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Deploying science to change hearts and minds: Responding to the opioid crisis

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ABSTRACT

The U.S. opioid epidemic, now in its third decade, continues to claim tens of thousands of lives each year. Despite strong scientific evidence to support the deployment of effective interventions from prevention to treatment, implementation and access to quality care continue to lag, in part, due to continued opioid prescribing, siloing of treatment services for those with opioid use disorder (OUD), public support for non-evidence-based practices, stigma, and discrimination. Primary prevention efforts should focus on avoiding exposure to opioids for chronic non-cancer pain, as there is little evidence of efficacy but substantial evidence of harms. FDA-approved medications for OUD (MOUD) have incontrovertible evidence supporting their efficacy, and their use saves lives. However, fewer than 10% of those in need are able to receive MOUD. The barriers include an inadequate workforce, inadequate reimbursement, challenges navigating the treatment system, and profiteering bad actors (e.g., treatment brokers, programs delivering non-evidenced-based care). Perhaps the greatest challenge (and deterrent from receiving MOUD) is stigma and lack of public knowledge about their efficacy. Detoxification is probably the most common form of "treatment" for OUD, but the evidence shows that detoxification actually increases the risk for overdose. Expansion of MOUD delivery in the criminal justice system, health care systems and communities is essential to stemming the tide of this epidemic. This article is a call to action for the scientific community to ensure that scientific evidence is guiding patient care, funding for treatment, and policy decisions that address the opioid epidemic.

The opioid epidemic has been declared a national emergency in the United States (Gostin et al., 2017; Pitt et al., 2018) and overdose (OD) deaths from prescription opioids, synthetic opioids, and heroin continue to increase, with more than 350,000 deaths from 1999 to 2016 (Seth et al., 2018). Despite efforts to stem the tide of this public health crisis, OD deaths continue to climb nationally contributing to a reduction in life expectancy (Murphy et al., 2018). While many efforts are underway at the national, state and local community levels to address this crisis and some progress has been made, the rate of OD deaths remains high along with untold costs of additional mortality and morbidity stemming from opioid use and unsafe injection practices. There is a substantial existing evidence base that should be informing the response to this crisis, which includes the well-known harms of opioid overprescribing, the incontrovertible evidence supporting the use of medications for the treatment of opioid use disorder (MOUD), such as methadone and buprenorphine, the efficacy of naloxone as an overdose prevention tool, and the protection afforded by access to syringe service programs to decrease transmission of infectious disease. Unfortunately, many of our most effective interventions are underutilized due to historical reasons (e.g., siloing of substance use disorder care outside of mainstream medicine), lack of public awareness and understanding of the nature of opioid use disorder (OUD), insufficient funding, and, perhaps most critically, stigma and outright discrimination. This brief treatise highlights some key evidence related to supporting an evidence-based approach to the crisis and is also a plea for the scientific community to ensure that our collective work is disseminated and is used to inform critical policy decisions related to prevention and treatment.

There are three primary approaches to addressing the opioid crisis; these include criminal justice approaches (interdiction, incarceration), prevention (primary through tertiary) and treatment for those already affected by OUD. This report will not review the history of

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criminalization of drug use or the efficacy of interdiction strategies. However, it is important to note that ever-increasing potent and dangerous drugs continue to pour across our borders via land and waterways and through the mail service. With regard to incarceration, confinement to jail or prison, along with periods of supervised release, are all critical opportunities to engage affected individuals in evidence-based care- opportunities too often lost. Many states are moving towards decriminalization or "diversion" programs, such as drug courts and decreasing felony penalties for possession to misdemeanor charges. It has been estimated that 80% or more of individuals incarcerated or under criminal supervision in the United States have a substance use disorder, yet many prisons and jails offer little in the way of evidence-based treatment. The criminal justice system is a critical touch point for engaging individuals in care. While other countries (e.g., the United Kingdom) have long offered MOUD in jails and prisons (Strang et al., 2000) the United States is just beginning to venture into treatment delivery with MOUD. When medication is offered, it is most commonly naltrexone (particularly the extended release formulation) as this is more palatable to the criminal justice communities. In contrast, buprenorphine and methadone are infrequently available during incarceration or at release (Schwartz et al., 2019; Magura et al., 2009), a time when the risk of overdose is especially high and the availability of medication particularly important. Thus, expansion of evidence-based treatment within the criminal justice system is one approach that could have an immediate and significant impact on the opioid crisis.

The second primary approach to address the opioid crisis is to improve our prevention efforts. The first line of prevention is to avoid exposure. The initial cause of the current opioid crisis has been largely attributed to the unconscionable (and sometimes illegal) actions of the pharmaceutical industry, pharmaceutical distributors and some providers. Beginning in the late 1990's, Purdue Pharma began aggressively marketing its sustained release formulation of oxycodone to physicians with the claims that it was non-addictive and effective for a wide range of pain conditions (and obtaining FDA-approved prescribing language that was unusually non-specific and disease agnostic). In reality, there was little to no evidence to support the claims of opioid efficacy for moderate-to-severe chronic non-cancer pain. This effective marketing strategy increased exposure to opioids through legitimate means on a disastrous scale in the United States, the consequences of which are still being realized.

In fact, long-term opioid use has been associated with worse pain and function outcomes, chronic work loss, and lower odds of returning to work (Sjogren et al., 2010; Turner et al., 2016; Volinn et al., 2009). A commissioned panel and resulting report from the NIH Pathways to Prevention Workshop sought to review the extant evidence supporting the efficacy and safety of opioids for chronic non-cancer pain in 2014. After an extensive review and weighing of the available published literature, this panel concluded that "particularly striking to the panel was the realization that evidence is insufficient for every clinical decision that a provider needs to make about the use of opioids for chronic pain"(Reuben et al., 2015). This panel also called for the conduct of prospective, randomized controlled trials to examine the simple question of safety and efficacy- a step that is typically completed before a drug is given FDA approval for a specified indication. One recent study examined the effects of opioid versus non-opioid medications for patients with moderate-to-severe back pain or hip or knee osteoarthritis pain in Veterans Affairs primary care clinics (Krebs et al., 2018). Using a multi-site, randomized, parallel-group, treat-to-target approach, patients (n = 240) were randomly assigned to receive either an opioid regimen (e.g., immediate-release opioids, sustained-release opioids, transdermal fentanyl) OR a non-opioid regimen (e.g., acetaminophen/NSAID's, adjuvants/topicals, tramadol/pregabalin) each with three escalating options. No significant differences in pain-related function, functional response, or health-related quality of life outcomes were observed, while a significant improvement of pain intensity was found in the non-opioid group. More medication-related adverse events were found in the opioid group. These results suggest that the opioid regimen was no better than non-opioids for analgesia. Due to the lack of superiority and to the known complications arising from chronic opioid use, these data do not support the use of opioids in these chronic pain conditions.

The extensive attention and publicity about opioid overprescribing coupled with new prescribing guidelines by the CDC and others have led to a downturn in opioid prescribing in the United States in recent years (Guy Jr. et al., 2017). However, not everyone is getting the message. For example, a study of nearly 3000 commercially insured patients showed that, after an emergency department or inpatient claim of prescription opioid or heroin overdose, 91% of patients continued to receive one or more opioid prescriptions (Larochelle et al., 2016). One-third of patients were receiving higher doses of opioids than before the overdose, while 58% of patients also received a benzodiazepine prescription after the overdose, a known contraindication due to enhanced respiratory depression. A recent publication utilized a creative strategy and notified the prescribing provider by letter after their patient had fatally overdosed (Doctor et al., 2018). By comparing prescribing practices from 1 month preceding the notification to three months after, a modest decrease (9.7%) in morphine milligram equivalents (MME) prescribing and a modest decrease (7%) in the likelihood of starting a new patient on opioids were observed. Critically, this group of 170 decedents had an average of 5.5 prescribers/person at the time of their death. These findings suggest that enhanced utilization of state prescription monitoring programs and coordination of care to ensure appropriate prescribing may be an underutilized tool that could reduce overprescribing. Clearly more work is needed to change practice behavior and to align prescribing with the evidence. If additional studies are published that support the findings from Krebs et al. (2018), perhaps the evidence demonstrating the absence of efficacy along with the known significant harms of chronic opioid therapy may lead to cessation of opioid prescribing for chronic non-cancer pain altogether.

For individuals already affected by OUD, accessing evidence-based care is life-saving but is fraught with structural and cultural barriers. The treatment gap reflects several major challenges, including insufficient treatment capacity (and providers), insufficient insurance coverage, poor treatment retention, and stigma against the use of MOUD, patients who receive MOUD and even providers who prescribe MOUD. Despite the known life-saving benefits of treatment with MOUD, detoxification (and "abstinence only" programs) remain a common and perhaps, the most common, "treatment" approach in the United States. This is in spite of decades of data demonstrating that detoxification can be a deadly form of "treatment" as it actually significantly increases the risk for fatal overdose with opioids (Newman and Whitehill, 1979; Kakko et al., 2003). Pitt et al. (2018) recently modeled the impact of 11 different policies on the opioid crisis. They showed that, without any interventions, an estimated 235,000 opioid-related deaths may occur from 2016 to 2020 and 510,000 deaths from 2016 to 2025. They determined that the interventions with greatest impact on reducing OUD-related were increasing access to MOUD treatment, naloxone availability, and needle exchange services.

With regard to treatment capacity, most of the nation's 1100 Opioid Treatment Programs (i.e., federally licensed methadone programs; OTPs) are located in urban centers, and growth in the number of OTPs has been modest in the past decade (Jones et al., 2015). Buprenorphine, in contrast to methadone, is more widely delivered in non-OTP settings in office-based opioid treatment (OBOT) in the United States (Kraus et al., 2011). The number of US physicians who are DEA-waivered to prescribe buprenorphine (Knudsen et al., 2017) along with actual buprenorphine dispensing have increased (Reuben et al., 2015; Alderks, 2017), but remain insufficient to meet the national need for treatment. Use of naltrexone (oral and depot) is limited except in criminal justice settings. While modest increases in the number of patients receiving MOUD have been achieved, the actual percentage of coverage has declined (from 25% in 2010 to 16% in 2014) due to increasing numbers of

affected individuals (Reuben et al., 2015; Morgan et al., 2018). This same study also revealed that retention in treatment with MOUD is very poor. Discontinuation rates of MOUD at 30 days after initiation of the prescription were reported at 70% for oral naltrexone, 52% for extended-release naltrexone, 58% for sublingual buprenorphine, and 31% for sublingual buprenorphine/naloxone. Understanding the structural barriers that prevent patients from remaining in treatment and improving recovery support services for those receiving MOUD are critical to enhancing the success and effectiveness of long-term care for those with OUD.

Perhaps one of the greatest barriers to expansion of treatment with MOUD (and contributing to the continued community support and even federal funding of non-evidence-based care/forced detoxification) is stigma against medication and a lack of understanding of the nature of OUD. Often times, “abstinence-only” programs actively prohibit persons on MOUD despite their stage of recovery or success in abstaining from illicit drug use. This arises from the misconception that FDA-approved medication is the same as uncontrolled illicit drug use- from the misconception that physical dependence (a physiological homeostatic process) is the same as an OUD- from the misconception that OUD is the same as all other substance use disorders rather than recognizing that a single lapse to illicit opioid use can lead to death- and, finally, from the misconception that OUD is a moral issue best treated by suffering rather than a life-threatening medical condition best treated by health practitioners with expertise and a toolkit of evidence-based treatments. Until we can sway public opinion, educate policy makers, openly engage patients and their loved ones, and stop providing tax dollars to support programs that are not only non-evidence-based but anti-evidence-based, this situation will not change. There are numerous opportunities for the scientific community to engage the public in order to change hearts and minds. When asked to speak to your local community about the epidemic (e.g., town hall, adult learning groups, school board, local churches), say yes. When asked for input on pending local or state legislation or revisions to treatment or reimbursement guidelines, say yes. When asked by the media to participate in a podcast, radio show, on-screen interview about the crisis- say yes. And volunteer- don't wait to be asked- to advocate through your institution or scientific organizations to speak to state and federal legislators. It is time for our community to leverage the science and lead a charge to ensure that policy, funding and treatment delivery for OUD aligns with the evidence.

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