Medicine

Subordinating Health Research to Ideology

Partisanship often dominates the discussion of issues related to public health. Even when researchers attempt an evidence-based review, their conclusions usually reflect a priori political positions rather than incorporate all reasonable interpretations of the data. In a perspective published in the *New England Journal of Medicine* on September 27, 2018, Garen Wintemute expresses concern that the recent mass shootings "are changing the character of public life" and "creating an unprecedented demand for action."[1] There are two policies that, in his opinion, can be used to stop mass shootings: background checks and the temporary removal of guns from people who pose a risk to themselves or others. Although Wintemute cites findings that such laws reduce firearm-related arrests and suicides, he gives no evidence that they reduce the incidence of mass shootings or any type of shooting for that matter.

Instead of illustrating the positive effect of legislation, he focuses on how our existing background check laws "fall short of their expected effectiveness when it comes to reducing population-level rates of violence," such as the Air Force's failure to report tens of thousands of events that would have prohibited airmen from procuring firearms. Wintemute laments the fact that in the Supreme Court decision *Printz v. United States*, a federal mandate for states and local agencies to report prohibiting events to the federal government was seen as unconstitutional. It is interesting that he thinks this would reduce mass shootings, considering that the current mandatory reporting laws have largely proven ineffective.

In fact, a number of sources indicate that more restrictive regulation would have little effect on firearm-related homicides. Wintemute references a study, which he coauthored, that "found no evidence of an association between the repeal of

1. Garen J. Wintemute, "How to Stop Mass Shootings," *New England Journal of Medicine* 379.13 (September 27, 2018): 1193–1196, doi: 10.1056/NEJMp1807277.

comprehensive background check policies and firearm homicide and suicide rates in Indiana or Tennessee."[2] In an article in *The Hill*, John Lott shows that, since 2000, all of the mass shooters in the United States obtained weapons legally without private transfers, often in states that already had universal background checks.[3] Other data suggest that additional, less talked about factors have a considerable effect on gun violence. According to the Federal Bureau of Investigation, the overall homicide rate in the United States was cut almost in half from 9.8 homicides per 100,000 persons in 1991 to 5.5 per 100,000 in 2004.[4] For those who advocate for stricter gun control laws, this is not part of the party line.

Few places are partisan talking points and emotional appeals as evident as in the context of school shootings. Contrary to vocal concern from school officials, the Department of Justice reported that "school crime rates are decreasing," and "school shooting are rare. … Today's students are less likely to be threatened or injured with a weapon, including a gun, at school than they were 10 years ago."[5] According to recent research conducted by James Fox of Northeastern University, "mass school shootings are incredibly rare events. … Mass murders occur between 20 and 30 times per year, and about one of those incidents on average takes place at school."[6] When we discuss hot-button political issues, we should set our agendas aside and try to look at the problem with nonpartisan glasses.

Balancing Beneficent Care and Community Needs

In the August 9, 2018, issue of the *New England Journal of Medicine*, William Grobman and colleagues reported on a multicenter randomized trial looking at the induction of labor at thirty-nine weeks of gestation among low-risk nulliparous women.[7] The patients were either induced at thirty-nine weeks or had expectant management. The results were surprising: induction of labor did not reduce perinatal death and severe neonatal complications, but it did reduce cesarean deliveries.

2. Rose M. C. Kagawa et al., "Repeal of Comprehensive Background Check Policies and Firearm Homicide and Suicide," *Epidemiology* 29.4 (July 2018): 494, doi: 10.1097/EDE.0000000000000838.

3. John Lott Jr., "Background Checks Do Not Diminish Crime Rates, but Can Increase Them," *The Hill*, accessed November 30, 2018, https://thehill.com/.

4. James Alan Fox et al., "Homicide Trends in the United States," Bureau of Justice Statistics, accessed November 30, 2018, https://www.bjs.gov/content/pub/pdf/htius.pdf.

5. "School Safety: By the Numbers," fact sheet, US Department of Justice, 1, November 2017, https://www.ncjrs.gov/.

6. Allie Nicodemo and Lia Petronio, "Schools Are Safer Than They Were in the 90s, and School Shootings Are Not More Common Than They Used to Be, Researchers Say," *News at Northeastern*, February 26, 2018, https://news.northeastern.edu/.

7. William A. Grobman et al., "Labor Induction versus Expectant Management in Low-Risk Nulliparous Women," *New England Journal of Medicine* 379.6 (August 9, 2018): 513–523, doi: 10.1056/NEJMoa1800566.

Previous research has shown an increase in the rate of cesarean delivery, especially in nulliparous women, and an increase in adverse maternal and perinatal outcomes.[8]

After reviewing these surprising results, the American College of Obstetricians and Gynecologists and the Society for Maternal–Fetal Medicine "determined that it is reasonable for obstetric care providers to offer an induction of labor to low-risk women after discussing the options thoroughly, as shared decision making is a critical element. Women eligible for induction must meet the following criteria: women who are planning their first delivery, are healthy and have no medical or obstetrical complications [or] women who are 39 weeks pregnant and had an ultrasound performed early in the pregnancy to confirm dating."[9] This represents a change in practice that could affect labor and delivery throughput. Induction of labor usually takes longer than natural birth, and with limited resources, this could place a strain on hospital infrastructure. This could create a conflict for providers: they would like to do what is best for mothers and their babies—induction of labor at thirty-nine weeks—but this may affect the overall ability of the hospital to provide safe obstetrical care by straining already limited resources.

Reminder of the Times We Live in

Smallpox, caused by the variola virus, was declared eradicated in 1980. However, it remains a concern because of its possible release as a bioweapon, and some nations, including Iraq and North Korea, possess stocks of smallpox.[10] In response to this threat, Douglas Grosenbach and colleagues evaluated the efficacy of oral tecovirimat as a treatment in nonhuman primate (monkeypox) and rabbit (rabbitpox) models.[11] They concluded that the treatment should be advanced as a therapy for smallpox. It is disturbing to think that this could happen in this day and age. It seems like something out of a Hollywood movie. However, it is just a reminder that evil definitely exists in our world.

Abstinence Is a Social Good

In the August 2018 issue of *Pediatrics*, Sharon Levy and colleagues assessed trends in abstaining from substance use in adolescents from 1975 to 2014.[12] They found that the proportion of high school seniors who have never consumed alcohol was more than five times greater in 2014 than in 1975. Similar trends were seen for tobacco and marijuana. Think about that—adolescents today are much more likely to

8. ACOG Committee on Practice Bulletins, "Induction of Labor," practice bulletin no. 107, August 2009, available at https://www.mnhospitals.org/.

9. American College of Obstetricians and Gynecologists and Society for Maternal–Fetal Medicine, "Leaders in Obstetric Care Respond to the Published Results of the ARRIVE Trail," news release, August 8, 2018, https://www.acog.org/.

10. Barton Gellman, "4 Nations Thought to Possess Smallpox," *Washington Post*, November 5, 2002, http://www.washingtonpost.com/.

11. Douglas W. Grosenbach et al., "Oral Tecovirimat for the Treatment of Smallpox," *New England Journal of Medicine* 379.1 (July 5, 2018): 44–53, doi: 10.1056/NEJMoa1705688.

12. Sharon Levy et al., "Trends in Abstaining from Substance Use in Adolescents: 1974–2014," *Pediatrics* 142.2 (August 2018), e20173498, doi: 10.1542/peds.2017-3498.

completely abstain from alcohol, tobacco, and marijuana, compared with adolescents in 1975. The study found that religious affiliation is associated with abstinence. The authors suggested various explanations for the decrease in substance use, such as a national law in 1984 that raised the drinking age to twenty-one. In addition, alcohol is seen as unhealthy, and a "reduced social tolerance accelerated the stigmatization of smoking." These social pressures have been reduced recently with respect to marijuana: "The impetus toward increased youth marijuana use has been furthered by a powerful marijuana lobby and emerging industry that work to portray marijuana as medicine and safer than alcohol, despite significant contrary evidence." In other words, a negative societal impression of a substance promotes lifetime abstinence, and when a substance is glorified or made to look beneficial, its use increases.

These findings have important implications with respect to sexual activity. It is interesting that we can expect adolescents to have the know-how and willpower to abstain from illegal substances, but we accept that they are ruled by their emotions when it comes to sexual activity! Furthermore, society's perception of a behavior can affect adolescents' ability to abstain from it—when society looks at something as normal or good, its use increases. At the University of California, San Francisco, for example, a key aspect of the approach to sexuality, sexual activity, and HIV prevention is that "all teens have sexual lives, whether with others or through fantasies. An important part of adolescence is thinking about and experimenting with aspects of your sexuality. This will help you grow and discover who you are."[13]

Imagine if we replaced *sexuality* with *substance use*. It would look glorious, something that should be explored. Similar to substance use, sexual behavior can negatively affect adolescents' physical and psychological health, but there is a push to normalize it nonetheless. The idea of abstinence, while advocated by some, is presented as only an alternative to jumping into the pool of sexual activity.[14] If we can expect our teens to have the willpower to resist substance use, why can we not expect them to do the same thing regarding sexual activity?

Overestimating Suicide Incidence in US Hospitals

One would think that we would be able to accurately measure how often something like suicide occurs in US hospitals. Surprisingly, we cannot. In 2003, the American Psychiatric Association estimated that there were fifteen hundred inpatient suicides in the United States each year and that one-third of these occurred with either one-on-one observation or checks every fifteen minutes.[15] Scott Williams and colleagues used two national databases to assess the incidence and method of sui-

13. "Guidelines for Teens: Thinking about Sexuality and Sexual Activity," *HIV InSite*, September 2000, http://hivinsite.ucsf.edu/.

14. See my Summer 2018 column. See also Arik V. Marcell, Gale R. Burstein, and Committee on Adolescence, "Sexual and Reproductive Health Care Services in the Pediatric Setting," *Pediatrics* 140.5 (October 2017), e20172858, doi: 10.1542/peds.2017-2858.

15. American Psychiatric Association, "Practice Guideline for the Assessment and Treatment of Patients with Suicidal Behaviors," *American Journal of Psychiatry* 160 suppl 11 (November 2003): 1–60.

cide in US hospitals for 2014–2015.[16] This was the first data-driven yearly estimate for US hospitals. They found that the incidence ranges from 48.5 to 64.9 inpatient suicides per year. This is a far cry from the approximately fifteen hundred that still is widely quoted. Hanging was the most common method, and 31 to 52 percent of suicides occurred during psychiatric treatment.

Better understanding the rate and causes of suicide is the first step toward reducing this tragic event. As noted in a 2018 review of suicide prevention measures, "It is obvious from the research literature that there are extensive gaps in our knowledge about what works to prevent suicide and how the different levels of intervention (USI) interact."[17] While it is beneficial to prevent inpatient suicides, the emphasis should also be moved upstream in the clinical arena to better assess who is at risk. Losing a loved one to suicide is tragic. Having it happen under the supervision of health care providers may be even more heartbreaking, since a hospital should be a place where one can feel that his or her loved one is safe.

Quest for the Perfect Child

Similar to how ultrasound has removed the mystery surrounding fetal development and congenital anomalies, prenatal genetic testing is becoming sensitive enough to detect even the most covert genetic disorders. As technology for prenatal diagnosis continues to improve, it seems like the quest for the perfect child becomes a greater preoccupation for parents. Our ability to detect smaller and smaller imperfections in the DNA is increasing. Jing Wang and colleagues prospectively analyzed 3,429 amniocentesis samples in China using next-generation sequencing methodology—copy number variation sequencing—in a high-risk pregnancy population.[18] They found that this technology reliably and accurately identified fetal anomalies, making it a suitable first-line test. They identified 146 fetal genetic abnormalities. The overall percentage of variants of unknown clinical significance was 1.43 percent. Imagine being told that your child may have a genetic syndrome that may or may not affect him later in life?

There is nothing wrong with the information that is gained from this advanced genetic testing. What is done with it is a different matter. The authors state, "Thus, the application of CNV-Seq was able to identify a significant number of additional anomalies that would have been missed by karyotyping, *avoiding the possibility of the birth of children with a chromosome disease syndrome if the abnormality was compatible with viability to term*" (emphasis added). As we can see, the clinical

16. Scott C. Williams et al., "Incidence and Methods of Suicide in Hospitals in the United States," *Joint Commission Journal on Quality and Patient Safety* 44.11 (November 2018): 643–650, doi: 10.1016/j.jcjq.2018.08.002.

17. Rory C. O'Connor and Gwendolyn Portzky, "Looking to the Future: A Synthesis of New Developments and Challenges in Suicide Research and Prevention," *Frontiers of Psychology* 9 (November 2018), 2139: 8, doi: 10.3389/fpsyg.2018.02139.

18. Jing Wang et al., "Prospective Chromosome Analysis of 3429 Amniocentesis Samples in China Using Copy Number Variation Sequencing," *American Journal of Obstetrics and Gynecology* 219.3 (September 2018): 287.e1–287.e18, doi: 10.1016/j.ajog.2018.05.030.

utility of this testing is to *avoid* the birth of children with genetic diseases. As physicians, should we share this with patients? Should we tell them that this test is being introduced to avoid the birth of children with genetic diseases? Who defines genetic disease? If we have traveled this far down the rabbit hole as a society, then it may not be a leap to say that this technology could be used to avoid the birth of children with other, less-severe "diseases" such as mild autism, low IQ, or even ADHD.

The fetus is under increasing attack from prenatal diagnostics aimed at finding out every possibly problem with an unborn child. Imagine if we used this screening at birth for euthanasia to avoid not the birth of these children, but the continuation of life? Could health care resources be better used elsewhere? Could you envision an economical argument for this type of testing? These issues are not far off, and we will need to provide an answer.

Jay Bringman, MD

Medicine Abstracts

American Journal of Obstetrics and Gynecology

J. Wang et al., **Prospective chromosome analysis of 3429 amniocentesis samples in China using copy number variation sequencing**, *Am J Obstet Gynecol* 219.3 (September 2018): 287.e1–287.e18, doi: 10.1016/j.ajog.2018.05.030 • *Background:* Next-generation sequencing is emerging as a viable alternative to chromosome microarray analysis for the diagnosis of chromosome disease syndromes. One next-generation sequencing methodology, copy number variation sequencing, has been shown to deliver high reliability, accuracy, and reproducibility for detection of fetal copy number variations in prenatal samples. However, its clinical utility as a first-tier diagnostic method has yet to be demonstrated in a large cohort of pregnant women referred for fetal chromosome testing. *Objective:* We sought to evaluate copy number variation sequencing as a first-tier diagnostic method for detection of fetal chromosome anomalies in a general population of pregnant women with high-risk prenatal indications. *Study Design:* This was a prospective analysis of 3429 pregnant women referred for amniocentesis and fetal chromosome testing for different risk indications, including advanced maternal age, high-risk maternal serum screening, and positivity for an ultrasound soft marker. Amniocentesis was performed by standard procedures. Amniocyte DNA was analyzed by copy number variation sequencing with a chromosome resolution of 0.1 Mb. Fetal chromosome anomalies including whole chromosome aneuploidy and segmental imbalances were independently confirmed by gold standard cytogenetic and molecular methods and their pathogenicity determined following guidelines of the American College of Medical Genetics for sequence variants. *Results:* Clear interpretable copy number variation sequencing results were obtained for all 3429 amniocentesis samples. Copy number variation sequencing identified 3293 samples (96%) with a normal molecular karyotype and 136 samples (4%) with an altered molecular karyotype. A total of 146 fetal chromosome anomalies were detected, comprising 46 whole chromosome aneuploidies (pathogenic), 29 submicroscopic microdeletions/microduplications with known or suspected associations with chromosome disease syndromes (pathogenic), 22 other microdeletions/microduplications (likely pathogenic), and 49 variants of uncertain significance. Overall, the cumulative frequency of pathogenic/likely pathogenic and variants of uncertain significance chromosome anomalies in the patient cohort was 2.83% and 1.43%, respectively. In the 3 high-risk advanced maternal age, high-risk maternal serum screening, and ultrasound soft marker groups, the most common whole chromosome aneuploidy detected was trisomy 21, followed by sex chromosome aneuploidies, trisomy 18, and trisomy 13. Across all clinical indications, there was a similar incidence of submicroscopic copy number variations, with approximately equal proportions of pathogenic/likely pathogenic and variants of uncertain significance copy number variations. If karyotyping had been used as an alternate cytogenetics detection method, copy number variation sequencing would have returned a 1% higher yield of pathogenic or likely pathogenic copy number variations. *Conclusion:* In a large prospective clinical study, copy number variation sequencing delivered high reliability and accuracy for identifying clinically significant fetal anomalies in prenatal samples. Based on key performance criteria, copy number variation sequencing appears to be a well-suited methodology for first-tier diagnosis of pregnant women in the general population at risk of having a suspected fetal chromosome abnormality.

Annals of Family Medicine

N. L. Schoenborn et al., **Older adults' preferences for discussing long-term life expectancy: Results from a national survey**, *Ann Fam Med* 16.6 (November–December 2018): 530–537, doi: 10.1370/afm.2309 • *Purpose:* Clinical practice guidelines recommend incorporating long-term life expectancy to inform a number of decisions in primary care. We aimed to examine older adults' preferences for discussing life expectancy in a national sample. *Methods:* We invited 1,272 older adults (aged 65 or older) from a national, probability-based online panel to participate in 2016. We presented a hypothetical patient with limited life expectancy who was not imminently dying. We asked participants if they were that patient, whether they would like to talk with the doctor about how long they may live, whether it was acceptable for the doctor to offer this discussion, whether they want the doctor to discuss life expectancy with family or friends, and when it should be discussed. *Results:* The 878 participants (69.0% participation rate) had a mean age of 73.4 years. The majority, 59.4%, did not want to discuss how long they might live in the presented scenario. Within this group, 59.9% also did not think that the doctor should offer the discussion, and 87.7% also did not want the doctor to discuss life expectancy with family or friends. Fully 55.8% wanted to discuss life expectancy only if it were less than 2 years. Factors positively associated with wanting to have the discussion included higher educational level, believing that doctors can accurately predict life expectancy, and past experience with either a life-threatening illness or having discussed life expectancy of a loved one. Reporting that religion is important was negatively associated. *Conclusions:* The majority of older adults did not wish to discuss life expectancy when we depicted a hypothetical patient with limited life expectancy. Many also did not want to be offered discussion, raising a dilemma for how clinicians may identify patients' preferences regarding this sensitive topic.

Epidemiology

R. M. C. Kagawa et al., **Repeal of comprehensive background check policies and firearm homicide and suicide**, *Epidemiology* 29.4 (July 2018): 494–502, doi: 10.1097/EDE.0000000000000838 • *Background:* In 2016, firearms killed 38,658 people in the United States. Federal law requires licensed gun dealers, but not private parties, to conduct background checks on prospective firearm purchasers with the goal of preventing prohibited persons from obtaining firearms. Our objective was to estimate the effect of the repeal of comprehensive background check laws—requiring a background check for all handgun sales, not just sales by licensed dealers—on firearm homicide and suicide rates in Indiana and Tennessee. *Methods:* We compared age-adjusted firearm homicide and suicide rates, measured annually from 1981 to 2008 and 1994 to 2008 in Indiana and Tennessee, respectively, to rates in control groups constructed using the synthetic control method. *Results:* The average rates of firearm homicide and suicide in Indiana and Tennessee following repeal were within the range of what could be expected, given natural variation (differences = 0.7 firearm homicides and 0.5 firearm suicides per 100,000 residents in Indiana and 0.4 firearm homicides and 0.3 firearm suicides per 100,000 residents in Tennessee). Sensitivity analyses resulted in similar findings. *Conclusion:* We found no evidence of an association between the repeal of comprehensive background check policies and firearm homicide and suicide rates in Indiana and Tennessee. In order to understand whether comprehensive background check policies reduce firearm deaths in the United States generally, more evidence on the impact of such policies from other states is needed. See video abstract at, http://links.lww.com/EDE/B353.

JAMA

P. Martin et al., **Effect of a pharmacist-led educational intervention on inappropriate medication prescriptions in older adults: The D-PRESCRIBE**

randomized clinical trial, *JAMA* 320.18 (November 13, 2018): 1889–1898, doi: 10.1001/jama.2018.16131 • *Importance:* High rates of inappropriate prescribing persist among older adults in many outpatient settings, increasing the risk of adverse drug events and drug-related hospitalizations. *Objective:* To compare the effectiveness of a consumer-targeted, pharmacist-led educational intervention vs usual care on discontinuation of inappropriate medication among community-dwelling older adults. *Design, Setting, and Participants:* A cluster randomized trial (D-PRESCRIBE [Developing Pharmacist-Led Research to Educate and Sensitize Community Residents to the Inappropriate Prescriptions Burden in the Elderly]) that recruited community pharmacies in Quebec, Canada, from February 2014 to September 2017, with follow-up until February 2018, and randomly allocated them to intervention or control groups. Patients included were adults aged 65 years and older who were prescribed 1 of 4 Beers Criteria medications (sedative-hypnotics, first-generation antihistamines, glyburide, or nonsteroidal anti-inflammatory drugs), recruited from 69 community pharmacies. Patients were screened and enrolled before randomization. *Interventions:* Pharmacists in the intervention group were encouraged to send patients an educational deprescribing brochure in parallel to sending their physicians an evidence-based pharmaceutical opinion to recommend deprescribing. The pharmacists in the control group provided usual care. Randomization occurred at the pharmacy level, with 34 pharmacies randomized to the intervention group (248 patients) and 35 to the control group (241 patients). Patients, physicians, pharmacists, and evaluators were blinded to outcome assessment. *Main Outcomes and Measures:* Discontinuation of prescriptions for inappropriate medication at 6 months, ascertained by pharmacy medication renewal profiles. *Results:* Among 489 patients (mean age, 75 years; 66% women), 437 (89%) completed the trial (219 [88%] in the intervention group vs 218 [91%] in the control group). At 6 months, 106 of 248 patients (43%) in the intervention group no longer filled prescriptions for inappropriate medication compared with 29 of 241 (12%) in the control group (risk difference, 31% [95% CI, 23% to 38%]). In the intervention vs control group, discontinuation of inappropriate medication occurred among 63 of 146 sedative-hypnotic drug users (43.2%) vs 14 of 155 (9.0%), respectively (risk difference, 34% [95% CI, 25% to 43%]); 19 of 62 glyburide users (30.6%) vs 8 of 58 (13.8%), respectively (risk difference, 17% [95% CI, 2% to 31%]); and 19 of 33 nonsteroidal anti-inflammatory drug users (57.6%) vs 5 of 23 (21.7%), respectively (risk difference, 35% [95% CI, 10% to 55%]) (*P* for interaction = .09). Analysis of the antihistamine drug class was not possible because of the small sample size (n = 12). No adverse events requiring hospitalization were reported, although 29 of 77 patients (38%) who attempted to taper sedative-hypnotics reported withdrawal symptoms. *Conclusions and Relevance:* Among older adults in Quebec, a pharmacist-led educational intervention compared with usual care resulted in greater discontinuation of prescriptions for inappropriate medication after 6 months. The generalizability of these findings to other settings requires further research. *Trial Registration:* ClinicalTrials.gov Identifier: NCT02053194.4.

L. S. Rotenstein et al., **Prevalence of burnout among physicians**, *JAMA* 320.11 (September 18, 2018): 1131–1150, doi: 10.1001/jama.2018.12777 • *Importance:* Burnout is a self-reported job-related syndrome increasingly recognized as a critical factor affecting physicians and their patients. An accurate estimate of burnout prevalence among physicians would have important health policy implications, but the overall prevalence is unknown. *Objective:* To characterize the methods used to assess burnout and provide an estimate of the prevalence of physician burnout. *Data Sources and Study Selection:* Systematic search of EMBASE, ERIC, MEDLINE/PubMed, psycARTICLES, and

psycINFO for studies on the prevalence of burnout in practicing physicians (i.e., excluding physicians in training) published before June 1, 2018. *Data Extraction and Synthesis:* Burnout prevalence and study characteristics were extracted independently by 3 investigators. Although meta-analytic pooling was planned, variation in study designs and burnout ascertainment methods, as well as statistical heterogeneity, made quantitative pooling inappropriate. Therefore, studies were summarized descriptively and assessed qualitatively. *Main Outcomes and Measures:* Point or period prevalence of burnout assessed by questionnaire. *Results:* Burnout prevalence data were extracted from 182 studies involving 109 628 individuals in 45 countries published between 1991 and 2018. In all, 85.7% (156/182) of studies used a version of the Maslach Burnout Inventory (MBI) to assess burnout. Studies variably reported prevalence estimates of overall burnout or burnout subcomponents: 67.0% (122/182) on overall burnout, 72.0% (131/182) on emotional exhaustion, 68.1% (124/182) on depersonalization, and 63.2% (115/182) on low personal accomplishment. Studies used at least 142 unique definitions for meeting overall burnout or burnout subscale criteria, indicating substantial disagreement in the literature on what constituted burnout. Studies variably defined burnout based on predefined cutoff scores or sample quantiles and used markedly different cutoff definitions. Among studies using instruments based on the MBI, there were at least 47 distinct definitions of overall burnout prevalence and 29, 26, and 26 definitions of emotional exhaustion, depersonalization, and low personal accomplishment prevalence, respectively. Overall burnout prevalence ranged from 0% to 80.5%. Emotional exhaustion, depersonalization, and low personal accomplishment prevalence ranged from 0% to 86.2%, 0% to 89.9%, and 0% to 87.1%, respectively. Because of inconsistencies in definitions of and assessment methods for burnout across studies, associations between burnout and sex, age, geography, time, specialty, and depressive symptoms could not be reliably determined. *Conclusions and Relevance:* In this systematic review, there was substantial variability in prevalence estimates of burnout among practicing physicians and marked variation in burnout definitions, assessment methods, and study quality. These findings preclude definitive conclusions about the prevalence of burnout and highlight the importance of developing a consensus definition of burnout and of standardizing measurement tools to assess the effects of chronic occupational stress on physicians.

JAMA Internal Medicine

J. Baudry et al., **Association of frequency of organic food consumption with cancer risk: Findings from the NutriNet-Santé prospective cohort study**, *JAMA Intern Med* 178.12 (December 2018): 1597–1606, doi: 10.1001/jamainternmed.2018.4357 • *Importance:* Although organic foods are less likely to contain pesticide residues than conventional foods, few studies have examined the association of organic food consumption with cancer risk. *Objective:* To prospectively investigate the association between organic food consumption and the risk of cancer in a large cohort of French adults. *Design, Setting, and Participants:* In this population-based prospective cohort study among French adult volunteers, data were included from participants with available information on organic food consumption frequency and dietary intake. For 16 products, participants reported their consumption frequency of labeled organic foods (never, occasionally, or most of the time). An organic food score was then computed (range, 0–32 points). The follow-up dates were May 10, 2009, to November 30, 2016. *Main Outcomes and Measures:* This study estimated the risk of cancer in association with the organic food score (modeled as quartiles) using Cox proportional hazards regression models adjusted for potential cancer risk factors. *Results:* Among 68 946 participants (78.0% female; mean [SD] age at baseline, 44.2 [14.5] years), 1340 first incident cancer cases were identified during follow-up, with the most prevalent being 459 breast cancers, 180 prostate cancers, 135 skin cancers, 99 colorectal cancers, 47 non-Hodgkin

lymphomas, and 15 other lymphomas. High organic food scores were inversely associated with the overall risk of cancer (hazard ratio for quartile 4 vs quartile 1, 0.75; 95% CI, 0.63–0.88; *P* for trend = .001; absolute risk reduction, 0.6%; hazard ratio for a 5-point increase, 0.92; 95% CI, 0.88–0.96). *Conclusions and Relevance:* A higher frequency of organic food consumption was associated with a reduced risk of cancer. If these findings are confirmed, further research is necessary to determine the underlying factors involved in this association.

M. Panagioti et al., **Association between physician burnout and patient safety, professionalism, and patient satisfaction: A systematic review and meta-analysis**, *JAMA Intern Med* 178.10 (October 2018): 1317–1330, doi: 10.1001/jamainternmed.2018.3713 • *Importance:* Physician burnout has taken the form of an epidemic that may affect core domains of health care delivery, including patient safety, quality of care, and patient satisfaction. However, this evidence has not been systematically quantified. *Objective:* To examine whether physician burnout is associated with an increased risk of patient safety incidents, suboptimal care outcomes due to low professionalism, and lower patient satisfaction. *Data Sources:* MEDLINE, EMBASE, PsycInfo, and CINAHL databases were searched until October 22, 2017, using combinations of the key terms *physicians*, *burnout*, and *patient care*. Detailed standardized searches with no language restriction were undertaken. The reference lists of eligible studies and other relevant systematic reviews were hand-searched. *Study Selection:* Quantitative observational studies. *Data Extraction and Synthesis:* Two independent reviewers were involved. The main meta-analysis was followed by subgroup and sensitivity analyses. All analyses were performed using random-effects models. Formal tests for heterogeneity (I^2) and publication bias were performed. *Main Outcomes and Measures:* The core outcomes were the quantitative associations between burnout and patient safety, professionalism, and patient satisfaction reported as odds ratios (ORs) with their 95% CIs. *Results:* Of the 5234 records identified, 47 studies on 42 473 physicians (25 059 [59.0%] men; median age, 38 years [range, 27–53 years]) were included in the meta-analysis. Physician burnout was associated with an increased risk of patient safety incidents (OR, 1.96; 95% CI, 1.59–2.40), poorer quality of care due to low professionalism (OR, 2.31; 95% CI, 1.87–2.85), and reduced patient satisfaction (OR, 2.28; 95% CI, 1.42–3.68). The heterogeneity was high and the study quality was low to moderate. The links between burnout and low professionalism were larger in residents and early-career (≤5 years post residency) physicians compared with middle- and late-career physicians (Cohen $Q = 7.27$; $P = .003$). The reporting method of patient safety incidents and professionalism (physician-reported vs system-recorded) significantly influenced the main results (Cohen $Q = 8.14$; $P = .007$). *Conclusions and Relevance:* This meta-analysis provides evidence that physician burnout may jeopardize patient care; reversal of this risk has to be viewed as a fundamental health care policy goal across the globe. Health care organizations are encouraged to invest in efforts to improve physician wellness, particularly for early-career physicians. The methods of recording patient care quality and safety outcomes require improvements to concisely capture the outcome of burnout on the performance of health care organizations.

Joint Commission Journal on Quality and Patient Safety

S. C. Williams et al., **Incidence and methods of suicide in hospitals in the United States**, *Jt Comm J Qual Patient Saf* 44.11 (November 2018): 643–650, doi: 10.1016/j.jcjq.2018.08.002 • *Background:* There are no reliable estimates of hospital inpatient suicides in the United States. Understanding the rate and the methods used in suicides is important to guide prevention efforts. This study analyzed two national data sets to establish an evidence-based estimate of hospital inpatient suicides and the methods used. *Methods:* The study is designed as a cross-sectional analysis of data from 27 states

reporting to the National Violent Death Reporting System (NVDRS) for 2014–2015, and from hospitals reporting to The Joint Commission's Sentinel Event (SE) Database from 2010 to 2017. Categorical variables and qualitative reviews of event narratives were used to identify and code suicide events occurring during hospital inpatient treatment. *Results:* Based on the hospital inpatient suicides reported in the NVDRS during 2014–2015, 73.9% of which occurred during psychiatric treatment, it is estimated that between 48.5 and 64.9 hospital inpatient suicides occur per year in the United States. Of these, 31.0 to 51.7 are expected to involve psychiatric inpatients. Hanging was the most common method of inpatient suicide in both the NVDRS and SE databases (71.7% and 70.3%, respectively). *Conclusion:* The estimated number of hospital inpatient suicides per year in the United States ranges from 48.5 to 64.9, which is far below the widely cited figure of 1,500 per year. Analysis of inpatient suicide methods suggests that hospital prevention efforts should be primarily focused on mitigating risks associated with hanging, and additional suicide prevention efforts may be best directed toward reducing the risk of suicide immediately following discharge.

New England Journal of Medicine

W. A. Grobman et al., **Labor induction versus expectant management in low-risk nulliparous women**, *N Engl J Med* 379.6 (August 9, 2018): 513–523, doi: 10.1056/NEJMoa1800566 • *Background:* The perinatal and maternal consequences of induction of labor at 39 weeks among low-risk nulliparous women are uncertain. *Methods:* In this multicenter trial, we randomly assigned low-risk nulliparous women who were at 38 weeks 0 days to 38 weeks 6 days of gestation to labor induction at 39 weeks 0 days to 39 weeks 4 days or to expectant management. The primary outcome was a composite of perinatal death or severe neonatal complications; the principal secondary outcome was cesarean delivery. *Results:* A total of 3062 women were assigned to labor induction, and 3044 were assigned to expectant management. The primary outcome occurred in 4.3% of neonates in the induction group and in 5.4% in the expectant-management group (relative risk, 0.80; 95% confidence interval [CI], 0.64 to 1.00). The frequency of cesarean delivery was significantly lower in the induction group than in the expectant-management group (18.6% vs. 22.2%; relative risk, 0.84; 95% CI, 0.76 to 0.93). *Conclusions:* Induction of labor at 39 weeks in low-risk nulliparous women did not result in a significantly lower frequency of a composite adverse perinatal outcome, but it did result in a significantly lower frequency of cesarean delivery. (Funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development; ARRIVE ClinicalTrials.gov number, NCT01990612.)

D. W. Grosenbach et al., **Oral tecovirimat for the treatment of smallpox**, *N Engl J Med* 379.1 (July 5, 2018): 44–53, doi: 10.1056/NEJMoa1705688 • *Background:* Smallpox was declared eradicated in 1980, but variola virus (VARV), which causes smallpox, still exists. There is no known effective treatment for smallpox; therefore, tecovirimat is being developed as an oral smallpox therapy. Because clinical trials in a context of natural disease are not possible, an alternative developmental path to evaluate efficacy and safety was needed. *Methods:* We investigated the efficacy of tecovirimat in nonhuman primate (monkeypox) and rabbit (rabbitpox) models in accordance with the Food and Drug Administration (FDA) Animal Efficacy Rule, which was interpreted for smallpox therapeutics by an expert advisory committee. We also conducted a placebo-controlled pharmacokinetic and safety trial involving 449 adult volunteers. *Results:* The minimum dose of tecovirimat required in order to achieve more than 90% survival in the monkeypox model was 10 mg per kilogram of body weight for 14 days, and a dose of 40 mg per kilogram for 14 days was similarly efficacious in the rabbitpox model. Although the effective dose per kilogram was higher in rabbits, exposure was lower, with a mean steady-state maximum, minimum, and average (mean) concentration (C_{max}, C_{min}, and C_{avg}, respectively) of 374, 25, and 138 ng per

milliliter, respectively, in rabbits and 1444, 169, and 598 ng per milliliter in nonhuman primates, as well as an area under the concentration–time curve over 24 hours ($AUC_{0–24hr}$) of 3318 ng × hours per milliliter in rabbits and 14,352 ng × hours per milliliter in nonhuman primates. These findings suggested that the nonhuman primate was the more conservative model for the estimation of the required drug exposure in humans. A dose of 600 mg twice daily for 14 days was selected for testing in humans and provided exposures in excess of those in nonhuman primates (mean steady-state C_{max}, C_{min}, and C_{avg} of 2209, 690, and 1270 ng per milliliter and $AUC_{0–24hr}$ of 30,632 ng × hours per milliliter). No pattern of troubling adverse events was observed. *Conclusions:* On the basis of its efficacy in two animal models and pharmacokinetic and safety data in humans, tecovirimat is being advanced as a therapy for smallpox in accordance with the FDA Animal Rule. (Funded by the National Institutes of Health and the Biomedical Advanced Research and Development Authority; ClinicalTrials.gov number, NCT02474589.)

J.M. McWilliams et al., **Medicare spending after 3 years of the Medicare Shared Savings Program**, *N Engl J Med* 379.12 (September 20, 2018): 1139–1149, doi: 10.1056/NEJMsa1803388 • *Background:* Health care providers who participate as an accountable care organization (ACO) in the voluntary Medicare Shared Savings Program (MSSP) have incentives to lower spending for Medicare patients while achieving high performance on a set of quality measures. Little is known about the extent to which early savings achieved by ACOs in the program have grown and been replicated by ACOs that entered the program in later years. ACOs that are physician groups have stronger incentives to lower spending than hospital-integrated ACOs. *Methods:* Using fee-for-service Medicare claims from 2009 through 2015, we performed difference-in-differences analyses to compare changes in Medicare spending for patients in ACOs before and after entry into the MSSP with concurrent changes in spending for local patients served by providers not participating in the MSSP (control group). We estimated differential changes (i.e., the between-group difference in the change from the pre-entry period) separately for hospital-integrated ACOs and physician-group ACOs that entered the MSSP in 2012, 2013, or 2014. *Results:* MSSP participation was associated with differential spending reductions in physician-group ACOs. These reductions grew with longer participation in the program and were significantly greater than the reductions in hospital-integrated ACOs. By 2015, the mean differential change in per-patient Medicare spending was −$474 (−4.9% of the pre-entry mean, $P < 0.001$) for physician-group ACOs that entered in 2012, −$342 (−3.5% of the pre-entry mean, $P < 0.001$) for those that entered in 2013, and −$156 (−1.6% of the pre-entry mean, $P = 0.009$) for those that entered in 2014. The corresponding differential changes for hospital-integrated ACOs were −$169 ($P = 0.005$), −$18 ($P = 0.78$), and $88 ($P = 0.14$), which were significantly lower than for physician-group ACOs ($P < 0.001$). Spending reductions in physician-group ACOs constituted a net savings to Medicare of $256.4 million in 2015, whereas spending reductions in hospital-integrated ACOs were offset by bonus payments. *Conclusions:* After 3 years of the MSSP, participation in shared-savings contracts by physician groups was associated with savings for Medicare that grew over the study period, whereas hospital-integrated ACOs did not produce savings (on average) during the same period. (Funded by the National Institute on Aging.)

Pediatrics

Committee on Infectious Diseases, **Recommendations for prevention and control of influenza in children, 2018–2019**, *Pediatrics* 142.4 (October 2018), e20182367, doi: 10.1542/peds.2018-2367 • The authors of this statement update the recommendations of the American Academy of Pediatrics for the routine use of influenza vaccine and antiviral medications in the prevention and treatment of influenza in children. Highlights for the upcoming 2018–2019 season include the following: (1) Annual influenza immunization is recommended for everyone 6 months and

older, including children and adolescents. (2) The American Academy of Pediatrics recommends an inactivated influenza vaccine (IIV), trivalent or quadrivalent, as the primary choice for influenza vaccination in children because the effectiveness of a live attenuated influenza vaccine against influenza A(H1N1) was inferior during past influenza seasons and is unknown for this upcoming season. (3) A live attenuated influenza vaccine may be used for children who would not otherwise receive an influenza vaccine (e.g., refusal of an IIV) and for whom it is appropriate because of age (2 years of age and older) and health status (i.e., healthy and without any underlying chronic medical condition). (4) All 2018–2019 seasonal influenza vaccines contain an influenza A(H1N1) vaccine strain similar to that included in the 2017–2018 seasonal vaccines. In contrast, the influenza A(H3N2) and influenza B (Victoria lineage) vaccine strains included in the 2018–2019 trivalent and quadrivalent vaccines differ from those in the 2017–2018 seasonal vaccines. (a) Trivalent vaccines contain an influenza A(Michigan/45/2015[H1N1])pdm09–like virus, an influenza A(Singapore/INFIMH-16-0019/2016[H3N2])–like virus (updated), and an influenza B (Colorado/60/2017)–like virus (B/Victoria lineage; updated). (b) Quadrivalent vaccines contain an additional B virus (Phuket/3073/2013–like virus; B/Yamagata lineage). (5) All children with egg allergy of any severity can receive an influenza vaccine without any additional precautions beyond those recommended for all vaccines. (6) Pregnant women may receive an influenza vaccine (IIV only) at any time during pregnancy to protect themselves as well as their infants, who benefit from the transplacental transfer of antibodies. Postpartum women who did not receive vaccination during pregnancy should be encouraged to receive an influenza vaccine before discharge from the hospital. Influenza vaccination during breastfeeding is safe for mothers and their infants. (7) The vaccination of health care workers is a crucial step in preventing influenza and reducing health care–associated influenza infections because health care personnel often care for individuals at high risk for influenza-related complications. (8) Pediatricians should attempt to promptly identify their patients who are suspected of having an influenza infection for timely initiation of antiviral treatment when indicated and on the basis of shared decision-making between each pediatrician and child caregiver to reduce morbidity and mortality. Although best results are seen when a child is treated within 48 hours of symptom onset, antiviral therapy should still be considered beyond 48 hours of symptom onset in children with severe disease or those at high risk of complications (see Table 2 in the full policy statement).

S. Levy et al., **Trends in abstaining from substance use in adolescents: 1974–2014**, *Pediatrics* 142.2 (August 2018), e20173498, doi: 10.1542/peds.2017-3498 • *Background and Objectives:* Adolescent substance use is a prevalent modifiable health behavior; understanding long-term trends is essential to inform prevention efforts and public health policy. We investigated changes in the proportion of substance nonuse among adolescents over a 40-year period and associations between abstinence and individual risk and protective factors. *Methods:* Data from the nationally representative Monitoring the Future survey, administered 1975–2014, were analyzed to determine the annual proportion of abstinent students. The 2014 Monitoring the Future cohort was analyzed to determine associations between nonuse and risk and protective factors. *Results:* The prevalence of abstaining seniors between 1976 and 2014 increased fivefold for lifetime abstinence and more than doubled for past 30 days; similar increases were reported by younger students between 1991 and 2014. Trend lines were distinct for alcohol, which increased steadily over the past 38 years; tobacco, which increased dramatically over the past 20 years; and marijuana and illicit drugs, which increased slightly, although not consistently, between 1976 and 2014. In 2014, students that identified as male, African American, or other race and those who reported greater religious commitment were significantly more likely to report lifetime abstinence. Students that lived in

single-parent households, spent more evenings out, worked more hours during the school year, and reported lower grades and more truancy had lower abstinence rates. *Conclusions:* Abstinence is a realistic choice for a growing proportion of high school students. With the differences in abstinence trends for individual substances, we suggest strategies for advancing prevention efforts.

A. Sims, **Infant walker–related injuries in the United States**, *Pediatrics* 142.4 (October 2018), e20174332, doi: 10.1542/peds.2017-4332 • *Objectives:* To investigate the epidemiologic characteristics of infant walker–related injuries among children <15 months old who were treated in US emergency departments and to evaluate the effect of the 2010 federal mandatory safety standard on these injuries. *Methods:* National Electronic Injury Surveillance System data from 1990 to 2014 were analyzed. *Results:* An estimated 230 676 children <15 months old were treated for infant walker–related injuries in US emergency departments from 1990 to 2014. Most of the children sustained head or neck injuries (90.6%) and 74.1% were injured by falling down the stairs in an infant walker. Among patients who were admitted to the hospital (4.5%), 37.8% had a skull fracture. From 1990 to 2003, overall infant walker–related injuries and injuries related to falling down the stairs decreased by 84.5% and 91.0%, respectively. The average annual number of injuries decreased by 22.7% ($P = .019$) during the 4-year period after the implementation of the federal mandatory safety standard compared with the 4-year period before the standard. *Conclusions:* Infant walker–related injuries decreased after the implementation of the federal mandatory safety standard in 2010. This decrease may, in part, be attributable to the standard as well as other factors, such as decreased infant walker use and fewer older infant walkers in homes. Despite the decline in injuries, infant walkers remain an important and preventable source of injury among young children, which supports the American Academy of Pediatrics' call for a ban on their manufacture and sale in the United States.

Surgery

A. I. Eid et al., **Variation of opioid prescribing patterns among patients undergoing similar surgery on the same acute care surgery service of the same institution: Time for standardization?**, *Surgery* 165.5 (November 2018): 926–930, doi: 10.1016/j.surg.2018.05.047 • *Background:* Diversion of unused prescription opioids is a major contributor to the current United States opioid epidemic. We aimed to study the variation of opioid prescribing in emergency surgery. *Methods:* Between October 2016 and March 2017, all patients undergoing laparoscopic appendectomy, laparoscopic cholecystectomy, or inguinal hernia repair in the acute care surgery service of 1 academic center were included. For each patient, we systematically reviewed the electronic medical record and the prescribing pharmacy platform to identify: (1) history of opioid abuse, (2) opioid intake 3 months preoperatively, (3) number of opioid pills prescribed, (4) prescription of nonopioid pain medications (e.g., acetaminophen, ibuprofen), and (5) the need for opioid prescription refills. The mean and range of opioid pills prescribed, as well as their oral morphine equivalent, were calculated. *Results:* A total of 255 patients were included (43.5% laparoscopic appendectomy, 44.3% laparoscopic cholecystectomy, and 12.1% inguinal hernia repair). The mean age was 47.5 years, 52.1% were female, 11.4% had a history of opioid use, and 92.5% received opioid prescriptions upon hospital discharge. Only 70.9% of patients were instructed to use nonopioid pain medications. The mean and range of opioid pills prescribed were 17.4; 0–56 (laparoscopic appendectomy), 17.1; 0–75 (laparoscopic cholecystectomy), and 20.9; 0–50 (inguinal hernia repair), while the range of prescribed oral morphine equivalent was 0–600 mg for laparoscopic appendectomy/laparoscopic cholecystectomy and 0–375 mg for inguinal hernia repair. No patients required any opioid medication refills. *Conclusion:* Even within the same surgical service, wide variation of opioid prescription was observed. Guidelines that standardize pain management may help prevent opioid overprescribing.