This issue marks the twenty-eighth installment consolidating recent clinical updates, mental health policy news, popular press news patients may be reading, and changes in the landscape of psychiatry in Wisconsin.

OF GENERAL INTEREST

Wisconsin Farmers and Suicide:
Appearing in the Wisconsin State Journal (1/27/2019 [LINK] journalist David Wahlberg Sheds light on the record 915 suicide in Wisconsin in 2017 and the impact of economic challenges on agrarian suicide: Several years of low milk prices, the high cost of farm equipment, trade wars and other pressures contributed to the closure of 691 dairy farms in the state last year, the highest number of closures since 2011.

Facebook, AI and Suicide Prevention:
Since 2017, Facebook has used artificial intelligence to screen for potential suicidal ideation and its users. In an article at Medscape (1/15/2019, [LINK] phonetically aptly named journalist Deborah Brauser describes what is known about the process by which artificial intelligence screens postings and submits those deemed at risk to a specialist team for review. Thus far, this process has resulted in 3500 wellness checks worldwide among Facebook users.

Wisconsin Physician Burnout:
According to work published in the WMJ (Hauer, Waukau and Welch, [LINK] nearly 54 percent of Wisconsin physicians are experiencing burnout. Results also indicated that 47% planned to reduce their hours or retire in the next 5 years. The Wisconsin Medical Society has made it a priority to address this through pressing for EHR changes and encouraging more physician leadership in healthcare, among other goals ([LINK]).

Annual Burnout Cost: $4.6 Billion:
According to data published in the Annals of Internal Medicine (Han et al, [LINK]): On a national scale, the conservative base-case model estimates that approximately $4.6 billion in costs related to physician turnover and reduced clinical hours is attributable to burnout each year in the United States. This estimate ranged from $2.6 billion to $6.3 billion in multivariate probabilistic sensitivity analyses. At an organizational level, the annual economic cost associated with burnout related to turnover and reduced clinical hours is approximately $7600 per employed physician each year.

Op-Ed Compares The Sacklers/Purdue Pharma to El Chapo:
In an opinion article appearing at MedScape (2/4/2019, [LINK] author George Lundberg MD describes the impact of pharmaceutical advertising and prescribing practices on public health.

MOC?
Given the degradation of the maintenance of certification process, Ault (1/11/2019, Medscape, [LINK]) publicized the release of a 96 page draft-report from a 27 member independent commission established by the American Board of Medical Specialties (ABMS). The Continuing Board Certification: Vision for the Future Commission report, according to Ault, suggested “that the process was far enough off the rails that the term "maintenance of certification" should be abandoned.”
Eliminating “Stupid Stuff”:
Reported by Berg at the AMA (2/19/2019 [LINK]), Melinda Ashton, MD, executive vice president and chief quality officer at Hawaii Pacific Health, wrote an essay published by the New England Journal of Medicine ([LINK]). Providing physician is a way of categorizing “stupid stuff” in the electronic health record allowed for triage of excessive clicking into categories of never meant to happen, useful but needs work, and required but doesn’t make sense. The idea is to reduce the burden of the EMR and have it work for providers, not against them.

FDA Warns Against Abrupt Cessation of Opioids:
In a 4/8/2019 communication ([LINK]) the FDA warned:

Health care professionals should not abruptly discontinue opioids in a patient who is physically dependent. When you and your patient have agreed to taper the dose of opioid analgesic, consider a variety of factors, including the dose of the drug, the duration of treatment, the type of pain being treated, and the physical and psychological attributes of the patient. No standard opioid tapering schedule exists that is suitable for all patients. Create a patient-specific plan to gradually taper the dose of the opioid and ensure ongoing monitoring and support, as needed, to avoid serious withdrawal symptoms, worsening of the patient’s pain, or psychological distress (For tapering and additional recommendations, see Additional Information for Health Care Professionals).

CLINICAL PSYCHIATRY IN THE NEWS, IN BRIEF

FDA Approves Intranasal Esketamine:
Reported by the FDA on March 5th, intranasal esketamine what is approved for treatment resistant depression [LINK]. According to Reuters (March 7th, Medscape, [LINK]) Johnson & Johnson said its nasal spray depression treatment, called Spravato, will be priced at $590 for a 56 mg dose and $885 for 84 mg. Induction phase of therapy, lasting about a month with treatment twice a week results in a wholesale acquisition cost or list price in the range of $4,720 to $6,785, per Janssen spokesman Greg Panico via email statement.

FDA Declines to Approve Opioid Based MDD Rx:
As reported by Reuters (2/1/2019, [LINK]) the FDA declined to approve Alkermes once-daily pill combining samidorphan and buprenorphine as adjunctive treatment for depression citing the need for additional data to prove the effectiveness of the drug.

Poor Prospective/Retrospective Agreement in Childhood Maltreatment:
As reported in the APA Headlines of 3/27/2019:

Healio (3/26, Demko) reports that in a “large systematic review and meta-analysis” involving “16 studies with data on 25,471 participants,” investigators found “poor agreement between prospective and retrospective measures of childhood maltreatment, indicating that these two measures should not be used interchangeably to study risk factors associated with childhood maltreatment.” The findings were published online March 20 in JAMA Psychiatry. The author of an accompanying editorial wrote, “From a clinical perspective, these new findings do not negate the importance of listening to what a patient says, but they suggest that caution should be used in assuming that these retrospective reports accurately represent experiences, rather than perceptions, interpretations or existential recollections.”
Reducing Postoperative Delirium:
Appearing in JAMA (LINK) Subramaniam et al. Explores the use of IV acetaminophen combined with dexmedetomidine or propofol in older patients undergoing cardiac surgery. They found:
- Among older patients undergoing cardiac surgery, postoperative scheduled IV acetaminophen, combined with IV propofol or dexmedetomidine, reduced in-hospital delirium vs placebo.
- Additional research, including comparison of IV vs oral acetaminophen and other potentially opioid-sparing analgesics, on the incidence of postoperative delirium is warranted.

Chronic Psychosis Ages the Brain:
Research published in Biological Psychiatry (Sheffield et al. LINK) studied connectivity within the frontoparietal network (FPN) and cingulo-opercular network (CON) in 240 patients with schizophrenia and 178 healthy controls (HC)
- Consistent with accelerated aging, significant group by age interactions reflected significantly stronger relationships between efficiency and age in patients with psychosis than in HCs for both the CON (psychosis: r = −.37; HC: r = −.16) and FPN (psychosis: r = −.31; HC: r = −.05).
- Accelerated aging was not observed in either the subcortical or visual network, suggesting specificity for cognitive networks that decline earliest in healthy aging. Replicating prior findings, efficiency of both the CON and FPN correlated with cognitive function across all participants (rs > .11, ps < .031). Furthermore, patients with chronic psychosis (p = .004), but not patients with early psychosis (p = .553), exhibited significantly lower FPN efficiency compared with HCs.

Sleep-Wake Cycle, CSF and Tau:
According to research reported in Science (Holt et al, LINK) Aβ plaques increase in sleep deprived mice, writing that sleep-wake cycle regulates interstitial fluid tau in mice and cerebrospinal fluid tau in humans.

Tamoxifen for Mania?
As reported in the APA Communication of 2/19/19:
- Healio (2/18, Demko) reported that tamoxifen “shows potential as a treatment for episodes of mania in patients with bipolar disorder [BD], according to a” five-study systematic review and meta-analysis published online Feb. 11 in the Journal of Psychopharmacology.

According to Psychiatric News (2/15), the medication “was found to be superior to placebo in lowering mania scale scores, with greater improvements when used as a monotherapy.”

Adjunctive Psychopharmacology in Schizophrenia:
Use of antidepressants in schizophrenia appeared to reduce frequency of hospitalizations whereas use of benzodiazepines appeared to increase frequency according to work published in JAMA Psychiatry by Stroup et al. LINK:
- The study cohort included 81 921 adult outpatients diagnosed with schizophrenia (mean [SD] age, 40.7 [12.4] years; 37 515 women [45.8%]) who were stably treated with a single antipsychotic and then initiated use of an antidepressant (n = 31 117), a benzodiazepine (n = 11 941), a mood stabilizer (n = 12 849), or another antipsychotic (n = 26 014) (reference treatment). Compared with initiating use of another antipsychotic, initiating use of an antidepressant was associated with a lower risk (hazard ratio [HR], 0.84; 95% CI, 0.80–0.88) of psychiatric hospitalization, whereas initiating use of a benzodiazepine was associated with a higher risk (HR, 1.08; 95% CI, 1.02–1.15); the risk associated with initiating use of a mood stabilizer (HR, 0.98; 95% CI, 0.94–1.03) was not significantly different from initiating use of another antipsychotic. A similar pattern of associations was observed in psychiatric ED visits for
initiating use of an antidepressant (HR, 0.92; 95% CI, 0.88-0.96), a benzodiazepine (HR, 1.12; 95% CI, 1.07-1.19), and a mood stabilizer (HR, 0.99; 95% CI, 0.94-1.04). Initiating use of a mood stabilizer was associated with an increased risk of mortality (HR, 1.31; 95% CI, 1.04-1.66).

**Predicting Psychiatric Side Effects with Levetiracetam:**
Published by Josephson et al. at JAMA Neurology [LINK], authors sought to determine what factors predicted psychiatric side effects of Levetiracetam:

Among 1173 patients with epilepsy receiving levetiracetam, the overall median age was 39 (interquartile range, 25-56) years, and 590 (50.3%) were female. A total of 14.1% (165 of 1173) experienced a psychiatric symptom or disorder within 2 years of index prescription. The odds of reporting a psychiatric symptom were significantly elevated for women (odds ratio [OR], 1.41; 95% CI, 0.99-2.01; P = .05) and those with a preexposure history of higher social deprivation (OR, 1.15; 95% CI, 1.01-1.31; P = .03), depression (OR, 2.20; 95% CI, 1.49-3.24; P < .001), anxiety (OR, 1.74; 95% CI, 1.11-2.72; P = .02), or recreational drug use (OR, 2.02; 95% CI, 1.20-3.37; P = .008).

**Lisdexamfetamine = Placebo in Binge Eating:**
Published in Clinical Psychiatry (Kornstein et al., [LINK]) analysis of over 700 participants equivalent response to placebo and dose optimized lisdexamfetamine in the treatment of binge eating disorder.

**Positive Predictive Value in Suicide Near Zero:**
According to analysis published at JAMA Psychiatry (Belaher et al. [LINK]) which winnowed 7306 abstracts down to 17 cohort studies meeting inclusion criteria:

To date, suicide prediction models produce accurate overall classification models, but their accuracy of predicting a future event is near 0. Several critical concerns remain unaddressed, precluding their readiness for clinical applications across health systems.

**ADHD → Stimulants → Psychosis?**
Published in the New England Journal of Medicine (Moran et al., [LINK]) nearly 338,000 young adults and adolescents treated with stimulants were assessed:

The study population consisted of 221,846 patients with 143,286 person-years of follow up; 110,923 patients taking methylphenidate were matched with 110,923 patients taking amphetamines. There were 343 episodes of psychosis (with an episode defined as a new diagnosis code for psychosis and a prescription for an antipsychotic medication) in the matched populations (2.4 per 1000 person-years): 106 episodes (0.10%) in the methylphenidate group and 237 episodes (0.21%) in the amphetamine group (hazard ratio with amphetamine use, 1.65; 95% confidence interval, 1.31 to 2.09).

CONCLUSIONS: Among adolescents and young adults with ADHD who were receiving prescription stimulants, new-onset psychosis occurred in approximately 1 in 660 patients. Amphetamine use was associated with a greater risk of psychosis than methylphenidate. (Funded by the National Institute of Mental Health and others.)

**Daily Cannabis, High Potency and Psychosis:**
Appearing in The Lancet Psychiatry (Di Forti et al., [LINK]):

Between May 1, 2010, and April 1, 2015, we obtained data from 901 patients with first-episode psychosis across 11 sites and 1237 population controls from those same sites. Daily cannabis use was associated with increased odds of psychotic disorder compared with never users (adjusted odds ratio [OR] 3.2, 95% CI 2.2–4.1), increasing to nearly five-times increased odds for daily use of high-potency types of cannabis (4.8, 2.5–6.3). The PAFs calculated indicated that if high-potency cannabis were no longer available, 12-2% (95% CI 3.0–16.1) of cases of first-episode
psychosis could be prevented across the 11 sites, rising to 30·3% (15·2–40·0) in London and 50·3% (27·4–66·0) in Amsterdam. The adjusted incident rates for psychotic disorder were positively correlated with the prevalence in controls across the 11 sites of use of high-potency cannabis ($r = 0·7; p=0·0286$) and daily use ($r = 0·8; p=0·0109$).

**FDA Approves Brain Stimulation Device:**

Appearing at Medscape (Megan Brooks, 3/27/2019, [LINK](#)) the FDA approved a prescription based home cranial electrotherapy stimulator (Cervella, Innovative Neurological Devices). The device, retailing for $695, is said to deliver micro pulses of electrical current across the brain. Reportedly, clinical trials demonstrated that use of the device (which is guided by a smartphone app which also records usage) led to a reduction in anxiety levels, insomnia, and depressed mood. More information is available at the company’s website: [LINK](#)

**Caution Advised by FDA in Use of Genetic Tests Guiding Prescribing:**

As reported in the AMA Morning Report of 4/1/2019:

In “Health & Science,” the Washington Post (3/29, Marcus) delved into the debate among physicians whether “genetic testing helps” them “better prescribe antidepressants.” Last November, “the Food and Drug Administration...released a statement warning patients and doctors to be cautious about genetic testing that has not been approved by the FDA, including those that guide the prescribing of antidepressants.” The statement, prepared by the directors of the Center for Devices and Radiological Health and of the Center for Drug Evaluation and Research, said, “The FDA is aware of genetic tests that claim results can be used by physicians to identify which antidepressant medication would have increased effectiveness or side effects compared to other antidepressant medications.” Nevertheless, “the relationship between DNA variations and the effectiveness of antidepressant medications has never been established,” the statement added.

**Antipsychotics in Youth Increase Death?**

According to work published in JAMA Psychiatry (Ray et al., [LINK](#)) Antipsychotic use is associated with increased mortality among children and youth.

In this cohort study of 247,858 Medicaid-enrolled children and youths in Tennessee who were new users of antipsychotic or control medications, the group that received a higher dose of antipsychotic medication had a significantly increased risk of unexpected death compared with the group that received control medication.

**FDA Approves Device to Treat ADHD:**

As reported in 4/22/2019 APA Communications:

USA Today (4/20, Garrison) reported that on Friday, the FDA “announced...that it permitted marketing for the first medical device to treat” attention-deficit/hyperactivity disorder (AD/HD). Known as “the Monarch external Trigeminal Nerve Stimulation (eTNS) System, the prescription-only device is for children ages 7 to 12 who are not taking...prescription medication” for the disorder. In a statement, Carlos Peña, director of the Division of Neurological and Physical Medicine Devices in the FDA’s Center for Devices and Radiological Health, said, “This new device offers a safe, non-drug option for treatment of” AD/HD “in pediatric patients through the use of mild nerve stimulation, a first of its kind.”

CNN (4/20, Lamotte) reported that “the device should not be worn by children under the age of seven, or any child on an insulin pump, pacemaker or implanted neurostimulator.” The device “should also not be used near a cell phone, the FDA said, because the phone’s low levels of electromagnetic energy may interrupt the therapy.”
PSYCHIATRIC SUMMARY XXVIII
Summer 2019
By Frederick Langheim, MD, PhD

The Hill (4/20, Axelrod) reported that “eTNS, which is designed to fit inside one’s pocket, is connected by wire to a patch that is placed on the forehead while sleeping and delivers a “tingling” electrical impulse to branches of the trigeminal nerve.” The FDA said, “While the exact mechanism of eTNS is not yet known, neuroimaging studies have shown that eTNS increases activity in the brain regions that are known to be important in regulating attention, emotion and behavior.”

FDA Grants Breakthrough Status to Novel Antipsychotic:
As appeared in the APA communications of 5/23:
According to Medscape (5/22, Brooks, Subscription Publication), “the US Food and Drug Administration (FDA) has granted breakthrough therapy designation to" SEP-363856, “a potentially first-in-class psychotropic agent with a completely different mechanism of action [than] currently available antipsychotic agents.” While the “exact mechanism of action is unknown, SEP-363856 is thought to activate trace amine-associated receptor 1 (TAAR1) and serotonin 1A (5-HT1A) receptors.” The medication “does not bind to dopamine 2 (D2) or serotonin 2A (5-HT2A) receptors, which are thought to mediate the effects of currently available antipsychotic mechanisms.” Results from a four-week, “double-blind, placebo-controlled trial involving 245 adults hospitalized with an acute exacerbation of schizophrenia” were presented at the American Psychiatric Association’s annual meeting.

Gabapentinoids and Suicide:
As reported in the AMA Morning Rounds of 6/18/2019:
Reuters (6/17, Harding) reports that gabapentinoids appear to increase “users’ risks for suicidal behavior, unintentional overdoses, injuries and car accidents – and the risks are particularly high for teens and young adults,” researchers concluded after examining “Swedish registry data on 191,973 people age 15 and older prescribed pregabalin or gabapentin in 2006-2013.” The findings were published online June 12 in the BMJ.

MENTAL HEALTH IN THE POPULAR PRESS

Alarming Rise in Female Suicides for Ages 10-19:
As reported in the APA Communications on May 20:
Bloomberg (5/17, Koons) reported researchers “analyzed suicide trends in 10- to 19-year-olds between 1975 and 2016,” and found that “the rate of suicide decreased from the early 1990s until 2007, but has increased in years since for both genders.” In addition, the researchers found that while “boys die by suicide at a higher overall rate than girls, female youth suicides have surged most in recent years.” The findings were published in JAMA Network Open.

Additional coverage is provided by: the New York Daily News (5/17, Vavra), NPR (5/17, Ingber, Chatterjee), TIME (5/17, Ducharme), USA Today (5/17, Haller), HealthDay (5/17), and Medscape (5/17, Citroner, Subscription Publication).

Teenage Depression, Anxiety, Bullying:
As reported in APA communications February 21:
The New York Times (2/20, Zraick) reports “most American teenagers — across demographic groups — see depression and anxiety as major problems among their peers, a new survey [of 920 teens] by the Pew Research Center found.” Results show “that 70 percent of teenagers saw mental health as a big issue,” and that “fewer teenagers cited bullying, drug addiction or gangs as major problems; those from low-income households were more likely to do so.”
Newsweek (2/20, Fearnow) says, “The Centers for Disease Control and Prevention reports that one in five American kids ages 3 through 17 – or about 15 million people – have a diagnosable mental, emotional or behavioral disorder in any given year.”

Suicide = 2nd Leading Cause of Death in Texans Aged 10-24:
As reported in 3/ /2019 APA Communication:

The Houston Chronicle (3/8, Maness) reported, “According to a recent report from the Centers for Disease Control and Prevention, suicide is the second leading cause of death of people in Texas aged 10 to 24 years.” The Chronicle added, “Suicide used to be just the second leading cause of death in 15- to 24-year-olds, but as of 2016 it is now also the second leading cause among children 10 to 14 years as well, according to the CDC.”

New Medication for Postpartum Depression:
As publicized in the AMA morning report:

The New York Times (3/19, Belluck) reports the Food and Drug Administration approved Zulresso (brexanolone) for postpartum depression. The article points out that Zulresso is the first FDA-approved drug for the condition and “works very quickly, within 48 hours.”

The AP (3/19, Johnson) reports Zulresso is “an IV drug given over 2 ½ days,” and “will cost $34,000 without insurance, plus costs for staying in a hospital or infusion center.” The article adds that “postpartum depression affects about 400,000 American women a year,” and that while “it often ends on its own within a couple weeks...it can continue for months or even years.”

Americans Among Most Stressed in World:
According to APA Headlines on 4/26/2019:

The New York Times (4/25, Chokshi) reports on a Gallup poll which found that in 2018, “Americans reported feeling stress, anger and worry at the highest levels in a decade.” In the US, nearly 55 percent of adults “said they had experienced stress during ‘a lot of the day’ prior, compared with just 35 percent globally.” The poll “found that being under 50, earning a low income and having a dim view of President Trump’s job performance were correlated with negative experiences among adults in the United States.”

TIME (4/25, Ducharme) reports that negative emotions and experiences, including “stress, anger, worry, sadness and physical pain,” were “common around the world, tying 2017’s record-setting levels, the report found.” Gallup’s measure of global positive experiences “had been on the decline for a few years, but that trend reversed in 2018, with more people reporting good experiences the day before the survey than they did in 2017.”

Medical Marijuana Associated with Increased Opioid Overdose?
Multiple popular press sources picked up on a study out of Stanford published in PNAS (Shover et al, LINK) which appears to contradict previous work citing reduced opioid deaths in states with medical marijuana (Bachhuber et al, JAMA Internal Medicine, LINK). While the earlier study, using death certificates, found that medical marijuana laws were associated with reduced opioid overdose deaths, The more recent study found that:

Not only did findings from the original analysis not hold over the longer period, but the association between state medical cannabis laws and opioid overdose mortality reversed direction from −21% to +23% and remained positive after accounting for recreational cannabis laws.
MENTAL HEALTH POLICY

Increased Minimum Wage = Decreased Suicide?
A retrospective panel study published in The American Journal of Preventive Medicine (Gertner, Rotter and Shafer, [LINK]) examined the linear association between changes in minimum wage and suicide rates across all 50 states from the period 2006 to 2016. They reported:

There were approximately 432,000 deaths by suicide in the study period. A one-dollar increase in the real minimum wage was associated on average with a 1.9% decrease in the annual state suicide rate in adjusted analyses. This negative association was most consistent in years since 2011. An annual decrease of 1.9% in the suicide rate during the study period would have resulted in roughly 8,000 fewer deaths by suicide. Analyses by race and sex did not reveal substantial variation in the association between minimum wages and suicides.

UK School-based Mindfulness:
According to a 2/4/2019 news release from the government of the United Kingdom ([LINK])
Education Secretary Damian Hinds announces that up to 370 schools in England will take part in a series of trials testing different approaches to supporting young people’s mental health.
Children will benefit from mindfulness exercises, relaxation techniques and breathing exercises to help them regulate their emotions, alongside pupil sessions with mental health experts. The study will run until 2021 and aims to give schools new, robust evidence about what works best for their students’ mental health and wellbeing.

Federally Funded Bed-Finder:
Much like the state driven psychiatric bed locator in Wisconsin, 23 states are involved in a pilot to provide emergency rooms real-time access to psychiatric bed availability. As reported in APA Communications of 2/25/2019:
The Omaha (NE) World-Herald (2/23, Anderson) reported the federal Substance Abuse and Mental Health Services Administration and the National Association of State Mental Health Program Directors are jointly funding a program which selected 23 states to develop “centralized, real-time” healthcare registries that can help mental health emergency care professionals locate inpatient psychiatric beds. Nebraska is among the states – and the only one from the Midwest – participating in the program, through which each state received a $150,000 grant to develop the registries.

Marijuana Legalization Reduces Use among Youth?
In an article published by The American Journal of Drug and Alcohol Abuse ([LINK]), Levine Coley et al. argue that small but significant reductions in use of marijuana among youth correlate with legalization of marijuana use.

Illinois Legalizes Recreational Marijuana:
The AP (6/25, Subscription Publication) reports Illinois Gov. J.B. Pritzker signed a bill legalizing recreational marijuana in the state. The new law makes Illinois the 11th state to legalize recreational marijuana, but “the first to implement a comprehensive statewide cannabis marketplace designed by legislators.”

The Chicago Tribune (6/25, McCoppin) reports the new law “will allow the licensed growth, sales, possession and consumption of cannabis for adults 21 and older.” The new law also “provides for automatic expungement of arrests for marijuana possession under 30 grams, and” Pritzker said “he will pardon those with convictions for possession up to 30 grams.”
Reuter's (6/25, Pierog) reports legal sales of recreational marijuana are “projected to generate over $57 million in new tax and fee revenue in fiscal 2020, which begins on July 1. Marijuana-related tax revenue is estimated to climb to $140.5 million in fiscal 2021 and to $375.5 million in fiscal 2024, according to Illinois’ revenue department.”

Additional coverage is provided by: ABC News (6/25, Keneally), Fox News (6/25, O'Reilly), and The Hill (6/25, Rodrigo).