possible, which in some cases might be zero."

Horowitz said he has received hundreds of emails from patients and doctors around the world telling him of the success they have had with the slower tapering approach. He is also giving his own antidepressant tapering experiment a second try. **PN**

**"Tapering of SSRI Treatment to Mitigate Withdrawal Symptoms" is posted at https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(19)30032-X/fulltext. "A Method for Tapering Antipsychotic Treatment That May Minimize the Risk of Relapse" is posted at https://academic.oup.com/schizophreniabulletin/advance-article/doi/10.1093/schbul/sbab017/6178746. "Five Year Outcomes of Tapering Antipsychotic Drug Doses in a Community Mental Health Center" is posted at https://link.springer.com/article/10.1007/s10597-018-0313-1.**

## Children

*continued from page 22*

ing mental health services may not have access to them.

Resources for building resilience are crucial because the pandemic has had a significant impact on our youth. According to a report by the Alliance for Excellent Education, more than 8 million children had limited or no internet access, impeding their ability to participate in academic courses during the pandemic. Students have also lost teachers who left the education workforce because of pandemic stressors or death from COVID-19. And according to the Centers for Disease Control and Prevention, between April and October 2020, the proportion of emergency visits related to mental health increased by approximately 24% for children aged 5 to 11 years and 31% for children aged 12 to 17 years.

The adverse effects of adult unemployment also touch kids' lives in very direct ways. For every 1% increase in unemployment, there is a 20% increase in child neglect and a 10% increase in abuse of any type, according to a paper published March 19, 2020, by the Social Science Research Network (SSRN).

Children from diverse families are particularly affected by the pandemic. According to a report by the United Hospital Fund, Black and Hispanic children in New York experienced the death of a parent or caregiver at twice the rate of Asian and White children. Asian families have faced additional stressors. Although hate crimes overall decreased last year, a report this year by the Center for the Study of Hate and Extremism showed that anti-Asian hate crimes in 16 major U.S. cities had an overall increase of 149%.

The mental health challenges of COVID-19 will continue to manifest long after the pandemic is over. The time to develop innovative interventions that build resilience and disseminate treatment delivery and preventive interventions is now. Recognizing functional change is just part of the work. Maximizing resilience and adaptation opportunities that take into account the burden of the pandemic and its associated stressors is essential. Children need advocates who can initiate and lead collaborations with leaders in communities, school districts, technology, among others, to build effective programs and interventions. We need to disseminate these within the systems where our kids socialize, study, and play. Policy work that helps to sustain these resilience-building projects is critical as it recognizes that "resilient" does not mean symptom-free. **PN**

**The Alliance for Excellent Education report, "Students of Color Caught in the Homework Gap," is posted at https://futureready.org/homework-gap. The CDC report, "Mental Health–Related Emergency Department Visits Among Children Aged <18 Years During the COVID-19 Pandemic—United States, January 1–October 17, 2020," is posted at https://www.cdc.gov/mmwr/volumes/69/wr/mm6945a3.htm. The SSRN report, "Child Maltreatment, Unemployment, and Safety Nets," is posted at https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3543987. The United Hospital Fund study, "COVID-19 Ripple Effect: The Impact of COVID-19 on Children in New York State," is posted at https://uhfnyc.org/publications/publication/covid-19-ripple-effect-impact-covid-19-children-new-york-state/.**

## Medications

*continued from page 33*

when relevant circuit mechanisms targeted by that treatment are expressed. For example, a given treatment, such as an mGluR2 agonist, might be effective early in the course of illness when it compensates for deficits in cortical inhibition, but it might lose efficacy as the illness progresses and the same drug now exacerbates the impact of synaptic deficits.

In summary, there are now at least four promising new medications under study for the treatment of schizophrenia. The fact that three of these new drugs inhibit the release of glutamate and dopamine draws our attention to pathophysiologic models for schizophrenia that encompass excessive glutamate and dopamine release. The model considered here suggests that excessive glutamate and dopamine release emerges in the high-risk state and persists through the early course of schizophrenia.

Later in the illness, synaptic loss complicates both the biology and treatment of this illness. This illness phase-specific approach to pharmacotherapy is a framework for increasing the precision of schizophrenia pharmacotherapy. However, the developmental model proposed is a general one, and we recognize that there are important differences in the biology of schizophrenia across patients that might account for why an individual patient might not fit this model. The approach outlined above would be more effective were it based on biomarkers of circuit function in individual patients. This type of biomarker-driven approach might yield even more precise matching of inhibitory treatments to evidence of network disinhibition or dopaminergic hyperactivity in individual patients. For example, genomic biomarkers might also drive the development of novel therapeutics, particularly those patients with specific rare loss of function mutations that produce substantial increases in schizophrenia. If individuals with those mutations could be identified as early as possible, it would create the possibility of instituting specific medication treatments or gene therapies well in advance of the onset of psychotic symptoms. As so frequently happens in psychiatry, discovering pharmacotherapies that work through novel mechanisms focuses our attention on new aspects of the biology and new opportunities for the treatment of this disorder.

This work was supported by UO1 MH121766-01. **PN**

**References and the author's disclosure statement appear in the online version of this article posted at https://psychnews.psychiatryonline.org/doi/10.1176/appi.pn.2021.11.37.**

## Brain Stimulation

*continued from page 37*

There is equally exciting research with other forms of brain stimulation, including cervical or transauricular vagus nerve stimulation (VNS); transcranial direct or alternating current stimulation (tDCS or tACS); and the newest method, pulsed ultrasound. The technologies are amazing, with closed-loop sensing devices and other Star Wars–like advances. However, the limiting factor for their use is that psychiatry does not have enough trained translational clinical researchers who can help move these wonderful ideas from the shelf to the patient's bedside.

### Future Lies in Better Access, Less Expensive Technology

Although the growth and flourishing of brain stimulation methods has been a marvelous story, rates of depression, addiction, and suicide continue to climb. These brain stimulation methods have not yet made a significant dent in terms of large-scale mental health. Some of this may be in part due to lack of knowledge. Sadly, in the United States, likely less than 5% of depressed patients who meet criteria for treatment with TMS actually receive treatment. Another factor in addition to lack of education may be the relatively high cost and inefficiency of how we use these technologies.

Can we develop less expensive forms of brain stimulation that might be used at home? Transcranial direct current stimulation, transcutaneous auricular vagus nerve stimulation, and other technologies are being tested now for home use. If they work, they may begin to make a larger impact, particularly during and after the COVID-19 pandemic, when patients are looking for home-based treatments.

Luckily, I'm still on my brain stimulation surfboard. This amazing wave of brain stimulation methods continues to swell and grow. Brain stimulation methods are helping psychiatrists to treat our patients, decrease patients' distress, battle stigma, and discover how the brain works in health and disease. What a wonderful ride it has been and will continue to be. **PN**