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AMERICAN PSYCHIATRIC ASSOCIATION

PSYCHIATRIC NEWS

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AP Foto/Mark Wallheiser

SEE STORY BELOW

Days after the shooting in Parkland, Fla., students from Marjory Stoneman Douglas High School held a rally at Florida's state capitol in Tallahassee to demand that lawmakers pass stricter gun-control legislation. "Never again" and "Vote them out," they chanted.

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Reducing burnout among physicians requires systemic changes.

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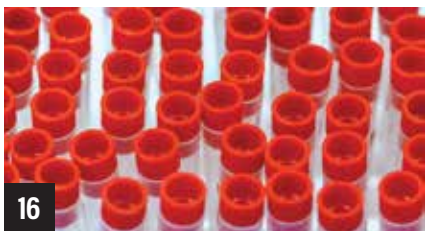
Expert on gun violence shares advice on reducing patients' suicide risk.



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FDA approves first blood test to diagnose traumatic brain injury.

Psychiatrists Help Florida Shooting Victims Push for Meaningful Change

APA members are working to ensure victims' needs are met after the latest mass shooting and meet with state officials to help prevent similar tragedies. **BY LINDA M. RICHMOND**

Psychiatrists in Florida were quick to support victims' needs after a mass school shooting last month that resulted in the deaths of 17 students and adults, while many closest to the tragedy are demanding action to prevent more bloodshed.

"Leaders in child psychiatry, especially in child trauma, have reached out to Florida psychiatrists who live and work in that area to offer their support," R. Scott Benson M.D., a child and adolescent psychiatrist in Pensacola, Fla., and a member of APA's political action committee (APAPAC), told *Psychiatric News.*

"The agencies that we work with have partnered with the school board to provide immediate crisis counseling," Bhagi Sahasranaman, M.D., a child psychiatrist in Broward County, told *Psychiatric News* in the aftermath of the shooting.

Benson and Sahasranaman were part of a Florida mental health and child welfare work group that was pulled together six days after the shooting. Attendees discussed ways to expand mental health services and intervene with families who frequently call law enforcement to handle domestic violence. Afterward, the two psychiatrists were part of a smaller group that met with Gov. Richard L. Scott. "Overall, I felt like it was a really positive meeting, although I wish bigger steps could have come out of it," Benson said.

Following the meeting, Scott proposed barring gun purchase and possession for individuals with mental illness, a $450 million investment to improve school security, and $50

see **Shooting** *on page 20*

PERIODICALS: TIME SENSITIVE MATERIALS

Health Care Groups Oppose Religious Exemptions for Providers

Medical and other health care organizations object to HHS actions that would open the door to religious discrimination against minorities, including LGBTQ patients. **BY REBECCA GREENBERG**

APA and more than 30 other health care organizations representing clinicians, patients, and administrators across the country sent a letter last month to Alex Azar, secretary of the Department of Health and Human Services (HHS), to express their concerns about actions that would allow health care professionals to refuse treatment to individuals on religious grounds.

Among those actions are the issuance of a proposed rule, "Protecting

see **Exemptions** *on page 18*

PSYCHIATRIC NEWS

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AMERICAN PSYCHIATRIC ASSOCIATION

FROM THE PRESIDENT

More Help for More Moms: Increasing Access Through Innovation

BY ANITA EVERETT, M.D., AND KRISTIN BUDDE, M.D.

When we think about innovation in psychiatric practice, our first thoughts are often about exciting new interventions and drug discoveries such as ketamine infusions and transcranial magnetic stimulation. Sometimes innovation in a field like psychiatry represents an advance in *what* is done, while other times innovation aims to enhance *how* things are done. In all the excitement about new therapeutic innovations—the *what*—it can be easy to forget that that even the most incredible interventions have limited benefit if they cannot be broadly accessed. Innovation design that is focused on the *how* of services delivery is a key component retooling health care so that gaps in access are addressed.

Take the problem of caring for pregnant women and new moms. As many as 21.9 percent of new moms experience depression in the first year of motherhood, which (taking the almost 4 million live births in 2015 as a reference point) amounts to 875,000 cases of postpartum depression each year. This is a problem in serious need of innovation for the mother, the family, and ultimately the next generation of children.

Anita Everett, M.D., is president of APA. Kristin Budde, M.D., M.P.H., is a fourth-year psychiatry resident at Yale University School of Medicine.

But where to begin?

Let's use some of the tools of innovation to think about solutions to this problem. First, define the problem. A problem could be framed as how to get more people into a particular specialty clinic or hiring more physicians to see more patients, but that is not our problem. Our problem is untreated mental illness in peripartum women. Paradoxically, narrowing the problem enables us to come up with broader designs possibilities.

Now let's take out a second innovations tool: analogous learning. Are there other analogous systems that have solved analogous problems successfully? For our current problem, can we learn from models in collaborative care, which creates access to stepped psychiatric treatment in primary care? Can we learn or adapt from models employed for general pediatrics whereby expert child psychiatry telephone consultation is made available to pediatricians regarding psychiatric and psychopharmacologic treatment of children? Is there something we can incorporate from low-resource countries that utilize paraprofessional community health workers to extend the reach of health care?

There are two innovative programs of which we are aware that have developed innovative solutions to our problem. The first is the MCPAP for Moms program in Boston (*Psychiatric News*, June 2, 2017). This program built upon

see **From the President** *on page 5*

IN THIS ISSUE

DEPARTMENTS

Register Now for Annual Meeting

APA's 2018 Annual Meeting will be held in New York City from **May 5** to **9**. Register now to take advantage of the low advance registration fees. For more information about the meeting, see pages 8 and 9. To register, go to psychiatry.org/annualmeeting/registration.

OVERCOMING BURNOUT

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Broad System Factors Influence Physician Wellness, Patient Care

Does the system in which doctors practice today guarantee they will experience stress and burnout? This article is part of a series on physician wellness and burnout spearheaded by APA President Anita Everett, M.D. **BY DAVID POLLACK, M.D.**

Systems matter.

That's a crucial lesson that APA's presidential Work Group on Psychiatrist Well-Being and Burnout has learned about what accounts for health and wellness—or for burnout—among America's physicians: the broader system and contextual framework in which a physician is working may be the most significant factor shaping that physician's reactions to stress.

As has been reported in *Psychiatric News*, the work group has met throughout this past year. We split into subcommittees to handle different components of the review and recommendations. We reviewed literature on a range of subjects and looked at other interventions and informational guidelines.

The products and ideas coming out of the committee's work have led to the creation of an online resource for psychiatrists (and other health professionals) to provide screening information on relative risks of burnout and depression, as well as support for addressing some forms of stress and distress. We reviewed and selected two screening instruments (Oldenburg and PHQ-9) to help members identify their relative risk of burnout or depression. The tools can be found on APA's website at psychiatry.org/burnout. A number of psychiatrists have accessed the online module for the screening and informational components. On the basis of our preliminary analysis of the results, we are concerned about the degree of burnout and mood symptoms of psychiatrists.

The work group has also created the Ambassadors Toolkit, which can be accessed at https://www.psychiatry.org/File%20Library/Psychiatrists/Practice/Well-being-and-Burnout/APA-Well-being-Ambassador-Toolkit-Manual.pdf. The toolkit includes a PowerPoint slide deck and companion manual to help you advocate for systemic reform in your home institution or organization. The slide deck can be modified to match the needs of your organization as you spread awareness of physician burnout and assist your organization in addressing the wellness and burnout needs within your work community.

In the process of reviewing and implementing support for APA members, we have attempted to understand the personal and clinical experiences of individuals with various forms of toxic stress associated with the health profession. At the same time, we have recognized the importance of taking a broader, more systems-based perspective of the problems and how they emerge within, are affected by, and affect other parts of the system.

At a symposium on physician well-being in 2015 by the Accreditation Commission on Graduate Medical Education, Dewitt Baldwin, M.D., presented a comprehensive "concept map" (see http://www.acgme.org/Portals/0/PDFs/Symposium/DBaldwinSymposiumPresentation.pdf), which depicts progressively broader areas of focus, all of which influence physician well-being. These start with the individual and extend outward through the program, institution/organization, specialty, profession, and the health care system. Encompassing all of these is the wider political environment, and policy decisions at the local, state, and national levels.

In addition, several APA leaders have been participating in the National Academy of Medicine's Action Collaborative on Clinician Well-Being. The collaborative has derived a slightly simpler scheme (see image) illustrating four broad systemic factors affecting physician well-being and resilience:

- **Learning/practice environment:** This comprises such issues as autonomy, collaborative versus competitive environment, mentorship, professional relationships, team structures and functionality, and workplace safety and violence.

- **Regulatory, business, and payer variables:** These include, among others, documentation and reporting requirements, compensation issues, maintenance of licensure and certification, reimbursement structure, and shifting administrative rules.

- **Sociocultural factors:** These may include the workplace culture of safety and transparency, discrimination and overt and unconscious bias, media portrayal, patient behaviors and expectations, political and economic climates, and stigmatization of mental illness.

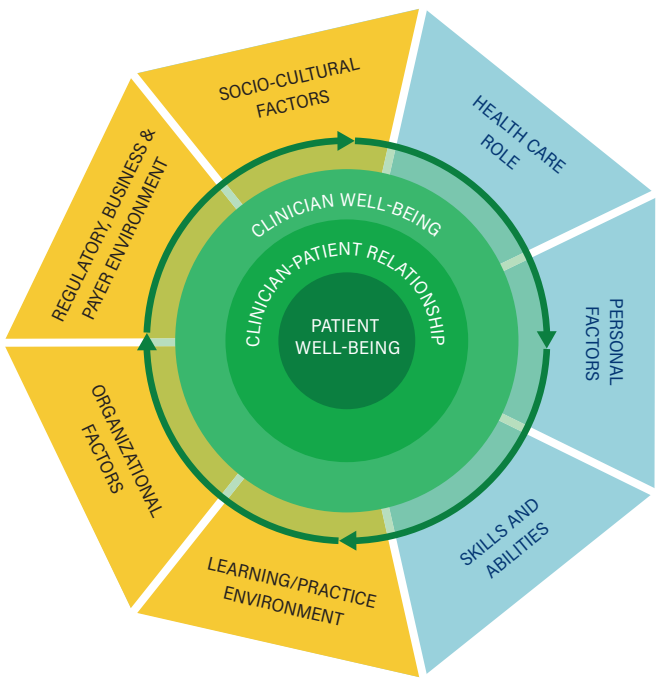
- **Organizational factors:** These comprise the organization's mission and values; culture, leadership, and staff engagement; data collection requirements; diversity and inclusion; level of support for all health care team members; professional development opportunities; scope of

continued on facing page

David Pollack, M.D., is a professor for public policy in the Department of Psychiatry and Division of Management at the Oregon Health and Science University and a member of the APA Work Group on Physician Well-Being and Burnout.

A Widening Circle of Factors Influence Physician Well-Being

Four broad systemic factors (in yellow) interact with individual physician factors (in light blue) to influence clinician well-being and, in turn, patient care.



Source: National Academy of Medicine/Action Collaborative on Physician Well-Being

National Academies Report Details Health Impact of E-Cigarettes

Among the 47 conclusions reached by the expert committee are items related to smoking cessation and the harm reduction potential of e-cigarettes. **BY NICK ZAGORSKI**

A comprehensive new report from the National Academies of Sciences, Engineering, and Medicine (NASEM) provides some mixed signals in relation to a central question about the public health impact of electronic cigarettes: do they have a value in helping people quit smoking?

The report cited strong evidence to suggest that electronic cigarettes, or e-cigarettes, contain fewer harmful compounds than traditional cigarettes and that smokers who completely switch to e-cigarettes can reduce their health risks in the short term. However, there is no substantive evidence that e-cigarettes can actually aid in smoking cessation.

The role of e-cigarettes in smoking cessation has been a topic of much debate since these devices first came on the market. Some health professionals, for example, believe they can be a form of nicotine replacement therapy just like patches, while others worry that their resemblance to regular cigarettes reinforces negative smoking behaviors that make it harder to quit.

As noted in the NASEM report—which included the results of over 800 peer-reviewed studies—there are some data from observational studies that suggest e-cigarettes can promote smoking cessation, but evidence from more controlled studies is lacking.

The report identified just a handful of randomized clinical studies, and most of these showed only that e-cigarettes that contain nicotine are more effective at promoting smoking cessation than e-cigarettes without nicotine. There are insufficient data to know how these devices compare with current FDA-approved cessation products such as varenicline or nicotine patches.

People who completely transition from traditional cigarettes to e-cigarettes appear to have improved health outcomes in the short term (one year or less), the report concluded.

Douglas Ziedonis, M.D., M.P.H., a professor of psychiatry at the University of California, San Diego, was cautiously optimistic about this finding:

"The short-term benefits are encouraging, but remember that addiction is a long-term issue," he told *Psychiatric News*.

Ziedonis said that while the concept of reducing harm in patients by encouraging switching to e-cigarettes is laudable, there are not enough data on the long-term behaviors of smokers who made the switch. "Many smokers, for example, will just flip-flop between tobacco products, and that is not helpful for their health," he said.

Until more evidence about cessation efficacy and long-term health outcomes becomes available, Ziedonis recommends that psychiatrists continue to focus on cessation strategies with their patients, though the use of e-cigarettes as part of the process can and should be a topic of conversation.

Ziedonis said he believes the objective NASEM report will be a great resource for mental health professionals, even those who do not specialize in addiction psychiatry. "Smoking is associated with psychiatric disorders, and questions about e-cigarettes are only going to get more common in psychiatry offices," he said. **PN**

"Public Health Consequences of E-Cigarettes" is posted at http://nationalacademies.org/hmd/Reports/2018/public-health-consequences-of-e-cigarettes.aspx.

continued from facing page

practice; and workload, performance, compensation, and value attributed to work elements.

These broad systemic factors interact with one's genetic, cultural, and personality factors—designated in the map as "health care role," "personal factors," and "skills and ability"—to create those experiences that contribute to toxic stress and ultimately impact patient care.

A concept map like Dr. Baldwin's helps to graphically articulate a systems-based view that can stimulate relevant policy discussion, process improvement, and research. Now is a time when such an approach is needed.

A public health systems perspective on physician burnout helps to identify upstream or antecedent events/factors that contribute to the prevalence and severity of burnout so that effective interventions can be developed and implemented at all levels—individual, team, organization, and health care system.

Don Berwick, M.D., former administrator of the Centers for Medicare and Medicaid Services and president of the Institute for Healthcare Improvement, has somewhat famously said, "Every system is perfectly designed to get the results it gets"—meaning that, whether intended or not, the design of a system (including alignment of incentives) will dictate and reinforce the outcomes that are observed.

The same holds true for understanding physician health and wellness: we have a system perfectly designed, in some ways, to produce burnout. Developing individual interventions is useful and necessary, but we cannot ignore or abandon the potential for larger-scale improvements by taking a public health and systems perspective. **PN**

APA's burnout and wellness toolkit can be accessed at https://www.psychiatry.org/burnout. The 2015 ACGME symposium on physician wellness, including a conceptual map of systemic factors, can be accessed at http://www.acgme.org/Portals/0/PDFs/Symposium/DBaldwinSymposiumPresentation.pdf. Information about the National Academy of Medicine Action Collaborative on Physician Resilience and Well-Being is posted at https://nam.edu/initiatives/clinician-resilience-and-well-being/.

Help Yourself and Your Colleagues With New Toolkit

Under the guidance of APA President Anita Everett, M.D., APA has launched a toolkit to help you determine whether you may be experiencing burnout and to provide resources to help you take charge of your well-being. New to the site is another valuable toolkit—the APA Toolkit for Well-Being Ambassadors—to help you advocate for systemic reform in your home institution or organization. The toolkit includes a PowerPoint slide deck and companion manual. Visit psychiatry.org/burnout and apapsy.ch/Ambassadors today.

Adam Scott

From the President

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the successful MCPAP, or Massachusetts Child Psychiatry Access Program, which has been successfully providing telephone consultation from child psychiatrists to general pediatricians for many years. Many states have emulated this program. MCPAP for Moms is a recent adaptation of MCPAP that aims to use the similar technique of telephone access to psychiatrists who provide consultation to frontline providers, the obstetricians. This innovation expands the number of providers who become equipped to identify and treat peripartum mood disorders. The developers of MCPAP for Moms, Program Director Marcy Ravech, M.S.W., and Medical Director Nancy Byatt, D.O., M.S., were recognized by APA with a Gold Achievement Award last fall.

In Connecticut, the New Haven Mental Health Outreach for Mothers (or MOMS Partnership) aims to explicitly foster collaboration between Yale academics, city officials, and community and health care supports for low-income mothers. It was awarded a Kresge Foundation grant in 2017 for its work. This program is designed in the style of modern local health departments "Public Health 3.0" model in that it convenes and supports a network of new public and private partners to focus on an identified problem: the impact of untreated mental illnesses in mothers. In this case, leaning on community supports allows mothers to get the care they need while connecting with their community.

In each case, a local group has designed a strategy that aims to solve the problem of access to care for women with peripartum mental health conditions. These are examples of innovative population health strategies that address *how* we solve the problem of good access to an appropriate level of care for a group of people. Realistically, our modern health care systems are complex and often based on traditional workflow designs that have been built to serve one patient at a time.

All of us—each one of us who cares for patients—can be innovators. Every time we streamline a clinical workflow and work with new partners to develop new ways to serve a new population, we are changing and improving our health care system. In fact, you're probably already an innovator.

Yes, our patients depend on us to continue researching, developing, and promoting new therapies. But let's not forget that we still need better systems to deliver those therapies. **PN**

"UMass Researcher Turns Idea Into a Nationally Recognized Program" is posted at https://psychnews.psychiatryonline.org/doi/full/10.1176/appi.pn.2017.3b1.

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Psychiatrists Often Needed to Ensure Success of International Adoptions

The success of international adoptions requires a team approach. **BY CAROL SORGEN**

When San Francisco psychologist Juli Fraga, Ph.D., counsels international (also referred to as intercountry) adoptees and their families, she brings with her a personal understanding of the mental health issues that can arise or persist even years after the initial adoption. Fraga was born in Korea, adopted by a white family in Nebraska, and grew up in an environment where there was little diversity.

"I never felt that I fit in," Fraga told *Psychiatric News,* adding that it was difficult for her parents to understand what she went through as they had never experienced racism themselves.

"Adoption in general is a form of trauma, and international and transracial adoptions add yet another dynamic to the situation," said Fraga. She noted that adoptees are often expected to be thankful for their new family while not acknowledging the loss that led them to that point.

"There's a sense of 'Look at what you've gained,'" said Fraga, which can be interpreted by the adoptee as "be grateful for your loss."

In "Mental Health in Internationally Adopted Adolescents: A Meta-Analysis," published in March 2017 in the *Journal of the American Academy of Child & Adolescent Psychiatry,* lead author Kristin G. Askeland, Ph.D., of the Department of Health Promotion, Norwegian Institute of Public Health, and colleagues reported that as a group internationally adopted youngsters show higher levels of mental health problems than their nonadopted peers. "This difference should be acknowledged, and adequate support services should be made available," wrote the authors.

Similar results were reported in "Alcohol and Drug Use Among Internationally Adopted Adolescents: Results From a Norwegian Population-Based Study," published on March 2, 2017, in the *American Journal of Orthopsychiatry.* Also led by Askeland, this study found that the increased risk of mental health problems among internationally adopted adolescents also led to more alcohol and drug use than among their nonadopted peers.

Mental health problems, such as reactive detachment disorder, disinhibited reactive disorder, posttraumatic stress disorder, developmental delays, and language disability are common among international adoptees, Adiaha Spinks-Franklin, M.D., a developmental-behavioral pediatrician at Texas Children's Hospital and the Texas Children's Center for International Adoption, told *Psychiatric News.*

"The older the child is at adoption, the more risk there is of mental health issues, because there have been so many years of trauma and neglect," said Spinks-Franklin.

Spinks-Franklin observed that it's not only adoptees themselves who can experience problems, but also the adoptive parents and other siblings. Issues include sibling jealousy as the adopted child requires more time, energy, and resources; stress and fatigue; and even remorse when the adopted child is not blending into the family as easily as anticipated.

Psychiatrists play a crucial role in working with international adoptees and their families, said Spinks-Franklin. "When seeing a child adopted from another country, consider the strong likelihood of early childhood trauma or neglect, as well as fetal alcohol syndrome or disorder, particularly if the child is from Eastern Europe," advised Spinks-Franklin. "Also, be aware that the child may be developmentally younger than his chronological age. As the child ages, problems can persist, or new problems—such as depression and anxiety—can present."

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RESIDENTS' FORUM

Preparing for a Sequel: '13 Reasons Why' and Suicide Contagion

BY MATTHEW C. FADUS, M.D.

"My friends esteem me; I often contribute to their happiness, and my heart seems as if it could not beat without them; and yet—if I were to die, if I were to be summoned from the midst of this circle, would they feel—or how long would they feel—the void which my loss would make in their existence?"

—Johann Wolfgang von Goethe, The Sorrows of Young Werther, 1774

The Sorrows of Young Werther, an 18th century novel by Johann Wolfgang von Goethe, describes the story of a young man, Werther, who falls in love with a woman named Charlotte. Charlotte, engaged to a man 11 years older than Werther, finds herself attempting to reconcile a friendship with Werther in addition to her new marriage. Werther becomes tortured by the marriage, and his desire for Charlotte overwhelms his ability to cope with a life without her. He dies by shooting himself with a pistol, which he borrows from Charlotte's husband.

Matthew C. Fadus, M.D., is a second-year psychiatry resident at the Medical University of South Carolina.

After publication of Goethe's novel, "Werther Fever" spread across Europe. Young men, rejected by women whom they love, were dying by suicide at alarming rates. They were found wearing the same characteristic yellow trousers and blue tailcoat as Werther, using a similar pistol, and discovered with a copy of *The Sorrows of Young Werther* at their side.

Young Werther's story and its effects across Europe have been described as the "media's first moral panic." The book was banned in Denmark, Germany, and Italy, and Werther's characteristic outfit was outlawed as well. The consequence of Goethe's novel was one of the first recorded incidents of suicide contagion, where exposure to suicide from family, friends, or media can influence vulnerable populations to attempt suicide. Suicide contagion is rooted in the idea that increased suicide exposure can lead some to view it as permissive, increasing suicide attempts and fatalities in temporo-spatial clusters.

In March 2017, the release of "13 Reasons Why," a Netflix drama series depicting the fictional suicide of 17-year-old Hannah Baker, had a ripple effect across the mental health community and throughout the country. Prior to her death, Hannah audiotapes herself describing 13 specific people whose actions led to her suicide, proving her suicide as a viable and vengeful conclusion to their mistreatment.

"13 Reasons Why" was one of the most popular series on Netflix in 2017 and perhaps the most widely discussed

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The importance of adoption-competent mental health professionals, including psychiatrists, has received increased attention in recent years. In December 2016, the Donaldson Adoption Institute released a policy perspective titled "A Need to Know: Enhancing Adoption Competency Among Mental Health Professionals." The report highlighted the difficulty that adoptive families face in finding practitioners who understand and are trained in the areas of permanency and adoption. Identifying practitioners who are adoption-competent is not always clear or easy to determine, the report noted, in part because adoption counseling has not yet been recognized as a professional specialty in health care, with accompanying guidelines for training, practice, and credentialing. Programs such as the National Adoption Competency Mental Health Training Initiative (NTI), however, are being established in the hope of filling that void.

NTI was created in October 2014 through a five-year, $9 million cooperative agreement between the Maryland-based Center for Adoption Support and Education (C.A.S.E.) and the Department of Health and Human Services, Administration for Children and Families, Children's Bureau. The evidence-informed, standardized web-based training is designed to help child welfare professionals and mental health practitioners better understand and address the mental health and developmental needs of children who are in the process of being adopted or have already been adopted.

Training modules specific to international adoptions include value-based education, such as the importance of racial and cultural identity from both a historical and contemporary perspective and development of skills, such as assisting parents in initiating conversations about race, ethnicity, and culture; supporting the significance and preservation of a child's connection to his or her ethnic/racial heritage and culture of origin; and assisting a child in integrating his or her racial/ethnic identity with other identities.

Ensuring that an international adoption is a success takes a team of providers, including teachers, pediatricians, psychologists, and psychiatrists as well, said Spinks-Franklin. "We all have to work together." **PN**

"Mental Health in Internationally Adopted Adolescents: A Meta-Analysis" is posted at http://www.sciencedirect.com/science/article/pii/S0890856716319955. "Alcohol and Drug Use Among Internationally Adopted Adolescents: Results From a Norwegian Population-Based Study" is posted at http://psycnet.apa.org/doiLanding?doi=10.1037%2Fort0000231.

television shows last year, as it was the most tweeted-about show of 2017. However, the notoriety of the show went beyond Twitter, Netflix, and other forms of media. The series left a grim trail of potential copycat suicides, and within three weeks of its release, Google searches for "how to commit suicide" and "how to kill yourself" increased 26 percent and 9 percent, respectively, according to a report published July 31 in *JAMA Internal Medicine*. Although unable to determine whether these internet queries preceded suicide attempts, studies in the past have pointed to a potential connection of increased rates of suicide and internet search trends.

One of the major criticisms of the series was its depiction of suicide, especially to the vulnerable and impressionable young audience who accounted for a significant portion of the show's viewership. The protracted and graphic scene of a 17-year-old girl slashing her wrists in a bathtub was the focus of the penultimate episode. It was viewed by millions, including adolescents aged 15 to 19 years old, who are two to four times more likely to die by suicide as a result of social contagion.

As it is estimated that up to 13 percent of teen suicides are attributed to the pattern of contagion, the need for responsible media production and coverage of mental health issues is greater than ever. The rate of suicide-related deaths of 10- to 14-year-old girls tripled over the last 15 years, and young teenagers are more impressionable than ever. The Netflix storyline legitimizing the graphic suicide of a 17-year-old girl as a vindictive fantasy went beyond being sensational or provocative—it was irresponsible.

The second season of "13 Reasons Why" has completed filming, and there is an expected release date later this year. With the implications of the first season clearly identified, we can only hope Netflix and the producers of the second season use their platform to make a positive impact on those suffering from mental health conditions. Suicide contagion is real, and with the rate of suicide in the United States at a 30-year high, we should protect a vulnerable and impressionable group of young people through responsible media production and use this sequel to continue to engage in healthy discussion of mental health issues. **PN**

References for this article are posted at https://psychnews.psychiatryonline.org/doi/full/10.1176/appi.pn.2018.3b13

NIAAA Creates Online Tool To Help Patients Obtain Treatment for AUD

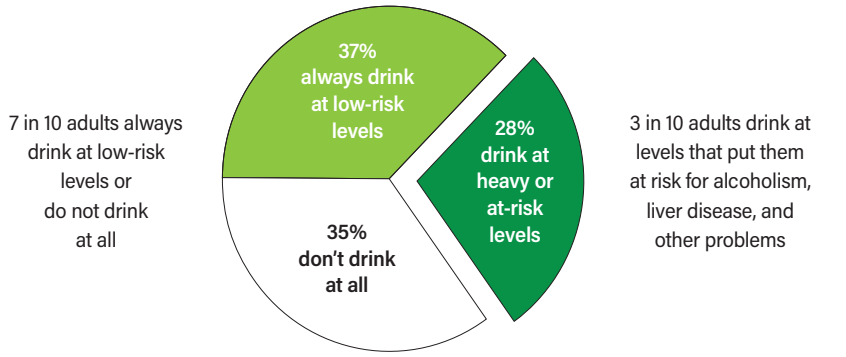
A new tool from the NIAAA provides comprehensive information about treatment options for alcohol use disorder.

BY REBECCA GREENBERG

More than 15 million adults in the United States struggle with alcohol use disorder (AUD), but only 1 in 12 receives treatment, according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA). Part of this problem has to do with limited information about treatment options and how to go about getting treatment, said Lori Ducharme, Ph.D., a sociologist and program director at NIAAA's Division of Treatment and Recovery Research.

The website links to directories of addiction specialists, including a list of board-certified addiction psychiatrists that is maintained by the American Board of Psychiatry and Neurology. It also outlines key components to look for when selecting a treatment program.

"There are plenty of directories out there where you plug in your ZIP code and get a list of providers, and you can also search Google, but there is really nothing that gives people a comprehensive strategy on what to do, how to assess the information they get, and make a choice based on what is good for them. This is especially true for people with co-occurring mental health needs, which is why we wanted to give people a variety of specialists who can assist them with AUD in their area."



Not knowing where to turn, some individuals call the NIAAA directly, often seeking help for a family member or friend. Inspired by these callers, Ducharme and a team at NIAAA developed the NIAAA Alcohol Treatment Navigator, an online tool that helps users gauge their drinking behaviors, provides information about treatment, and guides users through a step-by-step process to identify where they can receive high-quality, individualized treatment.

"We see this as a tool to empower consumers so that they get better information about addiction treatment and are more likely to find a particular option that will work for them," Ducharme said. "Many people think treatment is limited to Alcoholics Anonymous or a long-term residential rehab program. They have no idea about the variety of outpatient options or the variety of specialists who can deliver outpatient treatment; all of that is explained in the 'what to know about treatment' section."

Ducharme said the navigator can also be used by clinicians. "They can use this tool to build a rolodex of local resources or to keep on hand in case they need to make a referral. They can also show patients the navigator to help guide them toward an evidence-based choice."

Many people find it difficult to discuss their drinking behaviors when seeking care for the first time, Ducharme noted. Sample scripts are posted to help people ask questions when speaking with health care providers.

"Just like you would ask your primary care doctor or your surgeon questions about treatments in a routine health care environment, we want people to feel comfortable picking up the phone and asking questions about alcohol treatment." **PN**

The website of the NIAAA Alcohol Treatment Navigator is https://alcoholtreatment.niaaa.nih.gov.

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Climate Change Said to Be 'Ultimate Social Determinant of Health'

Activists say psychiatrists will be treating patients for the acute effects of extreme weather events and will also have a role in addressing helplessness and passivity in the face of climate change. **BY MARK MORAN**

A growing contingent of psychiatrist activists calling themselves the Climate Psychiatry Alliance (CPA) is seeking to draw attention to what they call a slow-motion catastrophe in the making.

"Psychiatrists and other mental health professionals have an ethical obligation to understand and treat the clinical and public health consequences of the slow-moving disaster that is climate change," said David Pollack, M.D., a professor of public policy at Oregon Health Science University and a founding member of CPA. "Climate is the ultimate social determinant of health, profoundly, and sometimes acutely, affecting all of those variables traditionally thought of as the social and environmental influences on health and illness. We believe that advocating for rational public policies at the local and national levels to address the risks to health and life posed by climate change is going to be a part of our ongoing practice as psychiatrists indefinitely.

"We must help to create and sustain our 'good enough' Mother Earth," Pollack said.

Two events—a symposium and a workshop—will be presented by the Alliance at the Annual Meeting in New York:

- **"When the Disaster Is Slow Moving: Implications for Psychiatry of Climate Change":** This symposium will explore a tripartite relationship of psychiatry with climate: the clinical challenge of helping patients engage with the reality of climate change, the professional responsibility to transform mental health care systems into environmental sustainability, and the contribution mental health professionals can make to psychosocial adaptation and resilience. Innovative programs aiming to train communities and individuals in "transformational resilience" will be reviewed and discussed.
Sunday, May 6, 8 a.m.-11 a.m.

- **"Mental Health Professionals in the Era of Deteriorating Climate Conditions: Do We Have an Ethical Duty to Warn and Protect?":** This workshop, divided into three sections, will address the question in the session title as well as other questions: the first section will provide an overview of the accelerating mental health toll from the impacts of climate change. The second section will look at ethical and legal precedents that serve to guide psychiatrists' actions, assisting them in evaluating the appropriateness and necessity of speaking up on this issue. The third section will review "good news," a broadening focus on what psychiatrists can do to reduce future harm to our climate and build resilience both in individuals and in communities. Existing successful efforts in these realms such as the "greening" of practices and "transformational resilience" training will be presented as models. This will be followed by a brainstorming breakout session organized by interest to discuss and to propose new "best practices."
Monday, May 7, 8 a.m.-9:30 a.m.

Both events will be chaired by Lise Van Susteren, M.D., a forensic psychiatrist in Washington, D.C. Speakers include, in addition to Pollack, Steven Moffic, M.D., retired tenured professor of psychiatry and behavioral health and family and community medicine at the Medical College of Wisconsin; Janet Lewis, M.D., a clinical assistant professor of psychiatry at the University of Rochester; Elizabeth Haase, M.D., an associate professor of psychiatry at the University of Nevada School of Medicine; Carissa Caban-Aleman, M.D., medical director of behavioral health for student health services at the Herbert Wertheim College of Medicine, Florida International University; and Sara Gorman, Ph.D., M.P.H., a mental health and public health consultant and writer in New York City.

Core members of CPA include members of a similar committee of the Group for the Advancement of Psychiatry that is focused on climate change (see https://ourgap.org/committees/climate). It also includes a growing number of others who have been concerned about the issue for years or are becoming so now.

Pollack emphasized that psychiatrists can help address the helplessness and passivity that may keep people from acting and help support what he and others call climate-change denial. "We can and should be the professionals who can say to people that we are falling prey to a collective, maladaptive psychological defense mechanism of denial that we use to protect ourselves from anxiety and distress, but which ultimately does not serve our best interests," he said.

At the March 2017 meeting of the APA Board of Trustees, the Board approved a position statement on mental health and climate change. It reads: APA "recognizes that climate change poses a threat to public health, including mental health. Those with mental health disorders are disproportionately impacted by the consequences of climate change. APA recognizes and commits to support and collaborate with patients, communities, and other health care organizations engaged in efforts to mitigate the adverse health and mental health effects of climate change."

Prior to that, the American Association of Community Psychiatrists approved a similar statement that says, "Persons with mental illnesses and behavioral health challenges are disproportionately impacted by the consequences of climate change. Psychiatrists are uniquely positioned to help reduce barriers to addressing climate change, such as denial, hopelessness, and behavioral passivity, and to enhance efforts to communicate the public health and mental health risks of climate change through mechanisms that result in sustained behavioral change."

Also at the Annual Meeting, the APA Committee on Psychiatric Dimensions of Disaster will present the course "Disaster Psychiatry Review and Updates: Terrorist Mass Killing, Climate Change, and Ebola" on Saturday, May 5, from 1 p.m. to 5 p.m. **PN**

Information and resources about climate change are posted on APA's website at https://www.psychiatry.org/patients-families/climate-change-and-mental-health-connections.

See You in New York!

APA's Annual Meeting will be held **May 5 to 9** in New York City. For registration information, see the box at the bottom of page 3.

For an up-to-date schedule of the meeting's scientific program, download the APA Meetings App to your smartphone or tablet at psychiatry.org/app. For more information about the app, see the ad on the facing page.

Mythbusters: C-L Psychiatrists Separate Fact From Fiction

Consultation-liaison psychiatrists seem to encounter more than their share of myths due to the collaborative nature of their work with other fields of medicine. **BY ROBERT BOLAND, M.D.**

In this "post-factual" age of "fake news," we have become all too familiar with the power of half-truths, opinions, and assertions to take on the appearance of facts. This is not new—medicine has a long history of taking anecdotes and repeating them so frequently that they become accepted dogma. One recent example was the unusual warning added to a 1980s letter to the editor in the *New England Journal of Medicine* that purported to show that the risk of iatrogenic addictions from opioid prescriptions is rare, warning that this modest letter has been "heavily and uncritically cited" (see http://www.nejm.org/doi/10.1056/NEJM198001103020221).

Robert Boland, M.D., is president of the Academy of Psychosomatic Medicine.

Most doctors have their pet peeves about something they were told or read in a textbook that might not have stood up to scrutiny. Although this pervades medicine, we consultation-liaison psychiatrists feel particularly drawn to this subject, working as we do between psychiatry and other fields of medicine, and in this interface half-truths and frank misunderstandings seem particularly common.

With this in mind, when the Academy of Psychosomatic Medicine—soon to be the Academy of Consultation-Liaison Psychiatry—was invited by our APA president to present a presidential symposium, I chose to ask representative members to present a favorite example of a myth that they have encountered. I purposely asked psychiatrists at different stages of their careers, so we have both the wisdom of prominent psychiatrists in our field as well as the new experiences of mid-career and younger consultation-liaison psychiatrists.

For example, among leaders of our field, Peter Shapiro, M.D., at Columbia University has devoted much of his career to understanding the interface between cardiology and psychiatry. He will critically review the "accepted" idea that QTc intervals are the best method for predicting whether psychotropics will cause arrhythmias.

Similarly, Sejal Shah, M.D., and in this regard David Gitlin, M.D., will examine whether the belief that psychiatrists are the best suited for performing suicide evaluations is itself a myth.

Alcohol use and abuse seem particularly prone to fake news, and Sparsha Reddy, M.D., will examine the relationship between Wernicke's encephalopathy and alcohol use, whereas I will take on the age-old question of whether alcohol really kills brain cells.

These are just a few examples of the myths, legends, and "old wives' tales" that can occur in a field that is both a science and an art. We have no doubt that many members of the audience will have their own examples of things that "just ain't so," and we hope to save time to share those as well. **PN**

"Mythbusters: Consultation-Liaison Doctors Separate Medical Fact From Fiction" will be held on Wednesday, May 9, from 8 a.m. to 11 a.m. For location, download the APA Meetings App (see ad below) or check the program guide distributed on site at the meeting.

Discount Pass Available for Restaurants, Popular Sites

Here's a chance to enjoy the Big Apple without robbing the piggybank. Registrants at APA's Annual Meeting are invited to use New York City's Delegate Discount Pass, which the city proudly calls the "ultimate guide to exclusive savings throughout the city" from participating restaurants, attractions, and tour companies. To redeem an offer, just show a printed or mobile version of the pass or use a promo code.

The pass and more information can be accessed at http://apapsy.ch/Discount_Pass.

Psychologist Sherein Abdeen, M.A., B.S. (right), conducts parenting training at one of the schools in Jerusalem where she has developed programs to identify and care for children with behavioral problems.

WHO Backs Palestinian Psychologist's Efforts To Integrate MH Care Into Jerusalem Schools

Training teachers and school principals to recognize symptoms of mental illness opens a door to better classroom behavior.

BY AARON LEVIN

The epiphany for Sherein Abdeen, M.A., B.S., came in her third year teaching chemistry and science to elementary and middle school youth in Jerusalem.

"There was something more important for me to do than teach chemistry," Abdeen recalled in a recent interview in East Jerusalem. Her fellow educators seemed to have no good ways aside from punishment for dealing with students with serious behavioral problems. So Abdeen left teaching to seek solutions to those problems.

She began by attending lectures by Palestinian psychiatrist Samah Jabr, M.D., at East Jerusalem's Al Quds University. She also developed a long-distance mentoring relationship with Elizabeth Berger, M.D., a clinical associate professor of psychiatry at George Washington University, where Jabr is a clinical associate professor and Abdeen is now a clinical instructor. (See "Psychiatry Residency Builds Global Reach by Using Local, Overseas Settings" at https://psychnews.psychiatryonline.org/doi/full/10.1176/appi.pn.2014.9a21.) To gain practical experience, she worked in Jabr's clinic from 2009 through 2014.

Next, Abdeen developed a three-pronged project to help out her former fellow teachers and their students with the assistance of the Palestinian Medical Education Initiative, run by Berger and Michael Morse, M.D., a former resident at George Washington and now at Medstar Georgetown University Hospital in Washington, D.C. Berger supervised the project by Skype—grounding the program in a medical model rather than the more common psychosocial programs that are often implemented in the West Bank.

Starting in one school, Abdeen trained teachers to recognize the problems and symptoms of mental illnesses. She did not stop there, however. She organized a committee at the school consisting of two teachers, the principal, a counselor, and herself. The committee met once a week, discussing two to five cases each session. The group talked over each case, and Abdeen offered suggestions about how the teachers could approach the students and their parents to improve the children's behavior. Abdeen provided her professional expertise to the committee, but she did not directly treat students. Difficult cases were referred to outside mental health professionals.

At the weekly meetings, each child was given a score, and the committee members chose actions designed to move that score down to zero over a period of weeks or months.

In 2015, she expanded the program to three private schools in the Jerusalem neighborhood of Beit Hanina with the support of GIZ, the nonprofit German Society for International Cooperation. The program next expanded in 2016 to a school in Bethlehem with funding by an Italian aid group. Then last year, the World Health Organization backed expansion of the program to five more Jerusalem schools run by the Palestinian Ministry of Education, when 60 teachers and principals began training on childhood mental disorders and building skills to deal with children affected by them.

Photos courtesy of Sherein Abdeen, M.A., B.S.

Sherein Abdeen, M.A., B.S., confers with a concerned mother about some of the parenting challenges she is facing.

She insists that principals must always be members of committees, both to be trained and to see the advantages of mental health approaches over disciplinary ones, as well as to ensure that the school is committed to the program.

Abdeen would like to expand teachers' training opportunities and add an incentive to participate by taking them out of the country to Europe or the United States to demonstrate other methods of behavioral control in the classroom. A trip to New York last year to deliver a paper at the American Academy of Child and Adolescent Psychiatry meeting offered her an insight into how families outside a conflict zone dealt positively with children and spouses.

Implementation has brought its challenges. For one thing, there are only so many schools that she can cover alone. Morse said he wants to "Xerox Sherein," but a more realistic option is finding the funds to train other professionals. In addition, teachers and principals already face heavy time burdens and complain that the ministry puts too many other projects on their agendas. So next year, Abdeen will expand only to schools that aren't so burdened. She finds that educators, too, have their blind spots, such as expressing skepticism about medications like stimulants or antidepressants. She asks them: "Is it better for the child to have problems or to improve by taking medication?"

Abdeen also works to help parents understand their children's behavior and engage in their care.

"Stigma is a big issue," she said. Educating parents who may know little about mental health takes up much of her energy. Some parents are only critical of their children and offer no positive communication, but she knows that solutions to children's psychiatric problems often require involving the whole family, she said. So she works to get parents to come into the school, meet with the committee, and then work together.

Her goal is to get everyone—teachers, principals, mothers, fathers—to understand the children and not blame them or give them negative feedback for their actions.

"I tell them not to look at the bad behavior but to look for what's behind the behavior," she said. "Why does the child have the need to act out and disturb the class? I help them to look for the good inside their child." **PN**

Researchers Sum Up Current Knowledge Of Bipolar Disorder, Call for More Study

Researchers confirm the progressive nature of bipolar disorder and find early intervention may prevent the more disabling aspects of the disorder. **BY LINDA M. RICHMOND**

The progressive nature of bipolar disorder, with milder phases occurring prior to the classic onset of the disease, makes it an ideal candidate for early intervention strategies, according to a research review published January 24 in *AJP in Advance*.

Bipolar disorder affects 1 percent of the world's population, and it is more prevalent in this country than in Canada and Europe, according to Eduard Vieta, M.D., Ph.D., of the Barcelona Bipolar Disorders Program at the University of Barcelona and colleagues. Mood symptoms emerge for up to 70 percent of individuals with the disorder before age 21.

For the review, the researchers examined more than 50 original studies evaluating prodromal symptoms and risk factors; biomarkers; screening tools; and early intervention treatment options, including psychotherapeutic and pharmacological interventions, for bipolar disorder.

Early identification may prevent or at least delay the onset of the disorder, co-author Boris Birmaher, M.D., the endowed chair in Early Onset Bipolar Disease and a professor of psychiatry at the University of Pittsburgh School of Medicine, told *Psychiatric News*. "This can give the young person a chance to develop normally, to finish school or maybe go to college, to foster interpersonal relationships, and to develop good coping skills before the full illness strikes."

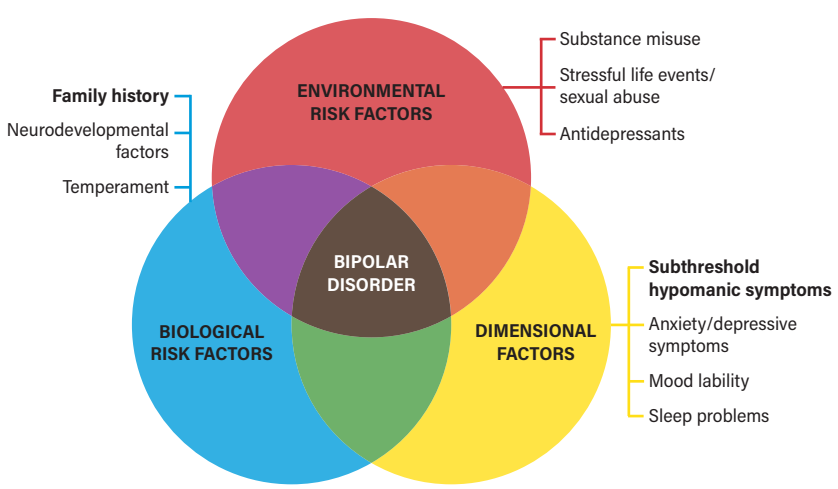
Failing to recognize and treat patients in the earliest stages of the disorder carries a high cost, such as increased risk for dropping out of school, using drugs, or death by suicide, Birmaher added. "The longer you wait, the more resistant to treatment this illness is."

A move toward early intervention will require changes in health insurance and government policies that dictate access to care, as well as better education of mental health professionals, general practitioners, and even the general public, co-author Estela Salagre, M.D., the scientific director assistant in the research consortium CIBERSAM (Centro de Investigación en Red de Salud Mental) and researcher in the Bipolar Disorders Unit of the Clinical Institute of Neuroscience in Barcelona,

see **Bipolar** *on page 20*

The Converging Risk Factors of Bipolar Disorder

The interaction between risk factors and prodromal symptoms may lead to bipolar disorder. Family history of the disorder is the strongest risk factor, while sexual abuse is related to a worse illness course. Subthreshold hypomanic symptoms are the strongest predictive factor.



Source: Eduard Vieta, M.D., Ph.D., et al., *AJP in Advance*, January 24, 2018

‘Cautious Optimism’ Marks Outlook for Ketamine, Mood Disorders

An APA work group consensus statement provides an overview and expert clinical opinion on critical issues and considerations associated with the off-label use of ketamine treatment for mood disorders. **BY MARK MORAN**

Ketamine for mood disorders—risks, benefits, pros, and cons—may be among the biggest stories in psychopharmacology today.

Dozens of articles on use of ketamine for major depression have appeared in *Psychiatric News* in the last two years—including a December 2017 report in the *American Journal of Psychiatry* (*AJP*) suggesting a single dose of the agent may be effective in treating suicidality—and hundreds of others have appeared in the medical and lay press.

Meanwhile, there has been a proliferation of ketamine infusion centers offering off-label treatment for mood disorders. The Ketamine Advocacy Network lists 25 centers around the country, but an online search suggests this number may more likely be in the hundreds. The network acknowledges that providers of ketamine infusion may not be included on their list for a variety of reasons: extraordinarily high fees; practices or protocols not supported by multiple peer-reviewed studies; or marketing strategies that include claims unsupported by evidence or serious factual errors about ketamine’s pharmacology or its mechanism of action.

Gerard Sanacora, M.D., Ph.D., lead author on a consensus statement produced by an APA work group last year, says the promise of ketamine—and its potential risks—make for a unique situation.

“Here is a drug that may have some real benefit for patients, especially those who have not experienced satisfactory relief from standard treatments that are available,” he told *Psychiatric News*. “Yet it’s a drug that carries a little bit more baggage than is typical.”

Because it was first approved as an anesthetic in 1970, ketamine cannot be patented, so pharmaceutical companies have no incentive to undertake extensive clinical trials for it to be approved for a new indication. Moreover, ketamine has been used recreationally as a “party” drug and carries with it the risk of abuse.

“With all this in mind, it was agreed that APA should develop some expert consensus with the understanding that there isn’t enough information to generate formal treatment guidelines,” Sanacora said.

Robert A. Lisak

Gerard Sanacora, M.D., says a registry of clinical trials on ketamine for mood disorders is necessary to help develop a body of knowledge about risks and benefits of long- and short-term use of the drug for mood disorders.

“We took the approach that since we can’t offer firm treatment guidelines, we could at least highlight the potential risks and benefits and make people aware of both the potential for this drug and the concerns that surround it without overstepping the boundaries of what’s known.”

The consensus statement was the product of a work group of the APA Council on Research Task Force on Novel Biomarkers and Treatments. Work group members, in addition to Sanacora, included past APA Presidents Alan F. Schatzberg, M.D., and Paul Summergrad, M.D. Other authors on the consensus statement were Mark A. Frye, M.D., William McDonald, M.D., Sanjay J. Mathew, M.D., Mason Turner, M.D., and Charles Nemeroff, M.D.

A paucity of evidence regarding the effectiveness of ketamine for mood disorders informs the entire consensus statement. “There still is relatively little high-quality peer reviewed published information beyond very short treatments,” Sanacora said.

The consensus statement cites an October 2015 paper in *AJP* that found seven published placebo-controlled, double-blind, randomized clinical studies on ketamine hydrochloride infusion as a monotherapy for the treatment of depression, comprising 147 treated patients. Five studies have been done looking at ketamine as an adjunct to electroconvulsive therapy, according to the *AJP* report. At least one study has compared ketamine with placebo for obsessive-compulsive disorder.

The promise of ketamine for mood disorders is real. “There is evidence that in a significant proportion of patients who have not received satisfactory benefit from standard antidepressant treatment, ketamine can offer a very rapid antidepressant effect,” Sanacora said. “We are talking about within four hours.”

Perhaps the most exciting possible use for ketamine is in suicidal patients. A meta-analysis published in *AJP* last October found that a single infusion of ketamine appears to significantly reduce suicidal thoughts in depressed patients in as little as one day, with benefits lasting for up to one week. “If this potential is borne out, we don’t want to prevent people from getting that treatment,” he said.

But the risks are just as real. “There are changes in cardiovascular function including increases in heart rate and blood pressure consistent with doing a moderate level of exercise. For most people this isn’t going to be a real problem, but you need to screen patients who cannot maintain this level of cardiovascular challenge,” he said.

There are also psychological effects, including changes in cognition and perception that can last for a couple of hours after dosing. And the longer-term risk is for abuse of a drug that has a history of being used recreationally and is still prominently a drug of abuse in some parts of the world. “The question about long-term use of ketamine is whether we are putting patients at risk of addiction,” Sanacora said.

He noted that there have also been reports in the media of clinics offering take-home kits of self-administered ketamine—a practice Sanacora said

see **Ketamine** *on page 21*

FROM THE EXPERTS

How to Reduce Risk of Suicide by Firearms

BY LIZA GOLD, M.D.

Suicide is the 10th-leading cause of death overall in the United States and the second leading cause of death for teenagers and young adults aged 15 to 24. In 2016, almost 45,000 people died by suicide—51 percent by firearms, the most common means, according to the Centers for Disease Control and Prevention. Psychiatric and substance use disorders are the strongest individual risk factors for suicide. As much as 90 percent of individuals who die by suicide have a diagnosable psychiatric disorder at the time of death, most commonly depression or substance abuse.

Only two interventions have been empirically demonstrated to be effective in decreasing suicide mortality: mental health treatment and restriction of lethal means. Suicide risk assessment (SRA) is the gateway to effective treatment. These assessments decrease the risk of suicide by identifying modifiable or treatable acute, high-risk suicide factors and available protective factors that guide patient treatment.

Psychiatrists are taught that a systematic SRA requires exploration of suicidal ideation, whether a plan has been formulated, and if so, whether the patient has the means to carry out the plan. We then work to restrict a patient’s access to lethal means. For example, if a patient has considered suicide by overdose, we may agree to limit the amount of medication prescribed at any one time. Similarly, if a patient identifies firearms as a method of choice, a firearm safety plan might include confirming that guns and ammunition have been separated, removed from the home, and safely secured in a location unknown to the patient.

Liza Gold, M.D., is a clinical professor of psychiatry at Georgetown University School of Medicine and co-editor of *Gun Violence and Mental Illness* from American Psychiatric Association Publishing. APA members may purchase the book at a discount at https://www.appi.org/Course/Book/Subscription/JournalSubscription/id-3385/Gun_Violence_and_Mental_Illness.

Regardless of whether a patient identifies firearms as a considered means of suicide, psychiatrists should always ask patients about their access to firearms because of the frequency of firearm suicide. The likelihood that a specific method of suicide will lead to death is related to its accessibility. The presence of firearms in the home is associated with a significantly

continued on facing page

What Pharmacogenetic Testing Can, Can't Tell You About Your Patient

There are FDA recommendations regarding some genetic variants and drug choice, but current technology mainly tests an individual's metabolizer status, indicating whether he or she may metabolize a drug quickly or slowly. ***BY MARK MORAN***

Key Points

A large and growing number of commercial entities are offering pharmacogenetic testing, using simple cheek swabs, and interpretation of tests to aid in prediction of response to medication. Patients may purchase these on their own and bring test results to clinicians.

- Most commercial entities test for variations in cytochrome P450 enzymes affecting speed of drug metabolization.
- The FDA has recommended that citalopram not be prescribed at doses higher than 20 mg/d without an EKG in patients who carry the CYP2C19 "poor metabolizer" phenotype.
- The FDA has recommended testing patients of Asian descent for the HLA-B1502 mutation before prescribing carbamazepine.
- A work group of the APA Council on Research is studying the subject of pharmacogenetics in psychiatry.
- Clinicians should be prepared to discuss pharmacogenetics with their patients and be able to understand, explain, and respond to genetic information.

Bottom Line: Pharmacogenetics is the future, promising to aid in predicting response to medication, improving outcomes, and saving money. Public expectations are likely to exceed the existing science. More and better research is necessary before broad pharmacogenetics testing may be regarded as clinically useful.

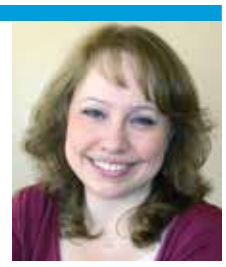
A 15-year-old girl presents with depression and obsessive-compulsive disorder. You suggest fluoxetine to treat both conditions, given its extensive testing in young people with depression; however, her mom tells you her daughter can't take fluoxetine "because of her genes." She hands you the printout of a commercial genetic test indicating that fluoxetine should only be used "with increased caution and more frequent monitoring."

If you haven't encountered a scenario like this yet, you may soon. Pharmacogenetics—the use of genetic testing to help predict efficacy and/or side effects of medications—is an advancing field that has garnered much publicity, assisted in part by former President Barack Obama's Precision Medicine Initiative. Online commercial entities offering pharmacogenetic testing claim improved health outcomes, reduced risk of side effects, and financial savings from avoiding trials of ineffective medications.

Some psychiatrists with expertise in genetics and pharmacology have a counter message for clinicians and the public: *Not so fast*.

"I believe in the promise of pharmacogenetics, but I also believe we are a long way off from being able to use it in a way that will really aid clinicians and benefit patients," said Erika L. Nurmi, M.D., Ph.D., during a presentation at the American Academy of Child and Adolescent Psychiatry's Pediatric Psychopharmacology Update last month in New York. "There is an evidence base for drug response based on genetic testing, but it is far behind public enthusiasm and the marketing claims of commercial companies."

> "I believe in the promise of pharmacogenetics, but I also believe we are a long way off from being able to use it in a way that will really aid clinicians and benefit patients."
>
> —Erika L. Nurmi, M.D., Ph.D.



Nurmi is the associate medical director of the Child OCD, Anxiety, and Tic Disorders Program in the UCLA Department of Psychiatry and deputy chief of mental health for the Greater Los Angeles VA. She studies psychiatric genetics and pharmacogenetics in her laboratory at the Semel Institute for Neuroscience and Human Behavior at UCLA.

"People are clearly ready for pharmacogenetics," she said, but the technology has not advanced enough for everyday clinical use. Important questions remain, including the following: Does the test accurately detect the genetic variant it claims in real-world settings? Does the test usefully change clinical management and improve health outcomes?

Nurmi said the association of a genetic variant with a specific phenotype affecting drug response is often oversimplified, ignoring the many factors that influence genetic expression. At the clinical level there are a range of factors—age, ethnicity, concomitant medication use, and history of substance use—that can affect drug response.

She said there has been a dearth of independent, randomized, controlled trials studying the value of prescribing informed by pharmacogenetic testing. Studies that exist tend to be supported and analyzed almost entirely by commercial entities, using proprietary algorithms for clinical decision-making and small sample sizes.

Existing guidelines on pharmacogenetic testing, such as those of the international Clinical Pharmacogenetics Implementation Consortium , are few and rely on theoretical interpretations of the limited data. A work group of the APA Council on Research is studying the use of pharmacogenetic testing in psychiatry.

see **Pharmacogenetics** *on page 19*

continued from facing page

increased risk of suicide. The association between higher rates of overall suicide and firearm suicide and higher rates of gun ownership is independent of psychopathology.

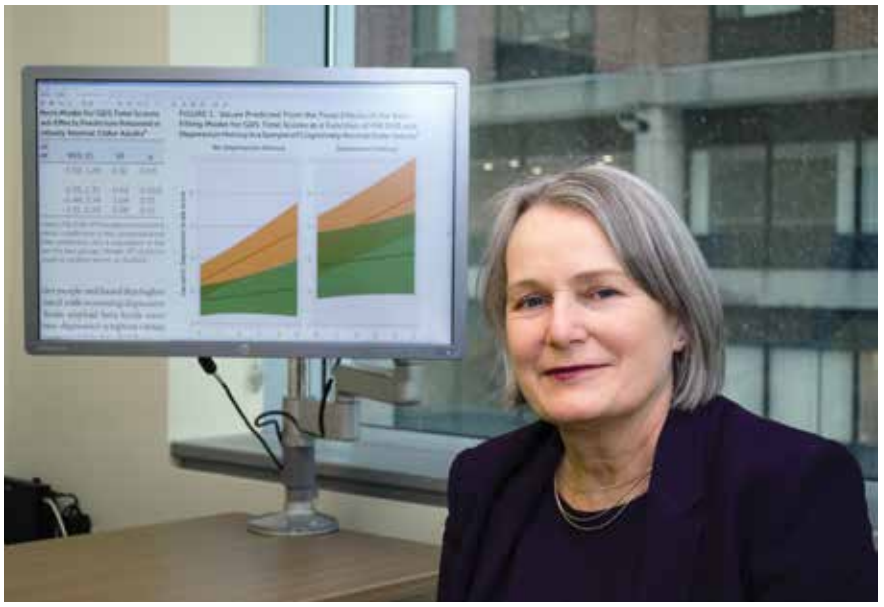
If a suicidal patient has access to firearms, even if that patient is not the owner and regardless of the presence or absence of other risk factors, steps should be taken to separate the individual from the firearms. Psychiatrists can work with high-risk patients to remove firearms from a patient's immediate environment, even if the removal is temporary. Outcomes data showing that reduced access to firearms is linked to lowered suicide rates are robust.

The following steps should be considered when patients have access to firearms:

- Ask about access to guns at home or elsewhere. Patients who have a gun at home often have more than one gun.
- Consider invoking emergency exception to confidentiality if a patient at high risk for suicide withholds consent to contact significant others.
- Involve significant others and the patient in designing a firearm safety plan, including discussions of clinical criteria for return of firearms.
- Educate patients that the risks of a fatal suicide increase when firearms are accessible and drugs or alcohol are used and that the safest option is removal of guns from the home.
- Designate a responsible individual to follow through with the gun safety plan.
- Confirm via callback from the designated person that the gun safety plan has been implemented.
- Document that the gun removal plan was implemented and that a callback was received from the designated individual.
- Repeat suicide risk assessments, particularly before a treatment decision that may restore access to firearms.

Despite the common belief that individuals intent on dying by suicide who lack access to their preferred means will find another means to end their lives, most studies have demonstrated that restriction of one method does not inevitably lead to substitution of another method. In addition, when method substitution occurs, particularly if the preferred method is firearms, chances of surviving the suicide attempt increase due to the fact that other methods are less lethal. **PN**

References for this article are posted at https://psychnews.psychiatryonline.org/doi/full/10.1176/appi.pn.2018.3b12.



Steven M. Smith

Nancy J. Donovan, M.D., says long-term follow-up of study participants with worsening anxiety is necessary to determine if their symptoms progress to clinical depression and/or mild clinical impairment and dementia.

Worsening Anxiety In Older Adults May Precede Alzheimer's

Identifying factors associated with a higher risk of developing Alzheimer's may be a key to stopping its progression.

BY REBECCA GREENBERG

Subtle changes in the brain occur years before an individual experiences the memory loss and severe cognitive impairment associated with Alzheimer's disease (AD). If clinicians could detect these changes early on, interventions might be possible, according to Nancy J. Donovan, M.D., a geriatric psychiatrist and professor at Brigham and Women's Hospital.

Donovan and colleagues are the authors of a study published January 12 in *AJP in Advance* showing that cognitively normal older adults with worsening anxiety had higher levels of amyloid beta, a brain protein implicated in Alzheimer's.

The study builds on observational research showing that depression and other neuropsychiatric symptoms often emerge during the "preclinical" phase of Alzheimer's—a period marked by the accumulation of deposits of fibrillar amyloid and pathological tau in a patient's brain.

"Certain older adults with elevated amyloid have normal cognition but may experience detectable changes in emotional regulation and anxiety," Donovan told *Psychiatric News*.

"Recognizing these characteristic changes may help us identify high-risk older adults and target them with AD-directed treatments or psychiatric treatments that could reduce risk of progression to cognitive impairment. For example, there are suggestions in the literature that we may be able to attenuate progression very early in AD using antidepression or antianxiety treatment."

A total of 270 participants aged 62 to 90 underwent baseline positron emission tomography (PET) scans to measure cortical amyloid beta along with annual depression assessments based on the 30-item Geriatric Depression Scale (GDS). The team calculated total GDS scores as well as scores for three GDS item clusters: apathy-anhedonia, dysphoria, and anxiety concentration. These scores were examined over one to five years (mean: 3.8 years).

"Rather than just looking at depression as a total score, we looked at specific symptoms such as anxiety," Donovan said in a press release. "When compared with other symptoms of depression such as sadness or loss of interest, anxiety symptoms increased over time in those with higher amyloid beta levels in the brain."

The data were acquired from the Harvard Aging Brain Study, a longitudinal dataset designed to differentiate changes associated with "normal" aging from symptoms of preclinical Alzheimer's dementia.

"Cross-sectional studies have generally not been able to demonstrate a significant association of high amyloid in the brain and depression, but we have been collecting data for several years, so we were able to see if high amyloid was related to increasing depressive

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Varenicline May Lower Heavy Drinking, Smoking In Men With AUD

The findings add to the converging evidence of the need for more specific and targeted treatments for women and men. **BY JOANN BLAKE**

Varenicline, an FDA-approved smoking-cessation medication (Chantix), may be effective in treating both alcohol use disorder (AUD) and smoking in men, according to a study published in the February issue of *JAMA Psychiatry*.

"Men appeared to derive benefit

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symptoms," Donovan told *Psychiatric News*. "Longitudinal analyses have greater power to address this question."

Follow-up is necessary to determine whether escalating depressive symptoms "give rise to clinical depression and/or mild cognitive impairment and dementia associated with Alzheimer's disease over an extended period," she said.

Donovan and her colleagues will monitor cognitive changes in the study participants for the next five years.

"Anxiety may be a manifestation of the disease process, but it also may also be a disease-potentiating factor, so if we could treat it, we may be able to attenuate progression or reduce risk of progression," she concluded. **PN**

"Longitudinal Association of Amyloid Beta and Anxious-Depressive Symptoms in Cognitively Normal Adults" is posted athttps://ajp.psychiatryonline.org/doi/full/10.1176/appi.ajp.2017.17040442.

from varenicline, compared with placebo, on measures of heavy drinking, whereas women did better taking placebo," wrote lead author Stephanie S. O'Malley, Ph.D., director of the Division of Substance Abuse Research in Psychiatry at Yale School of Medicine. "In the overall sample, more patients taking varenicline quit smoking (13 percent versus none on placebo) even though they were not seeking smoking cessation counseling," O'Malley told *Psychiatric News* by email.

Researchers conducted the phase 2, randomized, double-blind, placebo-controlled trial at two outpatient clinics (New York City and New Haven, Conn.) from September 19, 2012, to August 31, 2015. The researchers recruited men and women aged 18 to 70 who were seeking treatment for AUD. Individuals who met the criteria for alcohol dependence (according to *DSM-IV-TR*), reported heavy drinking (≥5 standard alcoholic drinks for men and ≥4 drinks for women) two or more times a week and cigarette smoking two or more times a week were included in the trial.

Patients who had been diagnosed with a serious psychiatric illness, experienced suicidal ideation, and had taken psychotropic medications other than a stable dose of selective serotonin reuptake inhibitors were excluded from the trial, said O'Malley. Previous clinical trials involving varenicline mostly have excluded participants with mental illness because of possible neuropsychiatric side effects that prompted the Food and Drug Administration in 2008 to issue a black-box warning. This warning was removed from the Chantix label in December 2016 after an analysis of more than 8,000 smokers with and without psychiatric illnesses found varenicline and bupropion did not significantly increase the risk of adverse neuropsychiatric events (*Psychiatric News*, January 6, 2017).

O'Malley and colleagues randomly assigned 131 participants to receive either 2 mg of varenicline or placebo daily for 16 weeks. Medication was titrated in the following standard doses: 0.5 mg once daily for three days, 0.5 mg twice daily for four days, and 1 mg twice daily for the remainder of the 16-week treatment. Daily medication adherence was monitored through a combination of pill counts returned from blister packs and self-reported compliance.

Stephanie S. O'Malley, Ph.D., notes that women subjects were less likely to comply with the study regimen for varenicline than men.

Over the course of the trial, participants attended 12 medical management sessions during which they met with a medical professional to discuss the tolerability of the assigned medication, medication adherence, and the importance of drinking goals as well as developing and implementing strategies for changing drinking behaviors. During these sessions, the participants were also asked about their drinking and smoking behavior, adverse effects of the medication, changes in mood, and more.

The varenicline (n=64) and placebo (n=67) treatment groups were similar in the median percentage of pills taken out of the total possible pills over the 16-week treatment period (85 percent versus 81 percent); however, women receiving varenicline took fewer pills (58 percent) than did men receiving the medication (91 percent). Women also were more likely than men to reduce or discontinue use of varenicline (37 percent versus 4 percent). In contrast, the percentage of placebo pills taken by men and women was similar (80 percent and 83 percent, respectively).

Women taking varenicline reported higher rates of abnormal dreams and nausea—common adverse effects of varenicline, which may have caused them to take fewer pills. "The medication management treatment protocol specially supported dose reductions in response to adverse events, because lower doses were found to be effective for smoking cessation in prior research, although this may not be the case for AUD," said O'Malley.

The mean change from baseline in the percentage of heavy drinking days in the overall sample by the end of the study was not different between the placebo and medication groups, but varenicline appeared to have different effects on drinking in men and women. Compared with placebo, varenicline resulted in a greater decrease in percentage of heavy drinking days in men and a smaller decrease in women. Even though the subjects were not seeking or provided smoking-cessation counseling, varenicline resulted in significantly higher rates of smoking abstinence compared with placebo (13 percent versus 0 percent) at the end of treatment.

"It may be premature to conclude that varenicline is not effective in reducing heavy drinking in women, given that severity of dependence, lower dose of varenicline, poorer adherence, and/or higher rate of abnormal dreaming or other adverse events affecting adherence, rather than sex per se, may underlie efficacy," wrote A. Eden Evans, M.D., Ph.D., and John F. Kelly, Ph.D., both of the Center for Addiction Medicine at Massachusetts General Hospital and Harvard Medical School, in an accompanying editorial in *JAMA Psychiatry*.

The question of whether it is more difficult for individuals to quit smoking and drinking at the same time, rather than addressing one problem at a time remains an important question for researchers, commented O'Malley.

"We know that individuals with AUD are more likely to die from smoking-related consequences than from alcohol-related problems, and individuals with AUD who quit smoking have a better long-term prognosis," O'Malley said. "We undertook this trial with the hope that varenicline … would be effective for helping patients seeking treatment for their drinking and that it might also reduce their smoking." **PN**

An abstract of "Effect of Varenicline Combined With Medical Management on Alcohol Use Disorder With Comorbid Cigarette Smoking: A Randomized Clinical Trial" is posted at https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2665215. The related editorial, "A Call to Action for Treatment of Comorbid Tobacco and Alcohol Dependence," is posted at https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2665214.

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Douglas Levere/University at Buffalo

Though Banyan's blood test may provide accurate results if used correctly, neurologist Brian Leddy, M.D., believes current clinical protocols will still be better tools to evaluate the risk of brain bleeding in most cases, given the three to four hours needed to obtain the results.

FDA Clears the Way for First Blood Test To Evaluate Head Injuries

The Brain Trauma Indicator cannot determine whether someone had a traumatic brain injury but can identify the presence of intracranial bleeding without using a CT scan. **BY NICK ZAGORSKI**

The Food and Drug Administration (FDA) in February approved the marketing of the first blood test to aid in the evaluation of traumatic brain injury (TBI). The test, called the Brain Trauma Indicator, measures the levels of the proteins ubiquitin C-terminal hydrolase L1 (UCH-L1) and glial fibrillary acidic protein (GFAP), which are both released from the brain into the blood in the immediate aftermath of a head injury. The plasma concentrations of these proteins can indicate whether a patient who has experienced a head injury has intracranial lesions—or brain bleeds.

Currently, the presence of intracranial lesions can be detected only by using computed tomography (CT) scans, which, while effective, are expensive and expose a patient to radiation. The Brain Trauma Indicator, marketed by Banyan Biomarkers, can predict the presence or absence of such lesions with nearly 99 percent accuracy if administered within the first 12 hours following an injury (test results take around 3 to 4 hours). This accuracy rating is based on a clinical study in which blood samples from 1,947 adults with suspected mild TBI (mTBI) were tested and the results were compared with CT scans.

MediaSource

Blood test developer Linda Papa, M.D., is exploring whether two proteins—UCH-L1 and GFAP—might be able to predict not only immediate intracranial lesions, but also potentially long-term risks in people with TBI.

"A blood-testing option for the evaluation of mTBI/concussion not only provides health care professionals with a new tool, but also sets the stage for a more modernized standard of care for testing of suspected cases," FDA Commissioner Scott Gottlieb, M.D., said in a press release. "In addition, availability of a blood test for mTBI/concussion will likely reduce the CT scans performed on patients with concussion each year, potentially saving our health care system the cost of often unnecessary neuroimaging tests."

While this TBI-related blood test is an important clinical breakthrough, some neurological experts have been sounding notes of caution about the limitations of the test.

"There are scenarios where this blood test can be very useful, but I believe these occurrences will be the exceptions rather than the norm," said John Leddy, M.D., director of the concussion management clinic at the University at Buffalo.

Leddy told *Psychiatric News* that there are multiple, validated clinical algorithms—such as the New Orleans Rules or the Canadian CT Head Rules—that doctors can use to assess a TBI patient and guide decision making about whether the patient needs a CT scan or not. According to Leddy, these algorithms usually provide a clear answer. "Even in a situation where the results are not definitive, can you afford to wait four hours for the blood test to come back with a patient who might have internal bleeding?" he asked.

Linda Papa, M.D., an emergency medicine physician at the Orlando Regional Medical Center who has led many of the research studies with UCH-L1 and GFAP, acknowledged that the current test does have its limitations.

"This blood test won't be efficient in emergency settings until we can develop a point-of-care version that provides results within an hour," Papa told *Psychiatric News*. "However, it is worthwhile to have a new option to guide care for the many instances of less-severe head injury where patients are already placed under observation for several hours."

Children and adolescents with TBI could especially stand to benefit, since research has shown that children are more sensitive to potential CT radiation damage. Papa noted that the current version of the test is only for adults, but that clinicians could use a test off-label if circumstances are appropriate. She and her colleagues have conducted multiple studies with children that suggest these two proteins are equally valid biomarkers in pediatric TBI.

In the future, Papa said she believes that in the future the blood test might be useful for predicting a TBI patient's long-term prognosis. Papa has recently completed a clinical study that monitored patients for six months following their TBI to see if UCH-L1 and GFAP levels correlate with long-term outcomes, and she is currently analyzing the data.

If there are associations between the plasma levels of these proteins and long-term outcomes, clinicians could use these blood tests to assess patients and plan more aggressive rehabilitation strategies in cases where the results suggest a risk of cognitive deficits or other problems. **PN**

DREADDs Could Guide More Targeted Treatments in Future

Evolving research on Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) may someday lead to new therapies for treatment-resistant neuropsychiatric disorders. **BY RICHARD KAREL**

An innovative experimental technique called DREADDs—Designer Receptors Exclusively Activated by Designer Drugs—which uses surgically implanted man-made receptors to modify brain function, may someday provide a therapy for treatment of severe refractory psychiatric disorders.

Animal studies have shown that DREADDs can be surgically delivered to a population of brain cells thought to be compromised in patients with psychiatric disorders. Once in place, the receptors can be activated or inactivated through an injection of a specific drug.

The hope is that by implanting and manipulating DREADDs in a precisely targeted brain region associated with a neuropsychiatric disorder, therapeutic benefits could be provided absent the unwanted side effects associated with drugs.

So far DREADDs have been studied only in rodents and nonhuman primates. But clinical application is the next frontier, according to Mike Michaelides, Ph.D., chief of the Biobehavioral Imaging and Molecular Neuropsychopharmacology Unit at the National Institute on Drug Abuse (NIDA).

"Given the absence of any significant psychopharmacological breakthroughs in recent years, there is a palpable hunger for better ways to treat mental disorders," he said.

Among those who see real-world clinical application on the horizon is psychiatrist Ned Kalin, M.D., chair of the Department of Psychiatry at the University of Wisconsin-Madison School of Medicine and Public Health. There he runs a laboratory, which combines molecular, preclinical animal models, and human functional imaging studies to understand the neurobiology underlying anxiety and mood disorders. Kalin's lab is now working with rhesus monkeys and has shown that DREADDs can be safely applied and that the implanted receptors will function within the neural circuits of these animals.

The next step, said Kalin, is testing DREADDS in monkeys who demonstrate anxiety-like behaviors, something he anticipates could take place within the next two years.

Anxiety is a good initial neuropsychiatric target because the neural circuitry of anxiety is better understood than for other psychiatric disorders, he noted. "There is every indication to believe that this is going to work, so it's not whether we're going to get there, but when are we going to get there," he added.

In 2016, psychologist and neuroscientist David Amaral, Ph.D., of the University of California, Davis, published an article demonstrating use of DREADD technology to modify activity in the rhesus amygdala—a brain region known to play a role in emotional learning in the context of fear and anxiety. That research, however, was exploratory and not directed specifically at modeling anxiety treatment. In rodents, however, DREADDs have pointed to the role of specific cells involved in anxiety-like behaviors, drug and alcohol seeking, and symptoms of Parkinson's disease.

Even as studies involving DREADDs in animal models advance, questions remain about their translational potential. One of these questions involves whether DREADDs may have unintended effects on off-target populations of brain cells. In a 2016 article in the *Journal of Neuroscience*, scientists reported that DREADDs implanted in rodents altered neuronal activity even in the absence of an activating drug.

Given that DREADD implantation involves invasive intracranial neurosurgery, there will also be hurdles getting FDA approval, Kalin noted.

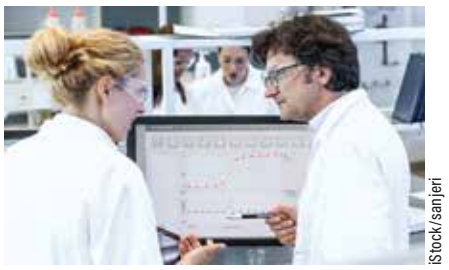
While Kalin said he currently sees no alternative to intracranial delivery of the DREADDs, he noted the FDA has approved invasive techniques in the past, including deep brain stimulation for Parkinson's disease. The delivery of DREADDs is key to the technology's therapeutic potential because it allows precise placement, he observed. "You can then have a very targeted circuit-based therapy that would allow you to get around all the problems with medications" that occur because they impact targets unrelated to the disorder.

In animal studies, scientists have

see **DREADDs** *on page 19*

JOURNAL DIGEST

BY NICK ZAGORSKI



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Women Less Likely To Be Listed First When Co-First Author Is Man

Women co-first authors are less likely to be listed first in a clinical science journal byline, according to an article in *JAMA*.

Overall, among studies published between 2005 and 2014 in five high-impact clinical journals (*Annals of Internal Medicine, BMJ, JAMA, Lancet, and the New England Journal of Medicine*), women co-first authors were listed first about 37 percent of the time when a man was the counterpart co-first author. This disproportionality was not seen in the top basic science journals (*Cell, Journal of Experimental Medicine, Nature, Nature Medicine, and Science*); between 2005 and 2014 women co-first authors were listed first 53 percent of the time.

Women co-first authors were about 18 percent more likely to be listed first when the senior author was also a woman, regardless of the type of science journal.

"It is unclear why differences were seen between clinical and basic science journals," Erin Aakhus, M.D., M.S.H.P., of the University of Pennsylvania Perelman School of Medicine and colleagues wrote. "Possible factors that were not measured include differences in author seniority or specialty, in the proportion of the total authors who were female, or gender bias."

Aakhus E, Mitra N, Lautenbach E, Joffe S. Gender and Byline Placement of Co-first Authors in Clinical and Basic Science Journals With High Impact Factors. *JAMA*. 2018; 319(6):610-611. https://jamanetwork.com/journals/jama/fullarticle/2672621

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Restoring Key Metabolite Improves Brain Function in Mouse Model of Alzheimer's

Defects in cellular energy metabolism have been implicated in many neurodegenerative diseases including Alzheimer's. One factor contributing to this dysfunction may be the depletion of NAD+, a metabolite that helps cells protect against stress and repair DNA damage.

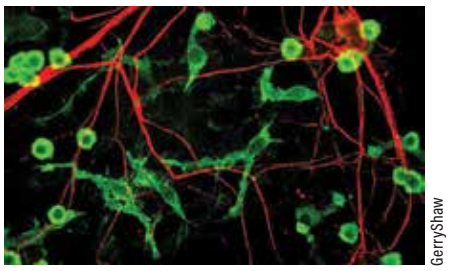
In a study published in *Proceedings of the National Academy of Sciences*, researchers at the National Institute on Aging and colleagues showed that restoring NAD+ improved outcomes in mice predisposed to develop Alzheimer's disease (AD).

The study involved mice genetically manipulated to mimic several aspects of Alzheimer's disease, including abnormal levels of amyloid and tau proteins as well as defective DNA repair mechanisms. The researchers gave some of these mice drinking water with nicotinamide riboside (NR, a form of vitamin B3 and NAD+ precursor) for three months; the others received regular drinking water. Over the next three months, the animals in both groups were evaluated in various behavioral and metabolic tests; during this time the mice in the active group continued to receive NR.

While there was no difference between the groups in amyloid buildup, animals who received chronic treatment with NR had reduced neuroinflammation, tau accumulation, and hippocampal cell death. NR-treated mice also performed better on multiple cognitive tasks than control mice.

"This study suggests that NR/NAD+ can target several aspects of AD, including traditional endpoints like tau pathology and inflammation, maybe via DNA repair enhancement," the authors concluded. "We believe that this work sets the stage for using NAD+ for treating AD in humans."

Hou Y, Lautrup S, Cordonnier S, et al. NAD+ Supplementation Normalizes Key Alzheimer's Features and DNA Damage Responses in a New AD Mouse Model With Introduced DNA Repair Deficiency. *Proc Natl Acad Sci USA*. 2018; 115(8): E1876-E1885. http://www.pnas.org/content/115/8/E1876.



GerryShaw

Gene Expression Profiles Suggest Similarities, Differences Among Five Psychiatric Disorders

A study led by investigators at the University of California, Los Angeles, has found that gene expression profiles of people with alcohol use disorder, autism, bipolar disorder, major depression, and schizophrenia share several characteristics.

The researchers collected genetic samples from 700 postmortem brains of individuals diagnosed with one of the five psychiatric disorders above as well as samples from 293 brains of healthy individuals and 193 brains from people with inflammatory bowel disease as controls. They then sequenced the samples and compared the expression profiles of over 10,000 genes.

The genetic profiles from patients with autism, bipolar disorder, and schizophrenia showed the most overlap. All three disorders had similar gene expression profiles that indicated synaptic dysfunction and elevated production of astrocytes (a type of non-neuronal support cell in the

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Exemptions

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Statutory Conscience Rights in Health Care; Delegations of Authority," published in the *Federal Register* on January 26. It would allow providers to opt out of certain procedures such as abortion, sterilization, and assisted suicide.

Organizations that signed on to the letter include the Academy of Psychosomatic Medicine, the American Academy of Addiction Psychiatry, the American Academy of Child and Adolescent Psychiatry, and the American Academy of Pediatrics.

The organizations fear that the new policies could lead to discrimination and/or denial of care that could harm lesbian, gay, bisexual, transgender, and questioning (LGBTQ) patients. For example, a clinician would have the right to refuse hormone therapies or counseling to a patient in gender transition if the clinician rejects such treatment.

"The mission of HHS is 'to enhance and protect the health and well-being of all Americans.' This should be clearly articulated in all HHS plans, with a special focus on how to achieve better health outcomes for minority populations," stated the groups in their letter to HHS Secretary Azar. "Any authority that grants license to discriminate would be detrimental to LGBTQ patients' safe access to care and would undermine the progress we have achieved in addressing disparities among this patient population."

In mid-January HHS announced the creation of the Conscience and Religious Freedom Division within its Office of Civil Rights (OCR) to handle complaints from health care professionals who refuse to provide care for religious reasons.

In addition, the Centers for Medicare and Medicaid Services has issued guidelines that give states "flexibility" to take actions against providers that offer abortion services, while removing barriers for religious and faith-based organizations to participate in HHS programs and receive public funding.

"I am deeply concerned that our LGBTQ patients—who already face unique health challenges—may now be denied care because of who they are," APA CEO and Medical Director Saul Levin, M.D., M.P.A., said in a January 19 press release. "We know that discriminatory policies harm our patients' mental health and well-being. APA is firmly opposed to laws and regulations that trample on the civil rights of LGBTQ people, including the right to access health care."

In their letter, the health care organizations pointed out that LGBTQ patients are already at risk for mental health issues because of social prejudice and have higher rates of suicide than their peers—40 percent of gender minorities report attempting suicide.

Noting that HHS leaders are discouraging staffers from using certain words, including "transgender," "evidence-based," and "diversity," the letter also expressed concern that such omissions could have harmful repercussions on data collection for minorities.

"To reduce the cost of health care and achieve our goal of creating a healthier nation, the needs of specific populations must be examined and effectively addressed. We urge you to reconsider these actions and include strategies to focus on better access to health services and improved outcomes for minority populations, including millions of LGBTQ people in the United States," the letter concluded. **PN**

The letter is posted at https://www.psychiatry.org/File%20Library/Psychiatrists/Advocacy/Federal/Joint-letter-to-HHS-on-LGBTQ-patients.pdf. Comments on the proposed rule can be filed at https://www.federalregister.gov/documents/2018/01/26/2018-01226/protecting-statutory-conscience-rights-in-health-care-delegations-of-authority. The comment period ends March 27.

Pharmacogenetics

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Other experts on the subject corroborate Nurmi's caution. "Pharmacogenetics is very *au current*," Joseph Goldberg, M.D., a clinical professor of psychiatry at Icahn School of Medicine at Mount Sinai, New York, told *Psychiatric News*. "However, the present technology really just helps to affirm that someone may need a lower than usual medication dose to minimize certain side effects, or a higher than usual dose if they metabolize a drug too quickly. Mass media and test manufacturers seem to foster the misperception that pharmacogenetic testing will magically predict which drug works best for a given patient. The notion that current pharmacogenetic testing can tell patients which drug will work for them as if it were a crystal ball is a gross oversimplification of a complex medical decision-making process."

Most Tests Assess Metabolization

The promise of pharmacogenetic testing and precision medicine as envisioned in Obama's initiative is real. In oncology, where the science is most advanced, pharmacogenetic testing has vastly improved clinical outcomes. Such tests could one day yield enormous benefits in psychiatry, where response to psychopharmacology is highly variable and it can take months to determine whether the medication is helping a patient.

A recent report in *AJP* found that one genetic variant may have a role in predicting which patients will improve with antidepressants and which type of antidepressant may be most effective, adding to the foundational knowledge needed to advance a precision approach to personalized antidepressant choices.

What can pharmacogenetic testing today reliably tell you, and, more importantly, what can't it tell you?

Nurmi explained there are two broad domains affecting drug response that could be influenced by an individual's genetic profile: pharmacokinetics (what the body does to a drug, especially how quickly or slowly it metabolizes a medication) and pharmacodynamics (what the drug does to the body's cells, tissues, and organs).

The bulk of available commercial testing is around pharmacokinetics. Genetic variations affecting the expression of cytochrome P450 (CYP) enzymes are known to affect whether the body metabolizes a particular drug quickly or slowly. There are a couple of clinical possibilities that might be indicated by testing CYP:

- A patient with a variation indicating unusually fast metabolization (an "ultra-rapid metabolizer") may metabolize the drug in question so quickly that it does not reach therapeutic levels in the bloodstream at a normal dose.

- A patient with a variation indicating unusually slow metabolization (a "poor metabolizer") would be likely to process the drug so slowly that it builds up in the bloodstream causing adverse effects at a normal dose.

Patients who order tests online may bring results into clinicians' offices indicating, for instance, that a medication "should be used with caution and increased monitoring." It is up to physicians to read test results more closely to determine what they indicate about metabolizer status.

Variations in expression of several CYP enzymes can cause poor or ultra-rapid metabolization of common psychiatric drugs. Two in particular—CYP2D6 and CYP2C19—affect the metabolization of common selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, and atypical antipsychotics. For instance, it has been found that citalopram, which is metabolized by the CYP2C19 enzyme, may cause an increased risk of QT prolongation in poor metabolizers. For this reason, the Food and Drug Administration (FDA) has recommended that citalopram not be prescribed at doses above 20 mg/d in individuals identified as poor metabolizers. Electrocardiogram (ECG) monitoring and/or electrolyte monitoring should be performed if citalopram must be used in such patients.

With regard to pharmacodynamics, pharmacogenetic test results have only a handful of established correlates with clinical outcomes. Notably, a 2004 report in *Nature* found that the HLA-B1502 genetic mutation (common in individuals of Asian descent) is linked to risk for Stevens-Johnson Syndrome, a systemic reaction that involves a severe skin rash, when prescribed carbamazepine (sometimes used for seizures and aggression). For that reason, the FDA added a boxed warning requiring that people of Asian descent be screened for HLA-B1502 before starting carbamazepine.

Nurmi said research will invariably produce risk genes for mental illness that can be translated for pharmacogenetic testing in the clinic.

In the meantime, clinicians should educate themselves and be prepared to talk to patients and families about pharmacogenetics. "Prior to responsible implementation, the health care field needs to be able to understand, explain, and respond to genetic information provided to guide clinical care," she said. **PN**

Information about the Clinical Pharmacogenetics Implementation Consortium guidelines is posted at https://cpicpgx.org/guidelines. "Antidepressant Outcomes Predicted by Genetic Variation in Corticotropin-Releasing Hormone Binding Protein" is posted at https://ajp.psychiatryonline.org/doi/full/10.1176/appi.ajp.2017.17020172. "FDA Drug Safety Communication: Revised Recommendations for Celexa (Citalopram Hydrobromide) Related to a Potential Risk of Abnormal Heart Rhythms With High Doses" is posted at https://www.fda.gov/Drugs/DrugSafety/ucm297391.htm. "Medical Genetics: A Marker for Stevens-Johnson Syndrome" is posted at http://www.nature.com/articles/428486a.

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brain). Autism profiles showed one additional feature: changes in the expression of immune-related brain cells known as microglia.

The profiles of major depression and alcohol use disorder were more distinct.

These findings, published in the journal *Science*, provide molecular portraits of psychiatric pathology. These genetic signatures act as proxies for brain dysfunction and may lead to more targeted treatments of these disorders.

Gandal M, Haney J, Parikshak N, et al. Shared Molecular Neuropathology Across Major Psychiatric Disorders Parallels Polygenic Overlap. *Science.* 2018; 359(6376):693-697. http://science.sciencemag.org/content/359/6376/693.long

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Alcohol Cues May Induce Changes in Brain Glutamate In People With AUD

Growing evidence suggests that glutamate neurotransmission plays an important role in alcohol addiction. A study appearing in the *Journal of Alcohol and Alcoholism* has now provided the first evidence in humans that glutamate levels in the brain change in response to alcohol-related cues. Alcohol cues (sights or smells related to drinking) are a significant factor that leads to relapse in people with alcohol use disorder (AUD).

Researchers at Indiana University used magnetic resonance spectroscopy to measure forebrain glutamate levels in 17 people with AUD and 18 healthy controls. Two spectroscopy sessions were performed in succession, the first to establish baseline glutamate levels and the second to measure changes in response to different visual cues.

There were no significant differences between the two groups in baseline glutamate levels on average. When presented with visual cues, glutamate levels in the AUD subjects dropped after they were shown alcohol-related photos, but not neutral photos; the control subjects showed no differences in glutamate levels in response to the cues.

"This is the first study to document changes in glutamate levels during exposure to alcohol cues in people with alcohol use disorders and shines a spotlight on glutamate levels as an important target for new therapies to treat the condition," said study co-author Sharlene Newman, Ph.D., in a press release. **PN**

Cheng H, Kellar D, Lake A, et al. Effects of Alcohol Cues on MRS Glutamate Levels in the Anterior Cingulate. *Alcohol Alcohol.* January 10, 2018. [Epub ahead of print] https://academic.oup.com/alcalc/advance-article-abstract/doi/10.1093/alcalc/agx119/4796882

DREADDs

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used radioactive tracers to observe how DREADDs react when the appropriate activating drug is administered. The process uses positron emission tomography (PET), a technology long used in neuroimaging research. The radioactively tagged molecules show up as lighter and darker areas as the DREADD is turned up or down during drug administration, NIDA's Michaelides explained.

In future clinical applications, this would allow real-time monitoring of response in brain circuits. Clinicians would then have a way to fine-tune how much of the activating drug is administered based on individual response. In animal research scientists have used PET to observe the correlation between DREADD activation and behavioral changes, and the hope is that this same utility will be found in eventual clinical application, Michaelides said. **PN**

Amaral's study, "The Rhesus Monkey Connectome Predicts Disrupted Functional Networks Resulting From Pharmacogenetic Inactivation of the Amygdala" is posted at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5233431/. "DREADDs: Use and Application in Behavioral Neuroscience" is posted at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4792665/.

Shooting

continued from page 1

million in funding for mental health initiatives, including requiring all schools to have counselors and crisis intervention teams. As part of the plan, he also is vowing to create a "violent threat restraining order" that would allow Florida courts to confiscate firearms from individuals who threaten violence involving weapons. The state's legislature had just two weeks left in this session to pass legislation as of press time.

The governor's plan also includes increasing the legal age to purchase all firearms to 21 years old (currently it is 18 years old for rifles and shotguns) and banning bump stocks, devices that boost firearm firing speed. Florida has some of the least restrictive firearm laws in the nation, according to the Giffords Law Center to Prevent Gun Violence, which rated it an "F." However, even if the measure passes, youth of any age could still possess rifles, such as an AR-15, and other long guns.

If Florida's gun restrictions pass, it would be the first time in more than a decade that lawmakers there advance any legislation opposed by the NRA, according to the *Tampa Bay Times*.

Bhagi Sahasranaman, M.D., and R. Scott Benson, M.D., met with the Florida governor last month to discuss ways to improve mental health services following a mass shooting.

What Happened at Stoneman Douglas

Parkland, a small city with a million-dollar median home value and park-like design, was voted Florida's safest city in 2017. Its Marjory Stoneman Douglas High School has been an A-rated school for the past seven years by the Florida Department of Education. The school had diligently run safety drills and had established a single point of entry for the sprawling campus of 3,300 students. It even had an armed security guard on duty at the time of the shooting. "This shouldn't be happening here," said Sahasranaman, who lives just a few miles from the school.

And yet near the end of the school day on February 14—Valentine's Day—a former student who had been expelled for disciplinary reasons pulled a fire alarm and picked his way through one of its buildings with an AR-15 semiautomatic rifle, killing 14 students and three faculty members and inujring 14 before casually walking out and heading to a Subway inside a Walmart to buy a drink. He confessed after the shooting.

The mass shooting's effect on the community has been profound, with sadness, numbing anger, and intense anxiety, Sahasranaman said. She helped facilitate a psychiatric referral for one student who survived the tragic events at the school that day and needed a higher level of intervention. "Right now, everyone is in shock, dealing with the immediate situation," she explained. "The counseling will be more critical, and victims' needs will increase as time goes on."

After the shooting, Sahasranaman checked in on a close friend of hers, a math teacher who was in the building at the time, to offer support to her and her husband. The quick thinking by that teacher, "Mrs. V," saved many lives that day: rather than releasing her students at the sound of the fire alarm—the second one of the day—she realized something wasn't right and quickly locked the door and instructed students to huddle on the floor, covering her window with paper. "That was terror," Sahasranaman said. "She's devastated."

'They're Not Going to Take It'

What has set this mass shooting apart is the unprecedented level of activism by the survivors themselves, who are demanding tightened gun restrictions and for politicians to stop accepting money from the NRA.

"It's great to see these kids," Sahasranaman said. "They're amazing, and they're not going to take it. They're rallying against gun violence and demanding gun control. It's unfathomable that an 18-year-old can buy an assault rifle. They can't even buy a beer, but they can go and get an AR-15."

The United States has by far the highest gun ownership of any nation, with civilians owning about 90 guns for every 100 people—270 million firearms overall—according to estimates by Small Arms Survey, a gun research

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Bipolar

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told *Psychiatric News*. "Social stigma, too, is one of the biggest barriers to early intervention."

Bipolar disorder has a high genetic loading: the single greatest risk factor for developing the disorder is having a parent with the illness, particularly one who had an onset of the disease before age 21, the authors concluded. However, such children are also at increased risk for other psychopathology, such as major depressive disorder, anxiety disorder, or attention-deficit/hyperactivity disorder (ADHD), rendering a correct diagnosis more challenging.

Among the prodromal symptoms, the strongest predictor of conversion to bipolar disorder is subsyndromal manic symptoms, the authors wrote. Young people with these symptoms tend to have recurrent episodes of hyperactive, silly, and disruptive behaviors at school and home, beyond what are expected for their age, Birmaher said. For example, patients' parents comment that they cannot take their child to church. Unlike children with ADHD, the problems of these children are not continuous; they may last a few months and then stop, only to emerge again later. Sometimes a child becomes grandiose—for instance, he may genuinely believe that he is the best football player ever, even though he barely knows the game, Birmaher said.

Many patients with the early symptoms of bipolar disorder seem to be falling through the cracks. "Some psychiatrists don't believe the disorder exists, that you can't have children aged 6 to 12 years old with bipolar disorder. I understand them, because the disorder is hard to diagnose, especially if you don't ask the right questions and closely follow these children over time," Birmaher said.

The Pittsburgh Bipolar Offspring Study has been following 388 children of parents with bipolar disorder for more than 16 years. Researchers found that four-fifths of the children who were symptomatic at the outset of the study were not receiving any mental health treatment, despite having ADHD, behavior problems, anxiety, or depression. So far, about 28 percent of the children have developed bipolar disorder, compared with 1 percent of the control group from the same community being studied.

Bipolar disorder is also influenced by a number of environmental risk factors, researchers found, including stressful life events; sexual abuse; antidepressants, which can trigger mania; smoking, which research has shown plays a causal role in mental illness; and substance abuse. Children with very high academic attainment may also be at greater risk for bipolar disorder, according to the review.

Caution Needed With Early Treatment

Choosing preventive medication treatments is particularly complex. The potential benefits of any pre-onset interventions must be carefully weighed against the risks of such treatment, Salagre said. Moreover, patients at risk for bipolar disorder might not convert to the full-blown illness. Pilot studies assessing the protective properties of valproate sodium and quetiapine against the onset of mania have been mixed. Still, some treatments such as lithium are more effective in the earlier stages of the disease, the authors wrote.

"For patients whose prodromal symptoms affect their functioning, you can try treating with the standard treatments for bipolar disorder, but the reality is we don't know what's best," Birmaher said. For now, his treatment strategy is to use evidence-based psychotherapy and/or medication that addresses their presenting symptoms. However, although these young people may present with anxiety or depression, both Salagre and Birmaher cautioned that the standard SSRI treatment can trigger mania. "It's not necessarily contraindicated, but you need to be super careful when prescribing antidepressants. Parents, too, need to be told what side effects to watch for," Birmaher said.

The authors recommend cautious use of pharmacotherapy and very gradual dosage escalations. Patients who have an early bad experience with medication may drop out of treatment and resist taking psychotropic drugs for years to come, they noted.

Among the various types of psychotherapy examined, Salagre said family-focused therapy provided longer stability and worked better at reducing symptoms of bipolar disorder than other forms of therapy. Clinicians can also help at-risk patients by screening for stressful life events and encouraging lifestyle modifications, including substance use cessation, physical activity, and healthy diet, she added.

Ultimately, the authors called for more study on the development and identification of treatments that can best prevent or at least delay bipolar disorder, and this "should be considered a priority in psychiatry." **PN**

"Early Intervention in Bipolar Disorder" is posted at https://ajp.psychiatryonline.org/doi/10.1176/appi.ajp.2017.17090972.

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group in Geneva, Switzerland.

APA is calling on President Trump and Congress to take a series of steps that would reduce gun violence with commonsense solutions, increase funding for research on mental illness, and improve access to mental health care (see box).

APA CEO and Medical Director Saul Levin, M.D., M.P.A., pointed out that research has consistently shown that people with mental illness are not more likely to be perpetrators of violence, but more likely to be victims. Moreover, people with serious mental illness commit only about 3 percent of violent crimes each year, according to the 2016 book *Gun Violence and Mental Illness* from APA Publishing.

Public Health Dimension Needs to Be Addressed

Benson agreed that gun violence must be approached as a public health problem. "The overwhelming majority of mass shootings have been committed by angry young men," he pointed out. "I don't have a medicine that can fix them. And locking them all up is not an option. While every society in the world has its share of angry young men, the United States stands alone in its mass shooting toll."

The United States is home to 5 percent of the world's population, but accounts for 31 percent of global mass shootings, according to a 2016 study by the University of Alabama. "We can't prevent hurricanes, earthquakes, or tornadoes, but I believe we can do something to curb this gun violence," Benson said. "APAPAC should consider a candidate's position on guns as a factor in their decision to support."

Ultimately, Benson said that in the aftermath of gun violence, psychiatrists step in to help people in the community heal and regain their footing.

"We help people resolve the trauma. We're good at that," he said. "But we've had too many of these shootings. We shouldn't have to deal with these tragedies; nobody should." **PN**

APA, Coalition Partners Demand Immediate Action

In partnership with coalition members and alone, APA vigorously responded to the high school shooting in Parkland, Fla., and criticized remarks that framed the shooting as a "mental health issue" and referred to people with mental illness in stigmatizing and disparaging terms.

In a press statement issued February 16, APA and four other frontline organizations representing 450,000 physicians and medical student members urged "national leaders to recognize in this moment what the medical community has long understood: we must treat this epidemic no differently than we would any other pervasive threat to public health. We must identify the causes and take evidence-based approaches to prevent future suffering."

Among other actions, the organizations asked for the appropriation of funding for research at the Centers for Disease Control and Prevention (CDC) to study gun violence and the establishment of constitutionally appropriate restrictions on the manufacturing and sale, for civilian use, of large-capacity magazines and firearms with features designed to increase their rapid and extended killing capacity.

On February 23, APA called on President Trump, Congress, and the country to enter into a meaningful dialogue to improve mental health care in this country. Among the issues APA said need to be addressed are enforcement of the parity law to ensure "timely access to a full range of mental health and substance use disorder providers and services" and increased research funding to improve early detection of mental illness and the development of effective interventions.

"Recent disparaging and inaccurate remarks about mental illness serve only to perpetuate stigma and prohibit honest and open dialogue about an illness or disorder that affects 1 in 5 people in the nation," APA stated.

In letters sent to all Congress members on February 22, APA and a coalition of 75 health organizations urged enactment of bipartisan solutions that address the public health threat of firearm-related injuries and fatalities.

"Federal policy should address gun violence with the same dedication applied to other successful public health initiatives over the past 25 years, such as immunizations, public sanitation, and motor vehicle safety," the letter stated. "Reducing injury and mortality through research and evidence-based prevention and intervention strategies has been proven to improve health, safety, and life expectancy. Strengthening firearm background checks and supporting funding for federal research and public health surveillance on firearm-related injuries and fatalities would provide meaningful progress in achieving a public health solution for this issue. … Our organizations stand ready to work with you to support that critical effort. Thank you for your consideration."

APA's news releases related to the Florida shooting can be accessed at https://www.psychiatry.org/newsroom/news-releases. The Senate letter can be accessed at http://apapsy.ch/Senate. The House letter can be accessed at http://apapsy.ch/House.

Ketamine

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creates the potential for drug diversion.

The work group consensus statement provides an overview and expert clinical opinion on six critical issues and considerations associated with the off-label use of ketamine treatment for mood disorders:

- **Treatment setting**. A clinical setting offering ketamine infusion should include sufficient means of monitoring patients and providing immediate care when necessary, especially for patients experiencing adverse effects on cardiovascular function. These measures include a means of delivering oxygen to patients with reduced respiratory function, medication, and, if indicated, means of rapidly managing potentially dangerous behavioral symptoms.

- **Patient selection**. Before initiating ketamine treatment, patients should undergo a thorough pretreatment evaluation process assessing relevant features of the patient's past and current general medical and psychiatric condition.

- **Medication delivery**. Most clinical trials and case reports use a dose of 0.5 mg/kg per 40 minutes intravenously. Limited information is available regarding different routes of delivery and different doses of ketamine.

- **Repeat infusions**. Several clinics providing long-term repeated administration of ketamine use a two- or three-week course of ketamine delivered two or three times per week, followed by a taper period and/or continued treatments based on patient response.

"However, there remain no published data that clearly support this practice, and it is strongly recommended that the relative benefit of each ketamine infusion be considered in light of the potential risks associated with longer-term exposure to ketamine and the lack of published evidence for prolonged efficacy with ongoing administration," Sanacora and colleagues wrote. "The scarcity of this information is one of the major drawbacks to be considered before initiating ketamine therapy for patients with mood disorders and should be discussed with the patient before beginning treatment."

- **Safety measures and continuation of treatment**. In addition to the risk of cognitive impairment and of substance abuse associated with long-term use of ketamine, there is also a risk of cystitis. For that reason, assessments of cognitive function, urinary discomfort, and substance use should be considered if repeated administrations are provided.

- **Clinician experience and training**. There are considerable differences in the experience and clinical expertise of clinicians currently administering ketamine, and no published guidelines or recommendations outlining specific training requirements.

So, what does the future look like for the use of ketamine for patients with mood disorders?

Sanacora said one important development will be clinical trials of "mirror" molecules of ketamine, such as esketamine, which are scheduled for phase three trials this year. Some chemical compounds, such as ketamine, are composed of left and right molecules that mirror each other; the mirror image of ketamine, if found to be effective, can be marketed profitably by a pharmaceutical company.

More and longer-term trials of ketamine are also a must. Sanacora and colleagues wrote in the consensus statement: "Although economic factors make it unlikely that large-scale, pivotal phase 3 clinical trials for [the originally approved ketamine compound] will ever be completed, there are several studies with federal and private foundation funding to address some of these issues. It is imperative that clinicians and patients continue to consider enrollment in these studies. … A second means of adding to the knowledge base is to develop a coordinated system of data collection. … After such a registry is created all clinicians providing ketamine treatment should consider participation." **PN**

"A Consensus Statement on the Use of Ketamine in the Treatment of Mood Disorders" is posted at https://jamanetwork.com/journals/jamapsychiatry/article-abstract/2605202?redirect=true. "The Effect of a Single Dose of Intravenous Ketamine on Suicidal Ideation: A Systematic Review and Individual Participant Data Meta-Analysis" is posted at https://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2017.17040472. "Ketamine for Rapid Reduction of Suicidal Thoughts in Major Depression: A Midazolam-Controlled Randomized Clinical Trial" is posted at https://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2017.17060647.