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Good afternoon Chairman Gowdy, Ranking Member Cummings and Members of the Committee. Thank you for the opportunity to speak today.

My name is Caleb Alexander and I am a practicing primary care physician and prescription drug expert at the Johns Hopkins Bloomberg School of Public Health, where I co-direct the Johns Hopkins Center for Drug Safety and Effectiveness. I am honoured to speak with you today. Much of my research is focused on identifying clinical and policy solutions to the opioid epidemic, and I will highlight two key points regarding the report from the President's Commission. However, as a physician, I know the power of stories to compel action, and I would first like to share a short one with you.

In 2011, Judy Rummler lost her son Steve to a heroin overdose. I work with Judy on policy reform and I asked her if I could share his story. She said "I am always happy to share Steve's story if it helps the cause." Steve's journey began with a lower back injury that evolved into chronic opioid use and addiction. Years before his death, he wrote of opioids, "At first they were a lifeline. Now they are a noose around my neck." Steve tried as best he could to get well and he did not want to die, but he ultimately succumbed from an overdose shortly after being discharged from a rehabilitation facility. Now, Judy keeps a picture of Steve along with a note, "If love could have saved you, you would have lived forever." Steve's story, and his family's resolve to ensure that other families don't have to experience what they have, is a reminder to me of what is at stake here, and of the loss that so many have endured.

During the past year, my colleagues at the Johns Hopkins Bloomberg School of Public Health and I have been reviewing hundreds of scientific studies and other data points on the epidemic. Last month, we released a report, entitled "From Evidence to Impact", in which we synthesize work from the field and provide a comprehensive set of evidence-based recommendations. Congressman Cummings, we were so honoured that you participated in the event marking the release of our report, and I have included our findings as part of my written testimony for the Committee's consideration.

In the remainder of my time, I would like to highlight two points regarding how the President's Commission can best be used to drive change.

First, the Commission's report provides a comprehensive framework for action. Simply put, the science is the science, and the report is based on evidence and lines up closely with our own appraisal in most areas. For example, both assessments agree that providers should be required to use prescription drug monitoring program (PDMP) databases, that the Center for Disease Control and Prevention's (CDCs) prescribing guidelines should be standard practice nationwide, and that high-quality, evidence-based addiction treatment should be available to those who seek it.

To enhance the use of PDMPs, Congress should pass the Prescription Drug Monitoring (PDMP) Act of 2017, which incentivizes states to mandate PDMP use by linking such mandates to the receipt of federal funding to fight the opioid epidemic. To promote the CDC's opioid guidelines, Congress should require that DEA licensure include mandatory, evidence-based training in the safe prescribing of controlled substances, and the federal government should also ensure that the CDC guidelines are consistently implemented in CMS and other federal delivery systems. There are many steps that Congress can take to improve the accessibility of high-quality, evidence-based addiction treatment, not the least of which is substantially expanding funding for these programs. The costs of the opioid epidemic are enormous, with estimates ranging from $80 to as high as $500 billion dollars per year. I believe it is Congressman John Delaney who has reminded us, "The cost of doing nothing is not nothing." Investments in addiction treatment are sound ones not only because of the incredible human toll that addiction

takes, but also because these short-term expenditures more than pay for themselves by reducing long-term direct and indirect costs associated with untreated opioid use disorder.

While the Commissions' report is remarkably thorough, there were a few areas that I believe were either underemphasized or not covered at all. For example, the Commission did not discuss harm reduction initiatives, yet the science is clear that providing sterile needles and syringes to people who inject drugs reduces HIV and Hepatitis C transmission and increases treatment seeking among those with substance use disorders. Similarly, while the Commission emphasized the importance of access to medication assisted therapy and the potential barriers posed by "fail-first" protocols or prior authorization requirements, they provided less discussion of the important role that health care insurance plays in promoting access to these treatments in the first place. Finally, while the Commission identified regulatory failures and called for the FDA to establish new guidelines for post-market surveillance, there are more immediate and effective steps they could have endorsed, such as calling upon the FDA to remove the most dangerous opioid formulations from the market and to revise the FDA label so that it better aligns with the science regarding the safety and effectiveness of these products.

Second, it is now critical for Congress and the Administration to develop a strategy to support the implementation of its recommendations. It is one thing to say we are going to send a man to the moon, it's quite another have a plan in place to do so. Of the 56 recommendations, arguably the two most important are that we need to: (1) reduce prescription opioid over-prescribing; and (2) provide high quality, evidenced-based treatment for addiction upon demand (disrupting the illicit fentanyl supply is also crucial). But how do we accomplish these goals? Let's just take the goal of reducing opioid over-prescribing. What specific steps is the federal government going to take to achieve this? What resources are required? Which agencies are responsible, what timeline will be followed and how will we know when we have been successful?

In short, we urgently need an action plan. I can't emphasize enough how important such a plan is if we are to make real progress. The Committee on Government Oversight could support this by asking for and reviewing the implementation plan for the Commission's most

important recommendations. My colleagues and I at Johns Hopkins are available to work with the Commission on such plans should we be able to be of service. This Committee can also exercise oversight capacity to ensure that other federal agencies act on the Commission's recommendations, especially the Department of Health and Human Services, the Drug Enforcement Agency and the Food and Drug Administration.

Chairman Gowdy, Ranking Member Cummings and Members of the Committee, we are missing more than *half a million* Americans from overdose that should be with us today. People like Steve Rummler and so many others. Incredibly, more deaths from opioids are expected in 2017 than ever before. As the Commission's Report makes clear, the origins of the epidemic are multiple but arise from within the healthcare system, including unsubstantiated claims about the safety and effectiveness of opioids, multifaceted campaigns by pharmaceutical companies and the failure of the FDA and DEA to regulate these products appropriately. Because of this, solutions will require involvement from patients, providers, regulators, industry, policymakers and other stakeholders.

As we look to 2018, there are reasons for hope. Patients and providers are increasingly using safer and more effective treatments for chronic, non-cancer pain. There is growing awareness that addiction is a treatable disease, and more and more Americans are living healthy and fulfilling lives in recovery. There is increasing consensus regarding evidence-based strategies that should be urgently scaled. Communities are increasingly mobilized, demanding affordable naloxone, reliable access to addiction treatment, stronger regulation by the FDA and DEA, and coordinated action by the federal government. This is a fixable crisis. But not without an implementation plan to accompany the Commission's recent recommendations.

Thank you for the opportunity to testify today. I look forward to your questions.

The opinions expressed herein are my own and do not necessarily reflect the views of Johns Hopkins University.

THE OPIOID EPIDEMIC

From Evidence to Impact

CLINTON FOUNDATION

JOHNS HOPKINS
BLOOMBERG SCHOOL
of PUBLIC HEALTH

THE OPIOID EPIDEMIC

From Evidence to Impact

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The growing crisis of the U.S. opioid epidemic affects all of us, not just those caught in its grip. It is destroying lives, ripping families apart, weakening our communities, and preventing our country from taking full advantage of our greatest resource—our people. We ignore the problem at our peril. We can't afford to lose a single person.

There is no single solution to this grave public health threat, but we know where to start. First we must acknowledge that opioid addiction is a disease that requires comprehensive treatment. Closing the path to addiction means addressing the overprescription of legal opioids and the proliferation of illegal opioids such as heroin and drugs laced with fentanyl. We also have to build the public health response so that families, first responders, and community groups have the support necessary to turn the tide on the epidemic, and in the meantime don't have to bear an impossible economic and emotional burden.

This report contains specific, proven recommendations for how to most effectively combat the epidemic—from allowing physicians to more effectively treat those suffering from addiction; to expanding coverage and accessibility of opioid overdose reversal drugs like naloxone; to changing the way that health care professionals, employers, and advocates talk about addiction to reduce stigma. These recommendations are a critical map for everyone working to fight the opioid crisis in America.

We all have a part to play. At the Clinton Foundation, we have worked since 2012 to help prevent overdose deaths, increase awareness and understanding of the scale of the problem, and frame this as a public health issue. Moving forward, it's up to all of us—leaders from the advocacy, nonprofit, government, and business sectors—to act together. By prioritizing this issue and advancing these recommendations, we can prevent more lives from being lost to this epidemic and ensure a brighter future for all Americans.

Bill Clinton

President Bill Clinton, Founder and Chairman of the Board, Clinton Foundation

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Executive Summary

While prescription opioids serve an invaluable role for the treatment of cancer pain and pain at the end of life, their overuse for acute and chronic non-cancer pain as well as the increasing availability of heroin and illicit fentanyl, have contributed to the highest rates of overdose and opioid addiction in U.S. history. Evidence-informed solutions are urgently needed to address these issues and to promote high-quality care for those with pain. This report is a response to that need. By providing an updated and expanded revision of a prior monograph, released in 2015, this report offers timely information and a path forward for all who are committed to addressing injuries and deaths associated with opioids in the United States.

The Opioid Epidemic: From Evidence to Impact reflects a commitment to the three principles that motivated the original report:

- Informing Action with Evidence;
- Intervening Comprehensively; and
- Promoting Appropriate and Safe Use of Prescription Opioids.

Those principles led to the delineation of 10 topic areas across the spectrum of the problem ranging from how clinicians treat pain to treatment for opioid-use disorders to harm reduction strategies.

The findings of the report are comprised of evidence from these 10 topic areas, as well as 49 recommendations that are informed by that evidence.

The first half of the report, Improving the Safe Use of Prescription Opioids addresses five topics:

1. Optimizing Prescription Drug Monitoring Programs
2. Standardizing Clinical Guidelines
3. Engaging Pharmacy Benefits Managers and Pharmacies
4. Implementing Innovative Engineering Strategies
5. Engaging Patients and the General Public

The second half of the report includes five additional topics and is focused on addressing the challenges of Identifying and Treating People with Opioid-Use Disorders:

6. Improving Surveillance
7. Treating Opioid-Use Disorders
8. Improving Naloxone Access and Use
9. Expanding Harm Reduction Strategies
10. Combating Stigma

This report is intended as a resource for policymakers; clinicians who prescribe opioids and those who treat people with opioid-use disorders; people with opioid-use disorders and their families; researchers; journalists; law enforcement officials; health system administrators; employers; service providers and agencies at the local, state, and federal levels; community organizations; and members of the general public. It provides guidance for those who are searching for solutions to address the unacceptable toll of opioid-use disorders in the United States as well as ways to reduce prescription opioid overuse and to maximize the quality of care for those with pain.

Recommendations for Action

OPTIMIZING PRESCRIPTION DRUG MONITORING PROGRAMS

1.1 Mandate prescriber PDMP registration and use.

1.2 Proactively use PDMP data for education and enforcement.

1.3 Authorize third-party payers to access PDMP data with a plan for appropriate use and proper protections.

1.4 Empower law enforcement and licensing boards for health professions to investigate high-risk prescribers and dispensers.

1.5 Work with industry and state lawmakers to require improved integration of PDMPs into Electronic Health Records systems.

1.6 Engage state health leadership to establish or enhance PDMP access across state lines.

STANDARDIZING CLINICAL GUIDELINES

2.1 Work with state medical boards and other stakeholders to enact policies reflecting the Centers for Disease Control and Prevention's (CDC's) Guideline for Prescribing Opioids for Chronic Pain.

2.2 Mandate electronic prescribing of opioids.

2.3 Standardize metrics for opioid prescriptions.

2.4 Improve formulary coverage and reimbursement for non-pharmacologic treatments as well as multidisciplinary and comprehensive pain management models.

ENGAGING PHARMACY BENEFITS MANAGERS AND PHARMACIES

3.1 Inform and support evaluation research of PBM and pharmacy interventions to address the opioid epidemic.

3.2 Continue the development and enhancement of evidence-based criteria to identify individuals at elevated risk for opioid-use disorders or overdose, and offer additional assistance and care to these patients.

3.3 Improve management and oversight of individuals who are prescribed opioids for chronic non-cancer pain.

3.4 Support restricted recipient (lock-in) programs among select high-risk patient populations.

3.5 Improve monitoring of pharmacies, prescribers, and beneficiaries.

IMPLEMENTING INNOVATIVE ENGINEERING STRATEGIES

4.1 Continue to support stakeholder meetings to advance technological solutions.

4.2 Sponsor design competitions.

4.3 Secure funding for research to assess the effectiveness of innovative packaging and designs available and under development.

4.4 Use research to develop implementation strategies in advance of identification of effective products.

4.5 Work with industry and government agencies to identify opportunities for the development and rigorous evaluation of abuse-deterrent formulations of prescription opioids.

ENGAGING PATIENTS AND THE GENERAL PUBLIC

5.1 Convene a stakeholder meeting with broad representation to create guidance that will help communities undertake comprehensive approaches that address the supply of, and demand for prescription opioids in their locales; implement and evaluate demonstration projects that model these approaches.

5.2 Convene an inter-agency task force to assure that current and future national public education campaigns about prescription opioids are informed by the available evidence, and that best practices are shared.

5.3 Provide clear and consistent guidance on safe storage of prescription opioids.

5.4 Provide clear and consistent guidance on safe disposal of prescription opioids and expand take-back programs.

IMPROVING SURVEILLANCE

6.1 Invest in surveillance of opioid misuse and use disorders, including information about supply sources.

6.2 Develop and invest in real-time surveillance of fatal and non-fatal opioid overdose events.

6.3 Use federal funding for interventions to address opioid-use disorders to incentivize inclusion of outcome data in those funded programs.

6.4 Support the linkage of public health, health care, and criminal justice data related to the opioid epidemic.

TREATING OPIOID-USE DISORDERS

7.1 Provide a waiver from patient caps for buprenorphine treatment for clinics that implement evidence-based models of care.

7.2 Require all state-licensed addiction treatment programs that admit patients with opioid-use disorders to permit access to buprenorphine or methadone.

7.3 Require all Federally Qualified Health Centers to offer buprenorphine.

7.4 Allocate federal funding to build treatment capacity in communities with high rates of opioid addiction and limited access to treatment.

7.5 Develop and disseminate a public education campaign about the role of treatment in addressing opioid addiction.

7.6 Educate prescribers and pharmacists how to prevent, identify, and treat opioid addiction.

7.7 Establish access to opioid agonist treatment with buprenorphine and methadone maintenance in jails and prisons.

7.8 Incentivize initiation of buprenorphine in the emergency department and during hospital stays.

IMPROVING NALOXONE ACCESS AND USE

8.1 Partner with product developers to design naloxone formulations that are easier to use by non-medical personnel and less costly to deliver.

8.2 Work with insurers and other third-party payers to ensure coverage of naloxone products.

8.3 Work with community-based overdose education and naloxone distribution programs to identify stable funding sources to ensure program sustainability.

8.4 Engage with the scientific community to assess the research needs related to naloxone distribution evaluations and identify high priority future directions for naloxone-related research.

8.5 Engage with the health care professional community to advance consensus guidelines on the co-prescription of naloxone.

8.6 Assess the effects of state laws expanding naloxone access to the general public.

EXPANDING HARM REDUCTION STRATEGIES

9.1 Establish and evaluate supervised consumption spaces.

9.2 Work with state and local stakeholders to establish and support needle and syringe service programs.

9.3 Evaluate and disseminate the use of test kits for fentanyl-laced opioids.

COMBATING STIGMA

10.1 Update employer human resources and benefits language to avoid stigmatizing language and include evidence about the effectiveness of treatment for opioid-use disorders.

10.2 Avoid stigmatizing language and include information about the effectiveness of treatment and the structural barriers that exist to treatment when communicating with the public about opioid-use disorders.

10.3 Educate health care providers about the benefits associated with destigmatizing language.

TOP TEN RECOMMENDATIONS FOR ACTION

1.1 Mandate prescriber PDMP registration and use.

2.1 Work with state medical boards to enact policies reflecting the Centers for Disease Control and Prevention's (CDC's) Guideline for Prescribing Opioids for Chronic Pain.

3.1 Inform and support evaluation research of PBM and pharmacy interventions to address the opioid epidemic.

4.3 Secure funding for research to assess the effectiveness of innovative packaging and designs available and under development.

5.4 Provide clear and consistent guidance on safe disposal of prescription opioids; expand take-back programs.

6.1 Invest in surveillance of opioid misuse and use disorders, including information about supply sources.

7.4 Allocate federal funding to build treatment capacity in communities with high rates of opioid addiction and limited access to treatment.

8.1 Partner with product developers to design naloxone formulations that are easier to use by non-medical personnel and less costly to deliver.

9.1 Establish and evaluate supervised consumption spaces.

10.2 Avoid stigmatizing language and include information about the effectiveness of treatment and the structural barriers that exist to treatment when communicating with the public about opioid-use disorders.

From the Editors

Prescription opioids serve an invaluable role for the treatment of cancer pain and pain at the end of life. Despite this, their overuse, especially for chronic non-cancer pain, remains a major public health challenge in the United States. Overdoses from heroin and illicit fentanyl have also come into sharp focus, with large increases in fatal overdoses from these drugs since 2010. In 2016, about 64,000 people died from drug overdoses in the United States,[1] and both experts[2] and projected data[3,4] suggest that deaths from opioids will increase further still in the years to come[5].

The opioid epidemic has manifested in many ways, and early reports of rising overdoses have been followed by many other signs of the serious effects that the epidemic has had on society's health and productivity. Rates of neonatal abstinence syndrome have increased 400 percent from 2000 to 2012. Where these cases reflect unstable home environments, children face significant social risks.[6] In some parts of the country, the epidemic has further strained an already vulnerable foster care system, with nearly half a million children in the system in 2015.[7] High rates of intravenous drug use among individuals with opioid-use disorders have led to local outbreaks of HIV and Hepatitis C. [8,9] The epidemic is so far-reaching that it is an important factor contributing to the declining life expectancy of the nation.[10]

Alongside these consequences is the fact that millions of Americans continue to experience high levels of chronic pain.[11] Such pain is a major source of disability and in addition to being associated with conditions such as depression and anxiety, chronic pain is also associated with increased mortality from other causes such as cardiovascular disease.[12] While several factors have contributed to the large increases in prescription opioid use in the past two decades, the high prevalence of chronic pain has been an important driver.

In 2014, at the invitation of the Clinton Foundation and the Johns Hopkins Bloomberg School of Public Health, a diverse group of experts came together to chart a path forward to address the opioid epidemic. The group, including clinicians, researchers, government officials, injury prevention professionals, law enforcement leaders, pharmaceutical manufacturers and distributers, lawyers, health insurers, and patient representatives, reviewed the current state of the evidence, identified strategies to address alarming trends in injuries and deaths from these drugs, and made recommendations for action that were released in 2015.[13] More than two years later, despite the efforts of many committed stakeholders, far too many lives continue to be lost.

While more injuries and deaths are occurring from opioids than ever before, the epidemic has also evolved. The volume of opioids prescribed, while still dwarfing that of other countries, plateaued in 2010 and since then, prescribing volume has modestly declined. In many communities, there is increasing awareness of the epidemic as well as a growing demand for prevention and treatment services. Increasing public support for such treatment has led to bipartisan efforts to improve funding and the delivery of more comprehensive and coordinated care for those with opioid-use disorders. Health care organizations, ranging from professional societies to health systems to pharmacies, are modifying their policies, procedures, and best practices to improve the care of those in pain and to identify and treat those with opioid-use disorders.

In this context, we have taken a fresh look at what remains a daunting challenge – stemming the tide of opioid–related injuries and deaths in the United States and improving care for those in pain. In addition to updating the evidence-base and timeliness of prior recommendations, we have also made several other modifications to our report, such as addressing the role of stigma and harm reduction in improving the treatment system. Our report reflects many changes from our previous analysis, but our commitment to the principles which motivated it remain unchanged:

INFORMING ACTION WITH EVIDENCE

An increasing number of evidence-based interventions exist to inform action to address this public health emergency; these should be scaled up and widely disseminated. Furthermore, many promising ideas remain evidence-informed, but have not yet been rigorously evaluated. The urgent need for action requires that we continue to rapidly implement and carefully evaluate these promising policies and programs. The search for new, innovative solutions also needs to be supported.

INTERVENING COMPREHENSIVELY

We support approaches that intervene all along the supply chain, and in the clinic, community, and addiction treatment settings. Interventions aimed at stopping individuals from progressing down a pathway that will lead to misuse, addiction, and overdose are needed. Effective primary, secondary, and tertiary prevention strategies are vital, including among those actively using opioids non-medically. The importance of creating synergies across different interventions to maximize available resources is also critical.

PROMOTING APPROPRIATE AND SAFE USE OF PRESCRIPTION OPIOIDS

Used appropriately, prescription opioids can provide relief to patients. However, these therapies are often prescribed in quantities and for conditions that are excessive, and in far too many cases, beyond the evidence base. Such practices, and the lack of attention to safe use, storage, and disposal of these drugs, contribute to opioid-use disorders and the overdose increases that have occurred. We support efforts to maximize the favorable risk-benefit balance of prescription opioids by optimizing their use in circumstances supported by evidence-based clinical practice guidelines.

In summary, this report provides a comprehensive, updated review of these target points of opportunity and summarizes the evidence in support of these recommendations for advancing the field through policy and practice. With rapid increases in the prevalence of opioid-use disorders and overdose deaths in this country as well as high rates of untreated pain, we are committed to assuring that what is known through research is translated to policymakers and practitioners. Uptake and implementation of these recommendations are needed to address the opioid epidemic that is continues to devastate families and communities throughout our country. Thank you for your personal efforts to help turn the tide.

G. Caleb Alexander, M.D., M.S.
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Improving the Safe Use of Prescription Opioids

Prescription opioids serve a vital role in the treatment of cancer pain and pain at the end of life. However, during the past two decades, their use in many other clinical settings, especially for the treatment of chronic non-cancer pain, has soared. Between 1999 and 2012, the volume of opioids prescribed increased more than 400 percent, such that by 2012, enough opioids were dispensed to provide every adult in the United States with a one-month continuous round-the-clock supply of pills.

These increases in use have been accompanied by consistent increases in rates of addiction, injuries, and overdose deaths, such that drug overdoses are now the leading cause of death among Americans under 50 years of age.[14] Since 2010, modest declines in opioid sales have been reported, though the United States remains a far outlier when it comes to opioid prescribing, and there is also enormous variation in rates of opioid use around the country. In addition, concerns regarding injuries and deaths from prescription opioids have been accompanied by a growing awareness of rapid increases in overdoses from heroin and illicit fentanyl.

The vast majority of prescription opioids that are misused come from medications that are prescribed, dispensed, and then used for non-medical purposes,[15, 16] both by patients who receive the prescriptions as well as friends and family members. Physicians and other health care providers overprescribe opioids for several reasons, and a small proportion of providers account for the majority of opioids prescribed.[17, 18] Health care providers who write or refill an opioid prescription provide a simple, discrete response which takes less time than educating a patient or providing counseling on non-pharmacologic therapies for pain management in busy practice settings where patients may expect to receive a prescription.[19] Referrals to multidisciplinary and subspecialty management for pain medicine are not accessible in all regions of the United States. Prescribers have a limited number of non-opioid medicines to treat patients who have moderate to severe chronic pain.[20] Pharmaceutical companies promote opioids through opioid related payments to advocacy and professional organizations[21] as well as directly to prescribers, which 1 in 12 US physicians received between 2013 and 2015.[22]

Challenges in the safe storage and proper disposal of prescription opioids also contribute to the opioid crisis. Most patients fail to store opioid products in locked locations, including patients with children and adolescents who are particularly vulnerable to risks of opioid misuse and overdose.[23, 24] Many patients also retain unused opioids instead of disposing with them using methods such as those suggested by the U.S. Food and Drug Administration (FDA).[25] Collectively, these practices create household reservoirs of opioids that facilitate misuse and diversion all across America. In some cases, prescription opioids are diverted intentionally, while in other cases, they are used without the knowledge of the person for whom they were prescribed. Approximately 70 percent of people who report non-medical use of prescription opioids state their most recently used drug came from a friend or family member.[26]

The non-medical use of prescription opioids impacts communities across the nation and remains a major challenge, despite modest reductions in opioid sales[27] and non-medical use[28] during the past few years. It is a problem that involves a legal product that is manufactured, marketed and dispensed by professionals through a system that is subject at multiple points to government oversight from different agencies at the federal and state level. That system has been ineffective in preventing the oversupply of prescription opioids to communities where demand for these products has grown. The supply of prescription opioids is connected to the manufacturing sector that controls production (e.g., the amount of product produced), chemistry (e.g., strength, composition, properties) and characteristics (e.g., crush resistance of pills, shelf life) of the drugs produced.

In the sections that follow, we consider five areas of effective response:

1. **Prescription Drug Monitoring Programs**, state-level programs governing the use of controlled substance prescribing information for providers, law enforcement and other stakeholders;
2. **Clinical Guidelines** that synthesize information regarding the safety, effectiveness and risk-benefit balance of prescription opioids in different clinical settings;
3. **Pharmacy Benefits Managers and Pharmacies**, two important stakeholders in the supply chain whose policies and procedures can reduce unsafe opioid use;
4. **Engineering Strategies**, such as innovative packaging solutions that can reduce non-medical opioid use as well as diversion;
5. **Patient and Public Engagement**, such as coordinated, community-based initiatives to raise awareness and facilitate action alongside other interventions that address the larger context in which the epidemic is occurring.

1. OPTIMIZING PRESCRIPTION DRUG MONITORING PROGRAMS

Prescription Drug Monitoring Programs (PDMPs) collect information about controlled substance prescriptions from in-state pharmacies and, for most PDMPs, mail order pharmacies that ship prescriptions into a state. Every state, as well as the District of Columbia and Territory of Guam, has a PDMP.[29] Through online access to their state's database, physicians and other prescribers can obtain clinical information regarding patients' controlled substance prescriptions to inform treatment decisions. Typically, information available through the PDMP includes drug name, type, strength, and quantity of drugs from previous prescriptions. Pharmacists can access PDMP data prior to dispensing a controlled substance prescription. PDMPs organize patient data in one location about controlled substance use in a way that can promote a culture of patient safety and quality of care.

One state-level survey revealed that 70 percent of physicians believed that the PDMP reduced the volume of opioids that they prescribed while increasing their comfort level with such prescribing; three-fourths of respondents (74%) reported that the data provided by the PDMP were very useful for informing opioid prescribing.[30] There is also evidence that PDMP implementation is associated with significant decreases in opioid prescriptions and opioid-related morbidity and mortality,[31, 32, 33] although the literature also includes findings suggesting otherwise,[34] and the effects of laws mandating PDMP registration and use remain an important area for further study.

PDMPs are under-used by prescribers. More than a quarter (28%) of primary care physicians in one national survey reported not being aware of their state's PDMP. While most clinicians (53%) reported having obtained data from their PDMP at some point, they accessed data in fewer than a quarter of the instances when they prescribed an opioid.[35] Physicians identify a number of barriers to PDMP use, including that retrieving the information is too time consuming in the context of busy clinical practice and that it is not user-friendly.[36]

While prescriber PDMP use may mitigate risks of opioid prescribing, practitioners may continue to unknowingly prescribe opioids to persons who will develop or already have opioid-use disorders. Such individuals are also at potential risk of heroin use as well as exposure to illicit fentanyl.[37] With the benefit of PDMP use, prescribers who identify persons with opioid-use disorders should refer them to appropriate treatment centers and addiction specialists.

To reduce illicit prescription opioid trafficking, law enforcement access to PDMP data is critical. Criminal enterprises such as "pill mills" that issue prescriptions for cash with no clinical evaluation, organized forgery, or doctor shopping rings facilitate non-medical prescription opioid use, and these supply channels should be a priority for law enforcement intervention.[57] Despite this, careful regulation of when and how law enforcement investigators access and use PDMP data is important. Concerns that unfettered access could lead to individuals with opioid dependence being subject to criminal prosecution as opposed to being directed to treatment must be considered.[38, 39, 40]

If PDMP registration can serve as a proxy for awareness, prescriber use remains a challenge, as even the highest rates of PDMP registration do not ensure use. For example, during the first quarter of 2012, Kentucky had the fifth highest proportion of registered prescribers of any state (49%), yet prescribers and pharmacists requested information for only six percent of the 2.9 million controlled substance prescriptions dispensed.[41] As of September 2017, 30 states mandated prescriber PDMP enrollment, and 28 required pharmacist enrollment.[42, 43, 44]

In response to the problem of low PDMP use, state lawmakers and PDMP administrators have made several adjustments, including:

- Authorization of delegates, such as approved prescribers' staff, to request PDMP data. As of September 2017, 48 states and the District of Columbia had laws authorizing delegates to request PDMP data, though only 36 had engaged in such reporting.[45]
- Establishment of interoperability with electronic health records and health information exchanges developed through the Affordable Care Act. The Substance Abuse and Mental Health Services Administration (SAMHSA) is providing grants to support this work in 16 states.[46] As of September 2017, PDMPs in 27 states offer health information exchange integration.[47]
- Proactive analysis of PDMP data and forwarding of unsolicited reports to prescribers and pharmacists noting when individuals' prescribing patterns are outliers. When prescribers receive unsolicited reports from PDMP administrators, they increase their own data requests, suggesting an increased vigilance with regard to prescribing decisions.[48, 49]

- Increased speed of data collection. Oklahoma collects data at the point of sale; another 42 states and the District of Columbia collect data daily, and eight states collect data every 3-8 days.[37, 50]
- Increased interstate PDMP data sharing so prescribers can observe prescriptions dispensed in other states. Forty-three states share data with other states and six others are working toward these agreements.[51]

States with low prescriber utilization are also increasingly mandating PDMP use. As of September 2017, 39 states mandate PDMP use under some circumstances.[37] Kentucky, in 2015, was the first state to mandate comprehensive PDMP use. Prescribers' PDMP use increased following the mandate,[52] and decreases in opioid prescribing, doctor shopping, and prescription overdose hospitalizations were noted in a 2015 evaluation. Although heroin treatment admissions rose during the study period, this increase began prior to the mandate. Like Kentucky, other comprehensive mandate states, such as Tennessee, New York, Ohio, and Wisconsin, experienced rapid increases in PDMP registrations, PDMP use, and prescribing of buprenorphine, indicative of increased treatment of opioid-use disorders.[53, 54] States also experienced decreases in high-risk prescribing, including for commonly misused controlled substances; combination prescribing of opioids, benzodiazepines, and muscle relaxants; and in multiple provider, or "doctor-shopping," episodes. As of September 2017, 24 states have enacted statutory mandates for comprehensive PDMP use and such mandates have been recommended by the National Governors Association,[55] Pew Charitable Trusts,[56] and Shatterproof, an organization representing families.[57] While specific criteria for use vary, in some settings use is mandated when opioids are prescribed for the first time, and if treatment continues, every 90 days thereafter, except for specific circumstances such as for prescriptions of three days or less without refills or for terminally ill patients.

Additional professional groups that could use PDMP data to reduce opioid overuse and diversion include:

Third-party health care payers and their pharmacy benefit managers (PBMs) that can intervene with prescribers, dispensers, and patients.[58,59]

Professional licensing boards that oversee clinicians and have an interest in identifying who may be self-prescribing for a possible opioid-use disorders as well as who has high-risk prescribing or dispensing patterns.[60,61,62]

Public health agencies that provide an early warning system for communities about the risks of opioid overdose and death[63,64] and intervene to prevent further harms.[65,66] This should include identifying persons at high risk due to co-prescribing of opioids and benzodiazepines, high volume morphine milligram equivalents, and other factors. Public health interventions should be employed as when disease registries identify persons who have positive infectious disease laboratory reports. Public health authorities can also take administrative action, such as revoking a state authorization to prescribe controlled substances, for prescribers who are practicing medicine far outside the standard of care.

RECOMMENDATIONS FOR ACTION

1.1 MANDATE PRESCRIBER PDMP REGISTRATION AND USE

States should mandate prescriber PDMP registration and use in order to achieve more comprehensive and effective use of PDMP data in treating patients. Access to this information should be a routine part of patient care as new ways are sought to maximize the value of PDMP information to clinicians and patients. Criteria guiding requirements for mandated use have been established. Such changes will require modifications to clinical workflow that in turn will require additional resources to address.

Rationale: Mandatory PDMP registration and use policies are associated with increased use, and most evidence suggests PDMP use is associated with decreased opioid prescribing and adverse events.

Current Status: Thirty states mandate PDMP registration and 39 mandate that prescribers register and use PDMPs in at least some clinical circumstances.

1.2 PROACTIVELY USE PDMP DATA FOR EDUCATION AND ENFORCEMENT.

States should analyze their PDMP data to identify:

1. High volume prescribers who deviate from standards of care for review;
2. Potential inappropriate or illegal activities for increased oversight of controlled substance prescribing; and
3. Inappropriate and/or illegal use for intervention. Primary recipients of PDMP data reports should include prescribers, dispensers, professional licensing boards, law enforcement agencies, and state and community prevention and treatment programs.

The types of information included in data reports should vary depending on recipients' roles. For example, reports to law enforcement should focus on identifying clinics or providers with exceptionally high volume prescribing that may signal illegal activities.

Rationale: Many PDMPs underutilize their data and do not engage in proactive reporting, nor do they participate in the Prescription Behavior Surveillance System or state-based equivalent reporting. Better use of PDMP data will help to identify opportunities for intervention and prevent non-medical use and overdose through education and enforcement.

Current Status: Forty states engage in proactive data analysis and reporting as of September 2017. Only five states provide unsolicited reports to all four primary recipient groups: prescribers, dispensers, professional licensing boards, and law enforcement agencies.[68]

Twelve states participate in the Prescription Behavior Surveillance System by sending de-identified PDMP data to and receiving reports from the Brandeis PDMP Center of Excellence. The Centers for Disease Control and Prevention and the Food and Drug Administration fund the project through an agreement with the Bureau of Justice Assistance.[69] States not participating in the Prescription Behavior Surveillance System can initiate their own data analysis and sharing with state and community prevention and treatment programs.

1.3 AUTHORIZE THIRD-PARTY PAYERS TO ACCESS PDMP DATA WITH A PLAN FOR APPROPRIATE USE AND PROPER PROTECTIONS

States should authorize Medicaid, Medicare, the Veterans Administration, Department of Defense, Indian Health Service, workers' compensation carriers, and private third-party health care payers to access PDMP data for their enrollees. This access should come with patient protections to assure, for example, that data sharing does not result in changes in coverage or pricing.[70] The authorization should also allow Pharmacy Benefit Managers to access the data as agents of the third-party payers for whom they manage benefits. See Section 3 of this report for more information on Pharmacy Benefit Managers.

Rationale: Access to PDMP data can provide third-party payers with the ability to identify and contact prescribers whose prescribing practices expose enrollees to unnecessary risks; identify enrollees who are obtaining high-risk prescriptions, contact their prescribers, create prescription limitations, and monitor compliance thereafter; and identify pharmacies where dispensing may put enrollees at risk. Such access may provide valuable information to inform internal policies that address opioid-use disorders associated with prescribed opioids. Careful consideration of enrollee protections is essential to protecting patients' rights and guarding against abuse.

Current Status: Thirty-six states and one territory authorize some combination of third-party payers to access PDMP data. Seven states provide access to Medicare and five states to commercial third-party payers.[71] Washington State authorizes Medicaid and Workers Compensation to access the PDMP data in bulk.[72]

1.4 EMPOWER LAW ENFORCEMENT AND LICENSING BOARDS FOR HEALTH PROFESSIONS TO INVESTIGATE HIGH-RISK PRESCRIBERS AND DISPENSERS

States should direct their PDMPs to proactively analyze these data to promote best standards of patient care and safety associated with opioid prescribing. Where such analyses reveal possible misconduct, that information should be provided to licensing boards and law enforcement for review.

Rationale: The centralized information source provided by PDMPs offers an opportunity for states to promote these data as tools for improving quality of care and patient safety. When questions about possible misconduct arise, licensing boards need access to PDMP data to review possible misconduct, and when warranted, share that information with the relevant law enforcement authorities.

Current Status: Forty-five states, Guam, and the District of Columbia permit their licensing boards to access PDMP data; 18 of the states send unsolicited reports to licensing boards.[73]

Twenty states proactively analyze and send unsolicited reports to law enforcement agencies, and 28 allow law enforcement to solicit reports.[74]

1.5 WORK WITH INDUSTRY AND STATE LAWMAKERS TO REQUIRE IMPROVED INTEGRATION OF PDMPS INTO ELECTRONIC HEALTH RECORDS SYSTEMS

Most PDMPs are largely web-based, standalone platforms requiring a separate workflow. This is inefficient and substantially decreases their utility and promise.

Rationale: PDMP use takes up to three times longer than other computer-based tasks, and the additional time and effort required is a large barrier to regular use.[75,76] Incorporating PDMPs into Electronic Health Records systems has the potential to reduce this burden and increase use.[67]

Current Status: The Office of the National Coordinator for Health Information Technology, in coordination with SAMHSA and others, has been involved in trials to integrate PDMPs into Electronic Health Records systems in a variety of settings, with generally positive results.[77] Twenty-seven states offer one or more forms of PDMP integration with Electronic Health Records and/or health information exchanges.[78]

1.6 ENGAGE STATE HEALTH LEADERSHIP TO ESTABLISH OR ENHANCE PDMP ACCESS ACROSS STATE LINES

Enact state policies that mandate interconnection of state PDMPs.

Rationale: In many areas of the U.S. PDMPs are of limited effectiveness if providers are unable to access information about prescriptions in neighboring states.[79]

Current Status: Forty-three states currently engage in interstate PDMP interoperability and six are working toward it as of 2017.[80]

2. STANDARDIZING CLINICAL GUIDELINES

A balanced approach to the opioid epidemic acknowledges both that appropriate and evidenced-based opioid prescribing benefits some groups of patients, and that urgent action is needed to minimize harm from the use of these products in many settings where they have an unfavorable risk-benefit balance.[81,82] Data-driven analyses and the clinical community broadly support opioids as part of a multimodal regimen in the treatment of acute pain after surgery,[83] cancer pain,[84,85] and pain in end-of-life, hospice, and palliative settings.[86] While indicated, opioid prescribing in some acute clinical contexts may contribute to harms by inadvertently transitioning patients from short-term to long-term use and facilitate the development of opioid-use disorders in some patient subgroups.[87,88] At the same time, policies to support appropriate access to prescription opioids may be associated with fewer unintended consequences than overly broad and blunt restrictions on opioid prescribing.[89]

Prescription opioids have been demonstrated as efficacious for the short-term treatment of chronic non-cancer pain, such as that caused by headaches, fibromyalgia, or lower back pain. For example, opioids have been shown to reduce nociceptive and neuropathic pain in chronic non-cancer settings for durations less than 16 weeks.[90,91] However, there is little to no moderate or high-quality evidence suggesting the long-term benefits from prescription opioids among patients with these diagnoses. In addition, data clearly shows that long-term opioid use increases the risk of adverse outcomes such as opioid misuse, overdose, and other adverse events.[92] Widely accepted clinical guidelines for chronic non-cancer pain do not recommend prescription opioids as first-line treatment.[93,94] Rather, these guidelines recommend non-pharmacologic and non-opioid pharmacologic therapies as the preferred treatment for chronic pain, a careful assessment of risks and benefits when considering opioid prescribing, and only prescribing opioids when benefits are anticipated to outweigh risks. Despite this, several factors, including a lack of studies assessing long-term outcomes of opioid therapy for chronic pain and misperceptions on the part of prescribers and patients regarding the appropriateness of opioids for chronic pain, persist. The net result is that many clinicians continue to prescribe opioids for patients with chronic non-cancer pain in a manner at odds with the best available evidence.

In 2016, the Centers for Disease Control and Prevention (CDC) published a Guideline for Prescribing Opioids for Chronic Pain. The Guideline provides the most recent and comprehensive synthesis of data on opioid prescribing for chronic non-cancer pain.[95] The CDC's guidelines carefully balance the risks and benefits of opioid prescribing. The synthesis of evidence details when to start or continue opioids, how to select opioids and conduct patient follow-up, and how to assess the benefits and risks from prescription opioids in patients with chronic non-cancer pain. Because the dose of opioid medication differs based on the type of opioid prescribed, prescribers need to calculate morphine milligram equivalents (MME) to understand the risks associated with opioid prescribing. A continuum of risks exists as MME increases, and no established MME dose fully mitigates the risk of opioid use. Despite this, recommended thresholds that

CDC GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN
United States, 2016

The CDC Guideline addresses patient-centered clinical practices including conducting thorough assessments, considering all possible treatments, closely monitoring risks, and safely discontinuing opioids. The three main focus areas in the Guideline include:

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

- Selection of non-pharmacologic therapy, non-opioid pharmacologic therapy, opioid therapy
- Establishment of treatment goals
- Discussion of risks and benefits of therapy with patients

OPIOID SELECTION, DOSAGE, DURATION, FOLLOW-UP, AND DISCONTINUATION

- Selection of immediate-release or extended-release and long-acting opioids
- Dosage considerations
- Duration of treatment
- Considerations for follow-up and discontinuation of opioid therapy

ASSESSING RISK AND ADDRESSING HARMS OF OPIOID USE

- Evaluation of risk factors for opioid-related harms and ways to mitigate patient risk
- Review of prescription drug monitoring program (PDMP) data
- Use of urine drug testing
- Considerations for co-prescribing benzodiazepines
- Arrangement of treatment for opioid-use disorders

Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49.
DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1

denote increased risk include doses of 50 MME/day, 90-100 MME/day, and 200 MME/day.

While much of the focus of the opioid epidemic has been on prescription opioids, there are many alternative pharmacologic and non-pharmacologic treatments that can be used to manage chronic non-cancer pain. Additional non-opioid pharmacologic agents include acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), select anti-depressants, muscle relaxants, select anticonvulsants, and topical analgesics. The appropriateness of these non-opioid treatments depends upon a variety of factors, including the origin and type of pain, patient age and comorbidities, and patient and clinician experience and preference, to name a few. There are also many non-pharmacologic therapies that can be used for the management of pain, including physical therapy, therapeutic massage, acupuncture, biofeedback, yoga, and heat or cold therapies. Efforts to improve care for those in pain as well as to reduce the overuse of prescription opioids, should be informed by knowledge and examination of these complements and alternatives to opioids,[96] and in some cases, the adequacy of insurance coverage supporting their use.[97]

There is also growing interest in the potential role of cannabis in the management of those with chronic non-cancer pain. Chronic pain is the most common indication for medical cannabis, and there is some suggestive evidence from ecological studies indicating that opioid use[98] and overdose are reduced after states implement medical cannabis laws.[99,100] However, there is a dearth of high-quality evidence from controlled trials on the effectiveness of cannabis as a supplement for opioids, and there is also evidence that cannabis use may increase risk of non-medical prescription opioid use and prescription opioid-use disorders.[101] In 2017, the National Academies of Sciences, Engineering, and Medicine noted that cannabis can effectively treat chronic pain, but also underscored that there is uncertainty and known adverse outcomes associated with cannabis use, such as the risk of motor vehicle accidents.[102] Most studies demonstrated short-term reductions in pain using oral cannabis extracts, such as nabiximol, in trials outside of the U.S., while a small group of U.S.-based studies suggested that a vaporized or smoked cannabis flower reduces chronic pain in the short-term. However, cannabis available for medical research differs in formulation, strength, and chemical composition from cannabis products sold to consumers in state markets. Consequently, the safety and efficacy of commercially available cannabis products is largely unknown.

Providers may prescribe opioids through a written or electronic prescription. Electronic prescribing of prescription opioids offers numerous advantages, including fewer dosing errors, reduced fraud, greater security through two-factor authentication, and enabling enhanced surveillance.[103] Electronic prescribing also facilitates the use of clinical decision support tools that can guide prescribers to implement evidenced-based practices during routine clinical care.[104] While federal regulations in the U.S. Drug Enforcement Agency's Practitioner's Manual only permit written prescriptions for opioids, the Agency permitted electronic prescribing for controlled substances in 2010 which effectively legalized electronic prescribing of controlled substances in all 50 states. However, only one in five providers work in health systems that enable electronic prescribing and fewer than 15 percent of controlled substance prescriptions are electronic.[105,106]

RECOMMENDATIONS FOR ACTION

2.1 WORK WITH STATE MEDICAL BOARDS AND OTHER STAKEHOLDERS TO ENACT POLICIES REFLECTING THE CENTERS FOR DISEASE CONTROL AND PREVENTION'S (CDC'S) GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

State medical boards should take concrete steps toward implementing the CDC's Guideline. Such steps might include use of the Guideline during disciplinary investigations as one factor for deciding whether a physician is practicing outside the standard of care. Such an approach will save the time and money involved in developing separate guidelines, and will contribute toward national parity with regard to prescription policies.

Rationale: The Guideline, issued in 2016, remains the gold standard for a comprehensive, evidence-based approach to prescribing opioids for chronic non-cancer pain in primary care. These evidence-based recommendations set the standard for how to address co-prescribed medications, safety information on dosing standards, and guidance from writing the first prescription to tapering patients.

Current Status: Since releasing the Guideline in 2016, the CDC has developed a variety of resources, including a companion smartphone app, to foster dissemination and implementation.[107] While dissemination of the Guideline has resulted in high rates of awareness among providers and policymakers, implementation across states remains an understudied area.

2.2 MANDATE ELECTRONIC PRESCRIBING OF OPIOIDS

Federal agencies and state jurisdictions should accelerate the adoption of electronic opioid prescribing through mandates to health systems and prescribers.

Rationale: Electronic opioid prescribing offers multiple advantages to written prescriptions, including improving surveillance of opioid prescribing and reducing rates of error, duplication, and forged prescriptions. Electronic prescribing also permits the use of clinical decision support systems, which help providers apply evidenced-based guidelines when prescribing opioids.

Current Status: Electronic prescribing of controlled substances is legal in all 50 states. As of September 2016, only one in five providers have health systems that enable electronic prescribing and fewer than 15 percent of transactions for prescriptions for controlled substances occur electronically.[108,109]

2.3 STANDARDIZE METRICS FOR OPIOID PRESCRIPTIONS

Federal Drug Enforcement Agency regulations should mandate that opioid prescriptions identify and record daily and total morphine milligram equivalents (MME) as measures of opioid exposure.

Rationale: The effective dose of opioid varies based on the type of opioid prescribed. MMEs require calculation and convey important information about the risk of opioids to prescribers, patients, and payers.

Current Status: The Drug Enforcement Agency has no mandate that opioid prescriptions include total and daily MMEs on opioid prescriptions.

2.4 IMPROVE FORMULARY COVERAGE AND REIMBURSEMENT FOR NON-PHARMACOLOGIC TREATMENTS AS WELL AS MULTIDISCIPLINARY AND COMPREHENSIVE PAIN MANAGEMENT MODELS

Payers should invest in care models for chronic pain that emphasize non-pharmacologic treatments as well as collaborative care by different medical specialties and non-physician caregivers.

Rationale: Evidence-based non-opioid treatments such as cognitive behavioral therapy, physical therapy, exercise, and acupuncture represent tools for the management of chronic pain that may help patients avoid initiation of opioid therapy or transition from long-term opioid use. Formularies drive patients and providers toward preferred treatment choices. Improving coverage of non-opioid alternatives would help to promote the use of pharmacologic and non-pharmacologic approaches that have a better risk-benefit balance than opioids for many patients.

Current Status: Formulary coverage and reimbursement for non-pharmacologic and multidisciplinary pain treatment does not have parity with traditional models of health care that emphasize medication prescribing and encounters with physicians, and even when covered, utilization management criteria such as prior authorization and quantity limits may prevent access to non-pharmacologic treatments.

3. ENGAGING PHARMACY BENEFITS MANAGERS AND PHARMACIES

Pharmacy Benefits Managers (PBMs) manage the pharmacy benefits for health plans and large employers, and thus, have an important opportunity to help reverse the opioid epidemic through coverage policies and programs, policies and procedures to reduce inappropriate prescribing and to intervene with individuals likely to be diverting prescription opioids or using them for non-medical purposes. Because PBMs work closely with health plans to design coverage benefits, some analyses have focused jointly on the role that PBMs and health insurers can play, especially in populations such as Medicaid recipients where non-medical use and opioid-use disorders are more common relative to other insured populations.[110]

PBMs can use several approaches to improve the safe use of prescription opioids. First, PBMs can use "formulary controls" to guide patients and prescribers toward the safest, most cost-effective medications and cover these drugs at a lower member cost share to encourage their use. The degree to which PBMs have effectively deployed these programs with a priority towards maximizing the safe use of opioids is not clear,[111] and opportunities undoubtedly remain. Some products, such as extended-release hydrocodone, promethazine with codeine syrup, and carisoprodol,[112] have been excluded from some formularies due to concerns about the potential for non-medical use. The ultimate goal of formulary design should be to ensure safe, cost effective therapy and better quality of care, consistent with the CDC's Guideline for Prescribing Opioids for Chronic Pain.[113]

In addition to formulary design, PBMs employ utilization management programs such as concurrent drug utilization review, prior authorization, precertification, and quantity limits to reduce non-medical use and diversion. Reports suggest significant reductions in opioid prescribing from these programs[114,115,116] though evaluations tend to be proprietary, as well as limited in the type of outcomes examined. Just as utilization management strategies may be deployed to restrict opioid use, removal of such programs may be undertaken to improve access to buprenorphine treatment for opioid dependence.[117] For patients who have particularly high-risk controlled substance use and whose utilization cannot be safely addressed using other mechanisms, insurers or PBMs may enroll the member in a pharmacy and/or prescriber restriction program. These programs, also known as "lock-in" programs, are applied to fewer than 1 in 1,000 individuals who are prescribed controlled substances, and have been used by state Medicaid programs for many years. Restricted recipient programs limit an individual to receiving their controlled substance prescriptions from one prescriber and one pharmacy for allowed insurance payment, or else the individual must pay cash. These interventions have demonstrated some positive impacts at the state level, including reduced use of controlled substances and emergency room visits as well as cost savings.[118,119]

Many PBMs also perform prescription claims reviews using software algorithms to identify prescribers, pharmacies, or patients who may be using opioids unsafely or else potential fraudulently prescribing, dispensing or using opioids. For example, PBMs may perform retrospective analyses to identify members visiting multiple prescribers or pharmacies, exceeding a threshold of morphine milligram equivalent (MME) daily or filling multiple simultaneous controlled substance claims. Since PBM surveillance criteria are proprietary, little is known regarding their validity, such as how closely they are associated with opioid-related injuries, deaths, health care use, or spending. However, some information about specific criteria used in select PBM interventions has been published.[120,121,122]

The Centers for Medicaid and Medicare Services (CMS) implemented an approach to identify high-dose and potentially unsafe opioid use in 2013. The criteria identify beneficiaries using high doses of opioids (>120 MME) for 90 or more consecutive days and also those who are receiving opioids from four or more prescribers and four or more pharmacies. Plans must implement utilization review and case management, usually performed by the PBM, for the identified beneficiaries and report back to CMS.[123] The non-profit Pharmacy Quality Alliance has also developed several quality metrics aimed at the opioid epidemic including one focused on the use of opioids at high dosage in persons without cancer. This measure was included in the Medicaid Adult Core Set of measures in 2016.[124] PBMs can use CMS and Pharmacy Quality Alliance criteria to identify at-risk members across their insured lives.

While more expensive and complicated to administer, payers and PBMs also have employed more intensive treatment programs for patients with opioid-use disorders and frequent health care use. For example, one payer implemented a Behavioral Health Medication Assistance Program that consisted of nurses and psychologists working with physicians to evaluate members at risk or in treatment for an opioid-use disorders. While impressive gains were reported, such as a 35 percent reduction in hospital admissions, as with many other analyses, these evaluations were based on proprietary data subject to several limitations.[125] Another PBM utilized a managed care pharmacist to implement a prescriber controlled substance intervention and reported a four to one return on investment.[126]

In one synthesis of the effect of insurer and PBM strategies to address opioid overuse, most studies examined some combination of patient review and restriction programs, drug utilization review programs, or prior authorization and quantity limit programs.[127] These assessments usually evaluated the effect of such programs on cost savings and changes in utilization; analyses of the effect of these strategies on health outcomes was rare. Many of these programs demonstrated significant reductions in the outcomes examined, such as the mean number of controlled substance claims, long-acting opioid prescriptions, carisoprodol prescriptions, and overall rates of opioid and sedative use. Despite this, studies were of low quality, often because of the absence of suitable comparison groups, long-term follow-up, and robust methods to address the potential for unmeasured confounding or co-interventions.[128]

Pharmacies also are an important stakeholder in the health care supply chain and distribution system for prescription opioids in the United States. Pharmacies' resources, programs, and policies vary across different types of pharmacies including retail chain pharmacies, mass retailers, food stores, and independent, government, and clinic-based pharmacies. State and federal law govern some elements of their conduct with respect to reducing non-medical opioid use and diversion. For example, the removal of prescriber dispensing privileges to curtail both diversion and inappropriate opioid prescribing is feasible and supported by state and federal law. Such actions are quite rare, yet given the high volume of opioids accounted for by a small group of prescribers, these actions may nevertheless have an important impact on the overall volume of controlled substances dispensed.[129] Both the Drug Enforcement Agency and state boards of pharmacy require pharmacists to use sound professional judgment when determining whether to fill opioid prescriptions.

Both PBMs and pharmacies play an important role in the increasing prevalence of electronic prescribing. Electronic prescribing for opioids has the potential to reduce forgery and fraudulent controlled substance prescriptions.[130] In 2016, fewer than 15 percent of the U.S. controlled substance prescriptions were electronically prescribed.[131,132] New York's Internet System for Tracking Over Prescribing (I-STOP) law was enacted in March 2016 and facilitated a 54 percent increase in electronic prescribing of controlled substances during 2016. Additional laws and evaluations to monitor their impact will be critical to maximizing the use of electronic prescribing as a tool for more effectively controlling the prescription opioid supply.

Many of the practices identified above, ranging from PBMs utilization management programs to pharmacy education programs, can be potentiated by the accessibility of PDMP data, since such data allows for a unified and comprehensive view of patients' prescription opioids prescribed as well as the ability to identify and personalize clinical outreach for specific patients based on their risk of potential injury or death from prescription opioids. The role of PDMPs in reducing non-medical opioid use and diversion is addressed in Section 1, including the interface between PDMPs, PBMs, and pharmacies. These interfaces have also been discussed elsewhere.[133,134]

Although not widely enacted, "take-back" programs that foster safer medication disposal by allowing for patients to return unused or unwanted opioids may also help to reduce the potential for diversion of opioids from licit to illicit channels. Pharmacies provide a convenient site for individuals to dispose of their unused opioid prescriptions, and recent federal law has clarified the legal framework in support of such activities. Evidence supporting the effectiveness of allowing pharmacies to take back and destroy prescription drugs is anecdotal, and additional discussion regarding these programs is presented in Section 5 of this report.

RECOMMENDATIONS FOR ACTION

3.1 INFORM AND SUPPORT EVALUATION RESEARCH OF PBM AND PHARMACY INTERVENTIONS TO ADDRESS THE OPIOID EPIDEMIC

PBMs and pharmacies are engaged in opioid interventions. Research is needed to evaluate the clinical and economic impact of these efforts. A stakeholder meeting to review research that is in progress and to identify priorities for new research is needed to inform investment in this area.

Rationale: Without high-quality evaluations of interventions, PBMs and pharmacies will lack a reliable evidence-base to inform how best to invest prevention dollars.

Current Status: The Patient-Centered Outcomes Research Institute (PCORI) has no funded projects on this topic. The CDC and the National Institute on Drug Abuse (NIDA) have sponsored modest extramural funding in this area. The private sector conducts research, much of which goes unpublished.

3.2 CONTINUE THE DEVELOPMENT AND ENHANCEMENT OF EVIDENCE-BASED CRITERIA TO IDENTIFY INDIVIDUALS AT ELEVATED RISK FOR OPIOID-USE DISORDERS OR OVERDOSE, AND OFFER ADDITIONAL ASSISTANCE AND CARE TO THESE PATIENTS

The Centers for Medicaid and Medicare Services (CMS) and the Pharmacy Quality Alliance have developed criteria to identify beneficiaries using high doses of opioids or using opioids in a high-risk manner, such as concomitantly with benzodiazepines. PBMs should be encouraged to use CMS and Pharmacy Quality Alliance criteria to identify at-risk members across their insured lives and to create evidence-based clinical programs for member or prescriber outreach.

Rationale: Criteria currently used to identify individuals at high risk for an opioid-use disorders or overdose require further refinement and validation.

Current Status: State Medicaid, managed care plans, and PBMs are using varying methods with varying degrees of evidence to support efforts to identify and respond to at-risk individuals.

3.3 IMPROVE MANAGEMENT AND OVERSIGHT OF INDIVIDUALS WHO ARE PRESCRIBED OPIOIDS FOR CHRONIC NON-CANCER PAIN

Encourage the states and CMS to incentivize PBMs through the Medicaid Innovation Accelerator Program and CMS Innovation Center to implement and rigorously evaluate innovative medication management strategies consistent with the CDC Guideline[135] for targeted management of individuals prescribed opioids for chronic non-cancer pain.

Rationale: Managed care plans and PBMs are uniquely positioned to implement utilization management programs for ensuring safe opioid prescribing consistent with the CDC Guideline.

Current Status: A systematic assessment of how plans and PBMs are currently implementing and evaluating management and oversight of individuals who are prescribed opioids for chronic pain does not exist.

3.4 SUPPORT RESTRICTED RECIPIENT (LOCK-IN) PROGRAMS AMONG SELECT HIGH-RISK PATIENT POPULATIONS

PBMs and plan sponsors should be encouraged to implement restricted recipient programs among select, high-risk patient populations in commercial, Medicaid, Medicare Advantage, and Part D plans.

Rationale: Lock-in programs among high-risk populations have demonstrated to be successful among select Medicaid programs. For high-risk patients, such programs offer an opportunity to enhance the coordination and quality of their care.

Current Status: In June 2016, the Comprehensive Addiction and Recovery Act (CARA) was signed, which included "lock-in" provisions for at-risk Part D beneficiaries. As of December 2016, the Department of Health and Human Services was determining the criteria for such programs.

3.5 IMPROVE MONITORING OF PHARMACIES, PRESCRIBERS, AND BENEFICIARIES

All PBMs should provide a list of pharmacies, prescribers, and beneficiaries to the National Benefit Integrity Medicare Drug Integrity Contractor (NBI MEDIC) that meet a threshold of concern for opioid prescribing. Based on these reports, MEDICs should share information about providers of concern with CMS.

Rationale: This information exists and can be used to address possible sources of diversion.

Current Status: Most PBMs are providing a list of pharmacies, prescribers, and beneficiaries that meet certain criteria of concern to NBI MEDIC. CMS is engaged with some follow-up of this information.

4. IMPLEMENTING INNOVATIVE ENGINEERING STRATEGIES

The U.S. Food and Drug Administration (FDA) highlighted the potential for innovative packaging solutions to be a part of the Agency's response to the role of prescription opioids in opioid-use disorders when it published a notice for public comment in the Federal Register in April 2014. Prescription packaging designs have evolved significantly in the past decade and now include many features – such as electronic systems for monitoring, accessing, and improving adherence to medication regimens – that also could help to prevent the diversion of prescription opioids. Examples of design strategies cited in the FDA notice include: prescription dispensing systems that remind patients to take a dose, track when a dose is taken, and limit further access until the next dose is due; radio-frequency identification-based systems; and microchips embedded within tablets. Often these technologies are packaged with data capture systems to provide feedback to providers on adherence, use, and tampering.[136]

The FDA has continued to examine packaging, storage, and disposal systems to enhance opioid safety, such as through a public and private sector workshop that was held in June 2017.[137] The group that was convened identified several promising packaging, storage, and disposal mechanisms including: locking technologies, disposal pouches, and calendarized blister packs for households with children; and calendarized blister packs, RFID-enabled monitoring, and dispensing technologies for adult patients. The summary report concludes:

> *"Building on injury prevention principles, a combination of passive protections, such as abuse deterrent drug formulations, and safety enhanced packaging, storage, and disposal solutions, may significantly help to improve the safe use of prescribed opioids. … To maximize the likelihood of a positive impact, experts thought that solutions should be passive, cost-effective, supported by payers, and appealing to patients, providers, and pharmacists alike, without imposing excess burden."* [138]

Although most prescription drug packaging innovations have been designed to improve medication compliance among patients using non-controlled substances for chronic conditions,[139,140] they could be adapted to help prevent prescription opioid misuse and diversion. For example, these products could reduce serious complications such as overdose by facilitating appropriate dosage and administration, and could help providers monitor for signs of non-medical use or diversion. In addition, products that limit access to the medication during non-dosing periods could help prevent use of the medication by non-prescribed individuals. The concept of personalization, i.e., use of a personal identification number, radio-frequency device, or fingerprint, facial recognition or other biometrics, has been proposed to prevent other types of injuries[141] and could be applied to prescription drug packaging as well. A pill dispenser that requires the prescribed patient's fingerprint before releasing the appropriate pain medication at the appropriate time, is an example of an application of personalized technology to prevent misuse and diversion through theft.

Evidence about the effectiveness of packaging designs to prevent non-medical prescription drug use and diversion is limited. One study of 37 individuals assessed the impact of an electronic medicine dispenser on diversion of buprenorphine-naloxone among patients being treated for opioid addiction. Researchers documented that 68 percent of patients receiving the dispenser preferred to use the electronic dispenser to store their tablets compared to the traditional prescription container; 16 percent reported that the dispenser prevented them from diverting their buprenorphine; 23 percent stated the dispenser prevented others from diverting their buprenorphine; and 58% believed the dispenser could prevent diversion of the medications dispensed in the electronic device. Additionally, 19 percent described the dispenser as "difficult" to tamper with while 58 percent described tampering with the dispenser as "impossible".[142] Another product, which couples a flow-controlled, tamper-resistant medication dispenser with an internet and phone accessible treatment portal, demonstrated sufficient promise to obtain funding from the National Institute on Drug Abuse. A phase II randomized controlled trial will assess use of the device and opioid misuse among patients from two pain management clinics.[143] Results from this trial were not available as of June 2017.

A review of the currently available and in-development opioid packaging designs concluded that many of the commercialized technologies such as locking caps, tamper-proof packages, and pill-dispensing products are most likely to deter unintentional misuse by elderly people or children and have limited application to prevent intentional misuse.[144] However, newer technologies, such as radio-frequency identification wireless technologies and simple technologies combined with radio-frequency identification – as well as other types of smart technologies – have the potential to play a role in deterring intentional opioid misuse by increasing communication between health care professionals and patients. The feasibility and differential impact of "tamper-resistant" rather than "tamper-evident" technologies has yet to be explored, but is a highly relevant question because of the intentional misuse issue. As part of their senior mechanical engineering design course, students at Johns Hopkins University created a prototype of a tamper-resistant, personalized dispenser that uses fingerprint recognition technology and is programmed to deliver a one-month supply of an opioid in the right time and correct dosage. The product is designed

so that only a pharmacist can open and lock the device. At the time of this report, this product was still in the prototyping and testing phase.[145]

Despite the very limited data on effectiveness, there are several products on the market for consumer use, and several state legislatures are considering bills requiring locking pill vials or similar technology. There is a need for research to understand the impact of these products on prescription drug misuse and diversion, their impact on rates of opioid-use disorders and opioid overdoses, and how they are used by people prescribed opioids for pain management. In addition to research questions on effectiveness, there are several outstanding questions that need to be explored before widespread adoption of these products can occur. These questions include:

- Where will these products enter the medication prescribing and use process? Will they be available for home use? Will pharmacists use them instead of traditional pharmacy dispensing vials? Will manufacturers move away from bulk product distribution, and incorporate these packaging designs for direct dispensing from the doctor's office or pharmacy?
- How will these products be regulated (e.g., as consumer products, medical devices, as combination drug devices)?
- Who will take on the costs for these products? Pharmacies? Patients? Insurers/PBMs?
- Who will control, monitor, and have access to the data available from these devices?

An additional design strategy to reduce non-medical use and overdose of prescription opioids is through the development of products designed to deter misuse. FDA, the pharmaceutical industry, Congress, and other stakeholders have called on drug developers to create opioids that are designed to make tampering and manipulation more difficult. To encourage product development, FDA has held multiple public meetings and issued guidance to industry. In April 2015, FDA issued a final guidance to assist industry in the development of opioid products with abuse deterrent features. The guidance explains FDA's current perspective on the types of studies that should be conducted to demonstrate that a given formulation can be expected to deter abuse by particular routes, and makes recommendations about how those studies should be performed and evaluated.[146]

Although FDA has approved labeling for 10 opioid analgesic products to indicate that they have design features intended to make non-medical use, typically via intranasal and injection routes, more difficult, FDA has concluded that misuse is still possible, and no products have been given a labeling claim for reducing opioid-use disorders or overdose deaths. Moreover, FDA has not granted a labeling claim for any product indicating that the product has demonstrated abuse-deterrence in a real-world setting. In fact, at a July 2017 meeting FDA stated:

> *"Determining the real-world impact of opioid formulations with properties designed to deter abuse is a key next step in understanding the utility of these products [abuse-deterrent formulations] in helping to curb the opioid abuse epidemic."* [147]

It is important to examine both the potential intended and unintended consequences of reformulated products. For example, in June 2017, the FDA requested that Endo Pharmaceuticals remove its reformulated product, extended-release oxymorphone (Opana ER), from the market due to post-marketing data demonstrating a significant shift in the route of non-medical use of Opana ER from intranasal to injection use after the product was reformulated.[148] The reformulated version was associated with a large HIV outbreak in Scott County, Indiana in 2015[149] as well as cases of thrombotic microangiopathy.[150] Additional questions have been raised regarding the ways that abuse deterrent-formulations have been marketed and promoted,[151] their costs[152] as well as unintended consequences including misperceptions that they may be less addictive or more effective than their non-abuse deterrent counterparts.[153,154] Regarding these products as "tamper-deterrent" rather than "abuse-deterrent" might help to reduce these misperceptions and unreasonable expectations about what these products can and cannot deliver, and their ultimate effect on the opioid epidemic.

Thus, while modified formulations that discourage non-medical use represent a promising technology, many questions regarding their real-world effectiveness as well as potential for unintended harms remain.

RECOMMENDATIONS FOR ACTION

4.1 CONTINUE TO SUPPORT STAKEHOLDER MEETINGS TO ADVANCE TECHNOLOGICAL SOLUTIONS

Work with the FDA to continue engaging with stakeholders to advance the conversation about packaging designs, and to identify high-priority future directions for engineering-related solutions and implementation of existing technologies.

Rationale: Engineering solutions to deter non-medical use of prescription opioids are promising and under development. There is a need for coordination of and support for the current efforts to ensure this line of innovation is adequately supported, quickly brought to market and rigorously evaluated.

Current Status: The FDA has convened one such meeting through the Duke-Margolis Center for Health Policy.

4.2 SPONSOR DESIGN COMPETITIONS

Partner with stakeholders to develop design competitions to incentivize innovative packaging and dispensing solutions.

Rationale: Design competitions have been used to encourage and support innovation in many areas. Engineering strategies for prescription packaging are a logical candidate for such a competition

Current Status: We are unaware of any design competitions on this subject.

4.3 SECURE FUNDING FOR RESEARCH TO ASSESS THE EFFECTIVENESS OF INNOVATIVE PACKAGING AND DESIGNS AVAILABLE AND UNDER DEVELOPMENT

Rationale: Data on the effectiveness of packaging interventions is limited. Research is needed to evaluate the engineering innovations under development and to inform future development.

Current Status: We are unaware of any funding source dedicated to evaluating engineering designs for prescription packaging.

4.4 USE RESEARCH TO DEVELOP IMPLEMENTATION STRATEGIES IN ADVANCE OF IDENTIFICATION OF EFFECTIVE PRODUCTS

Engage with key stakeholders, such as product developers, drug manufacturers, pharmacies, payers, regulators, chronic opioid therapy patients, and the public to explore potential barriers and incentives to product uptake.

Rationale: Innovations in prescription packaging are promising, but little is known about how to ensure the public will use these products and that the products will be integrated into existing payment policies. Research is needed to ensure that these aspects of translation are understood.

Current Status: We are unaware of any efforts to gather empirical data about how to ensure innovative engineering packaging for prescriptions is effectively integrated into the consumer market.

4.5 WORK WITH INDUSTRY AND GOVERNMENT AGENCIES TO IDENTIFY OPPORTUNITIES FOR THE DEVELOPMENT AND RIGOROUS EVALUATION OF ABUSE-DETERRENT FORMULATIONS OF PRESCRIPTION OPIOIDS

Rationale: Many formulations carry the potential for non-medical use, via intravenous injection, nasal inhalation, or other means. Development of drugs that deter this type of misuse may help limit the extent of and harms related to prescription opioid misuse.

Current Status: Previous abuse-deterrent formulations have shown limited effectiveness in terms of reducing abuse potential.[155] Future efforts must deter use by nasal inhalation as well as injection and oral routes if they are to be widely effective.

5. ENGAGING PATIENTS AND THE GENERAL PUBLIC

Much of this report emphasizes recommendations for changing prescriber behavior, reducing the supply of opioids, providing opioid-use disorders treatment, and decreasing the likelihood of overdose among those who are already using opioids. Here we focus on efforts to engage with patients and the general public to better understand opioid risks and alternatives for pain management. We also consider how we can collectively work to reduce opioid demand for the treatment of acute and chronic non-cancer pain, to promote safer use, and to minimize the widespread availability of these medicines for non-medical use.

Using clinical interactions to educate patients about the risks of prescription opioids and alternatives to pain management are beginning to be explored, but the literature is scant. Included in this effort are opioid treatment agreements, although there is a lack of evidence of their effectiveness in reducing opioid misuse and promoting adherence. Ethical issues regarding the use of patient contracts have also been raised, including concerns that they may harm the patient-provider relationship, further stigmatize opioid use,[156] or misconstrue the ability to prevent addiction. A recent multi-center trial of the patient provider agreement created by the Food and Drug Administration's Safe Use Initiative found that 94 percent of patients, but only 42 percent of providers, rated the tool as helpful, and there were no opioid-use related outcomes reported.[157]

The emergency department is another setting in which patient education regarding opioids is relevant[158] although there is limited research. One intervention study demonstrated that correct recall of instructions for taking analgesics increased from 40 percent to 71 percent after the introduction of written discharge instructions,[159] and a descriptive study found that none of the 20 patients discharged from an emergency department with an opioid prescription reported storing or disposing of them safely.[160] An ongoing project is testing the use of an m-Health patient decision aid in two emergency departments in Baltimore, Maryland and Morgantown, West Virginia.[161] Patients completed a personalized and tailored decision aid about pain treatment options and were encouraged to discuss the results with their doctor. Results of a small randomized trial found that the intervention effects were in the expected direction for knowledge, decisional conflict, and preference for a non-opioid approach to pain management.[162] Reductions in decisional conflict were statistically significant, although shared decision making and actual prescribing were not. More research is needed on how patient education can best facilitate patient empowerment, shared decision making, and a reduced demand for prescription opioids in managing pain.

Interventions at the community level have not been widely promoted as part of the national approach to controlling this epidemic. However, efforts to raise awareness about the risks associated with prescription opioids and alternatives available for pain management through public education campaigns are underway, including: The Medicine Abuse Project, aimed at preventing teen non-medical use and promoting treatment; Rx for Understanding, a school-based curriculum; the JED Foundation's college campus initiative; and the National Institutes on Drug Abuse's PEERx program. In 2017, the CDC has launched "It Only Takes a Little To Lose a Lot" Rx Awareness Campaign, which features testimonials of people affected by the epidemic as well as materials for others who want to implement their own consumer-directed campaigns. Assuring that public education initiatives are appropriately targeted, informed by evidence and rigorously evaluated is critically important to assuring that investments are well placed and effective.

Raising awareness is generally viewed as an important strategy for addressing prescription opioid-use disorders, and offers an opportunity for prevention when combined with other strategies. Best practices in health promotion and public health suggest that awareness-raising efforts will have maximum impact when combined with other interventions that address the larger context in which the problem is occurring. For this issue, raising awareness could be enhanced with attention to the policy context, such as naloxone availability as well as the need for other services, such as treatment for opioid-use disorders.

In response to increasingly high rates of unintentional opioid overdose deaths in Staten Island, New York, the city health department launched a comprehensive five-part public health strategy beginning in 2011. This included: creating and promoting prescribing guidelines; media outreach; town hall meetings; public service announcements; and enacting a law requiring the use of the State's PDMP. As a result, there was a 29 percent decrease in the opioid overdose death rate in Staten Island from 2011 to 2013, and no change in the other four New York City boroughs.[163]

Project Lazarus is a community-based initiative in North Carolina, in which 74 of 100 counties participated by implementing up to seven interventions: community education; provider education; hospital emergency department policies limiting prescribing and requiring PDMP use; training law enforcement in diversion control; programs to support pain patients; naloxone distribution; and addiction treatment. Interrupted time-series evaluation design estimated rates of unintentional and undetermined overdose deaths and emergency department visits during pre-intervention (2009–2012) and intervention periods (2013–2014). Provider education and policies limiting emergency department prescribing were associated with lower overdose mortality, although the

latter was also associated with more emergency department visits. Expansions of opioid agonist treatment were associated with increased mortality, but fewer emergency department visits.[164]

Public engagement efforts should be cognizant of the landscape of opioid use, sharing, storage, and disposal in U.S. homes. There are many deficiencies in how prescription opioids are stored and disposed of.[165] In a national survey of adults recently prescribed an opioid, more than one-fifth (21%) reported having shared it with another person. Few respondents stored the medication in a locked or latched place (21%), and among those with leftover opioid medications, 61 percent reported keeping them for future use. Nearly half of the adults with recent opioid medication use did not recall receiving information on safe storage (49%) or proper disposal (45%).[166] Only 12 percent of homes in which older children and teenagers were living had their opioids stored safely.[167] According to the 2015 National Survey on Drug Use and Health, more than half of the 969,000 12- to 17-year-olds who reported misusing prescription pain medicine cited a friend or relative as the source, and nine percent said they took the pills without asking, almost twice the proportion who reported buying pills from a drug dealer (5%).[168]

In 1995, CDC launched the National Campaign for Appropriate Antibiotic Use in the Community, which was renamed "Get Smart: Know When Antibiotics Work". One aim of the campaign was to decrease the demand for antibiotics by adults and parents of children with upper respiratory viral infections. Multiple studies have demonstrated positive impacts, suggesting that improving patient knowledge of risks, benefits, and alternatives to treatment may be a promising approach to reducing the number of prescriptions written.[169] Further studies have investigated the effectiveness of computerized patient education modules promoting awareness of appropriate antibiotic use, and provided initial evidence that these interventions can be effective in reducing demand.[170] For community prevention efforts, there are many parallels to the prescription opioid problem – i.e., the drugs are useful in certain circumstances but over-prescribed in many others, and patients are generally unaware of the potential individual and societal impacts associated with over-prescribing. Thus, community prevention interventions would do well to draw from the strategies used to reduce antibiotic overuse.

RECOMMENDATIONS FOR ACTION

5.1 CONVENE A STAKEHOLDER MEETING WITH BROAD REPRESENTATION TO CREATE GUIDANCE THAT WILL HELP COMMUNITIES UNDERTAKE COMPREHENSIVE APPROACHES THAT ADDRESS THE SUPPLY OF, AND DEMAND FOR PRESCRIPTION OPIOIDS IN THEIR LOCALES; IMPLEMENT AND EVALUATE DEMONSTRATION PROJECTS THAT MODEL THESE APPROACHES.

Rationale: Attention to the complex social and political context in which the problem of prescription misuse and overdose occurs has not been reflected in existing community campaign efforts. Broader stakeholder engagement may yield impactful new approaches.

Current Status: There are now several reports in the literature of community campaigns, some have evaluation data and others do not.

5.2 CONVENE AN INTER-AGENCY TASK FORCE TO ASSURE THAT CURRENT AND FUTURE NATIONAL PUBLIC EDUCATION CAMPAIGNS ABOUT PRESCRIPTION OPIOIDS ARE INFORMED BY THE AVAILABLE EVIDENCE, AND THAT BEST PRACTICES ARE SHARED

Rationale: Past success with reducing antibiotic use is generally attributed to a comprehensive national campaign. Applying lessons learned from that success to the current prescription opioid challenge will increase the likelihood that public education strategies benefit from the available evidence.

Current Status: Public education about the risks of prescription opioids and alternatives for pain management is needed, and many efforts are underway and will likely be developed. The extent to which these efforts are informed by the available evidence is unknown, and there is no central repository for collecting this evidence and sharing best practices.

5.3 PROVIDE CLEAR AND CONSISTENT GUIDANCE ON SAFE STORAGE OF PRESCRIPTION OPIOIDS

Rationale: The most common source of prescription opioids for non-medical purposes is family and friends, and national data indicate that one in five patients prescribed an opioid has shared it. National survey data reveal that very few parents with older children and teens keep their opioid prescriptions in a locked place. Ensuring prescription medications are not easily accessible may reduce intentional misuse by teens and adults and unintentional misuse by young children.

Current Status: While engineering solutions to packaging hold great promise, as detailed earlier in this report, clear guidance about safe storage options for patients who bring prescription opioids home is needed. National survey data reveal that nearly one-half of patients given an opioid prescription are given no information about safe storage. Messages should be appropriate for all populations, including those with low literacy and non-English speakers, and should be consistent across all sources –the prescriber, the pharmacist, in the patient packaging materials, and in community campaigns.

5.4 PROVIDE CLEAR AND CONSISTENT GUIDANCE ON SAFE DISPOSAL OF PRESCRIPTION OPIOIDS AND EXPAND TAKE-BACK PROGRAMS

Rationale: There are enormous volumes of unused opioids in homes throughout the U.S. that are too often diverted for non-medical use. Safe disposal options for prescription opioids are needed. Guidance from the federal government about how to safely dispose of prescription opioids can serve to launch community-based take-back initiatives that are responsive to local needs and culture.

Current Status: National survey data reveal that nearly one-half of patients given an opioid prescription receive no information about disposal options. Some pharmacies are taking back opioids. However, pharmacies are not universally providing this service or advertising this service to their patients. The Comprehensive Addiction and Recovery Act of 2016 expanded funding for take-back programs, but clear guidance on how to safely dispose of prescription opioids is lacking. Access to take-back programs is also limited and highly variable across jurisdictions. Messages should be appropriate for all populations, including those with low literacy and non-English speakers, and should be consistent across all sources–the prescriber, the pharmacist, in the patient packaging materials, and in community campaigns.

Identifying and Treating People with Opioid-Use Disorders

"Addiction is defined as a chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences. It is considered a brain disease because drugs change the brain; they change its structure and how it works."[171] Like many other chronic illnesses, addiction is influenced by genetics, the environment, and behavior. Also, like many other chronic illnesses, addiction is treatable.

In fact, opioid-use disorder is quite responsive to opioid agonist therapy, defined by the U.S. Surgeon General as a "combination of behavioral interventions and medications to treat substance-use disorders."[172] The Surgeon General has found that "[s]tudies have repeatedly demonstrated the efficacy of [opioid agonist treatment] at reducing illicit drug use and overdose deaths, improving retention in treatment, and reducing HIV transmission."[173] Indeed, in many studies, well more than half of patients receiving opioid agonist treatment show substantial improvement.[174] Communities that have expanded access to opioid agonist treatment have seen reductions in overdose deaths and other measures of population health improvement.[175]

Despite these facts, there are a variety of barriers that impede our nation's ability to identify and provide high-quality treatment to those with opioid use disorder. First, there is limited data available to track the opioid epidemic and the availability of treatment services in many areas. Overdose mortality surveillance depends on a patchwork system of medical examiners and coroners who do not use a consistent approach to classify cause of death. As a result, localities face difficulties developing an accurate picture of the epidemic and assessing whether intervention strategies are having the intended effect.

Second, there is inadequate access to opioid agonist treatment, which includes treatment that uses methadone and buprenorphine (a third FDA-approved treatment, naltrexone, is an opioid antagonist). Many people with opioid-use disorder do not receive treatment at all, and among those who do, just over a quarter received treatment with methadone or buprenorphine, the medications for opioid-use disorder with the strongest evidence of effectiveness.[176] Inadequate access is related to poor insurance reimbursement,[177] high regulatory barriers for methadone,[178] and relatively few prescribers of the medication buprenorphine.[179] Even among those receiving treatment, relapse is not uncommon,[180,181] reflecting the importance of high-quality, comprehensive, longitudinal care that is integrated with the other health care that patients receive.

Third, many people who use opioids for non-medical purposes die of overdose before they are able to reach treatment. An evidence-based strategy to address this challenge is greater availability of the overdose reversal drug, naloxone – for people who use opioids, for friends and family, for law enforcement, and for the general public.[182] As of July 2017, the Network for Public Health Law reports that all 50 states and the District of Columbia have passed laws to facilitate access to naloxone, and 40 states and the District of Columbia have Good Samaritan laws in place that provide some legal protections for people who respond to overdose events in good faith.[183] However, the high cost of naloxone and resistance in some communities is slowing the diffusion of this strategy.[184]

Fourth, the United States has been slow to pursue opportunities to engage people in the throes of addiction, provide lifesaving services, and support their transition to treatment. Despite strong evidence supporting syringe and needle exchange in reducing HIV and providing a path to addiction treatment, the federal prohibition on funding for these services only recently ended.[185] In Europe and Canada, it has been demonstrated that supervised consumption spaces reduce overdose in the surrounding community and provide a path to engagement and care for those not in treatment.[186] There is growing interest among U.S. localities in establishing supervised consumption spaces,[187] but questions about whether federal law enforcement will permit them to operate remain.

Finally, the immense stigma of addiction, opioid-use disorder, and its treatment creates many obstacles for integrating treatment into clinical care. Stigmatizing attitudes among the public and policymakers reduce support for policies to expand opioid-use disorder treatment, and stigma is also a barrier to treatment seeking for individuals with opioid-use disorders. Stigma is reflected in the derogatory language used to reference individuals suffering from opioid-use disorder;[188] in the ideology – common among many in the addiction treatment world – that one cannot receive medication to be in recovery; in the reluctance of traditional medical treatment providers to offer services; and in the use of law enforcement strategies unthinkable for other chronic illnesses, such as rulings by judges that prohibit individuals from receiving evidence-based treatment.[189]

These challenges are not the only ones facing those who are at risk of or who have an opioid-use disorder. While beyond the scope of this report, there has also been inadequate attention to the factors that may promote or protect against this brain disease, including intergenerational factors,[190,191] trauma,[192] and resilience.[193,194] In addition, there are a variety of supports that those with addiction may benefit from to maintain a stable recovery. These include employment, housing, health care, peer support, and other services. Even where such services exist, it can be difficult to develop strategies that account for the potential for relapse, such as what to do for individuals when they violate terms of zero drug tolerance while living in supportive sober housing. Expansion of recovery support is urgently needed, along with research designed to answer key questions about how to best help people move past their addiction, and into healthy and productive lives.

6. IMPROVING SURVEILLANCE

The opioid epidemic is rapidly changing, and active surveillance is vital. For example, early in the epidemic deaths were primarily due to prescription opioids. Between 2014 and 2015, deaths associated with the synthetic opioid fentanyl increased by a staggering 72 percent nationwide with even greater increases reported in states the following year. Fentanyl-related deaths in Maryland increased 229 percent between 2015 and 2016, marking the single greatest increase in drug-related deaths in the history of that state. [195,196]

Despite these disturbing trends, epidemiologic data are usually dated, posing an additional challenge for public health officials, policymakers, service providers, and other stakeholders to effectively intervene. Real-time surveillance of the populations at risk, types of drugs being used by people with opioid-use disorders and specifically used in overdose events, and geographic distribution of the problem are needed to reverse the current trend.

Various state-led efforts have attempted to address the need for real-time surveillance, though most are limited to data reflecting opioid-related hospitalizations and/or deaths. In 2014, the Rhode Island Department of Health, with support from the state legislature, launched an opioid surveillance system that requires emergency departments to report all cases of opioid overdose within 48 hours. [197] The goal is to identify outbreak clusters in real-time in order to design and implement responsive, targeted interventions. The system also has the capacity to identify geographically specific risk factors that can inform response and prevention. In the first full year of data collection, this system captured 1,523 hospital-reported adult overdose events, and identified socio-demographic risk factors as well as drug- and treatment-specific data, which can inform hospital, city, and state policies.

In the Fall of 2016, CDC announced a 12-state, $12.8 million dollar effort to support state-based opioid surveillance systems. The project, which includes Kentucky, Maine, Massachusetts, Missouri, New Hampshire, New Mexico, Ohio, Oklahoma, Pennsylvania, Rhode Island, West Virginia, and Wisconsin, is designed to enhance the timeliness of collection and dissemination of data on fatal and non-fatal opioid overdoses to better inform time-sensitive state and national prevention and response efforts. [198]

Other surveillance efforts, relying on data sources such as emergency medical services (EMS) transportation, hospital and emergency administrative data, PDMPs, and death certificates, have produced varying levels of detail.[199, 200, 201] Such systems, however, often operate at a delay of several months to a year or more, limiting their usefulness as a tool for timely surveillance and response.

RECOMMENDATIONS FOR ACTION

6.1 INVEST IN SURVEILLANCE OF OPIOID MISUSE AND USE DISORDERS, INCLUDING INFORMATION ABOUT SUPPLY SOURCES

Surveillance of opioid use, misuse, and opioid-use disorders helps to quantify the size and characteristics of the population that is at-risk for adverse outcomes related to opioid use. Such data in turn can allow us to understand the effectiveness of prevention programs and allocate resources for harm reduction and treatment. The National Survey of Drug Use and Health (NSDUH) is a household survey that measures use of opioids and other substances and screens for use disorders. In 2015 it was revised so that it now collects more data related to prescribed opioid pain reliever use as well as non-medical use, and motivations for non-medical use. The NSDUH remains the sole national survey to assess symptoms of opioid-use disorders in the population on an annual basis. The NSDUH has limitations, however, such as under-coverage of high-risk groups including incarcerated and homeless individuals, and a lack of geographic identifiers in public use files. Improving epidemiological surveillance will require additional efforts to strengthen the NSDUH and investments in complementary sentinel surveillance systems. This effort will involve collaboration with the Substance Abuse and Mental Health Services Administration and the CDC. Greater behavioral surveillance will inform understanding of both the use of opioid drugs and treatment services.

Rationale: Surveillance of opioid use, misuse, and opioid-use disorders is critical for the improvement of primary, secondary, and tertiary prevention efforts. Revising an existing surveillance tool is a cost-effective way to obtain needed information.

Current Status: Several federally-supported data collection efforts have attempted to monitor trends in opioid-use disorders with varying degrees of success. Few (e.g., RADARS) have proactively measured addiction prevalence from a variety of sources.[202] Investing in these tools will be critical to improving prevention efforts. For example, there is a need to revive programs that screen arrestees for opioid use, such as was historically provided by the Arrestee Drug Abuse Monitoring (ADAM) Survey, and to add more surveillance of opioid use and misuse to national surveys other than the NSDUH. Data from prescription drug monitoring programs provides another tool to quantify prevalence of prescribed opioid use, but does not necessarily indicate where misuse is occurring or capture use of opioids through diversion.

6.2 DEVELOP AND INVEST IN REAL-TIME SURVEILLANCE OF FATAL AND NON-FATAL OPIOID OVERDOSE EVENTS

Fatal and non-fatal overdoses are key indicators of the scope and lethality of the opioid epidemic. However, there are known data collection challenges that make timely, consistent, and longitudinal assessment of overdose events problematic. The most widely reported outcome is the national overdose death rate, yet this rate is inconsistently measured across areas and does not capture non-fatal overdoses.

Rationale: Real-time surveillance of all overdose events will help to inform appropriate responses to prevent overdose events and deaths, and can help to address fundamental questions about the epidemic such as the number of individuals who are switching to products with fentanyl adulterants.

Current Status: Current surveillance is afflicted with several key challenges that make it difficult to track the prevalence of overdose events in settings where they commonly occur. First, there are limited data on the number of individuals revived outside of hospitals (such as by first responders or family members). Second, there is likely under-coding of overdose in hospital admissions data, and such coding may be imprecise as hospital personnel may not adhere to consistent protocol for coding overdoses. Third, medical examiners and coroners vary in the rigor and consistency of procedures they use to classify overdose fatalities. As a result, there is known under-coding bias in state data, making it difficult to ascertain consistent cross-state and national trends.[203]

6.3 USE FEDERAL FUNDING FOR INTERVENTIONS TO ADDRESS OPIOID-USE DISORDERS TO INCENTIVIZE INCLUSION OF OUTCOME DATA IN THOSE FUNDED PROGRAMS

In the current era, there are widespread efforts to address the opioid epidemic through a variety of federal programs including initiatives with PDMPs, Medicaid programs, and direct grants to states (e.g., the State Targeted Response grants under the 21st Century Cures Act). These programs should include detailed guidance for data collection of program outcomes and approaches to sharing data where feasible, as these standards would enable grantees to track how programs are being implemented in different settings.

Rationale: Promising interventions are in the field, and may be more effectively disseminated if there is a repository of evidence to share across states and localities. Population-based outcome data are lacking and needed to inform decisions about replication and scale-up of promising interventions.

Current Status: While there is some provision for evaluating current programs, the data are often not consistently collected or disseminated. Moreover, programs are sometimes implemented in a manner that makes rigorous evaluation difficult. For example, the State Targeted Response grants include some minimal guidance for state data collection, but are not likely to be feasible for impact evaluations in most states.

6.4 SUPPORT THE LINKAGE OF PUBLIC HEALTH, HEALTH CARE, AND CRIMINAL JUSTICE DATA RELATED TO THE OPIOID EPIDEMIC

The impact of the opioid epidemic reaches across multiple service systems, and important indicators of harm related to the epidemic are captured in hospitals, public health programs (e.g., HIV screening or naloxone distribution), and law enforcement data. Although there are clear privacy implications to sharing data across entities, there are also real benefits in terms of efforts to increase overdose prevention.

Rationale: Because there are multiple pathways into harmful opioid use, no single data system can fully capture markers of risk. Measuring outcomes across systems provides a more complete picture. It also provides the foundation for better evaluation of the effectiveness of coordinated approaches.
Current Status: There are limited instances of data sharing across different service systems. While analyses have been conducted linking, for example, law enforcement data with drug treatment data, these are usually relevant to relatively discrete populations and done retrospectively. Massachusetts, under the Chapter 55 legislation, has made important progress in developing a legal framework for linking data across multiple service systems.

7. TREATING OPIOID-USE DISORDERS

Pharmacotherapies for opioid addiction include agonist maintenance with methadone, partial-agonist maintenance with buprenorphine, and antagonist treatment with immediate-release or extended-release naltrexone. Multiple well-designed randomized controlled trials provide strong evidence that buprenorphine maintenance and methadone maintenance are safe, efficacious, and cost-effective treatments for opioid addiction.[204] Both buprenorphine and methadone maintenance treatment are associated with reduced overdose risk, reduced risk of HIV infection, and improved maternal and fetal outcomes in pregnancy.[205,206] However, when used short term, especially in detoxification regimens, evidence of enduring benefit is lacking.[207]

Psychosocial approaches to treating opioid addiction include therapeutic communities, cognitive-behavioral therapies and 12-step facilitation, either provided in professional treatment or by mutual support groups such as Narcotics Anonymous. While 12-step programs are valued by many addiction professionals, it has been difficult to determine which elements of these programs may be of greatest therapeutic value. Psychosocial interventions, like medication treatments, may occur in outpatient or inpatient settings. While some studies support improved effectiveness of combining psychosocial therapies with buprenorphine and methadone maintenance, abstinence-based psychosocial approaches that shun opioid agonist treatment are associated with poor outcomes[208,209]

The ability to expand access to treatment with methadone is limited by a short supply of licensed programs in non-urban communities and requirements such as daily attendance. Unlike methadone maintenance, buprenorphine can be prescribed in an office-based setting. Unfortunately, there are barriers to buprenorphine treatment that include:

- **Federal limits on the number of patients a physician may treat with buprenorphine.** Physicians must apply to the Substance Abuse Mental Health Services Administration to provide buprenorphine treatment beyond the 30-patient limit for up to 100 patients with opioid dependency. Physicians who have prescribed buprenorphine to 100 patients for at least one year can now apply to increase their patient limits to 275 under new federal regulations.
- **Federal limits on nurse practitioners' and physician assistants' prescribing.** The Comprehensive Addiction and Recovery Act, signed into law on July 22, 2016, expanded buprenorphine prescribing privileges to nurse practitioners and physician assistants for five years (until October 1, 2021). Nurse practitioners and physician assistants must complete 24 hours of training for eligibility to obtain a DATA 2000 waiver and are limited to treating up to 30 patients.
- **Inadequate integration of buprenorphine into primary care treatment.** Physicians, nurse practitioners, physician assistants and other allied health care professionals receive little training in the recognition and treatment of opioid-use disorders.
- **Stigma against maintenance treatment for opioid addiction.** The misperception that maintenance medications substitute one drug for another is a commonly held view. These treatments have been underutilized because of misunderstandings about the drugs and their effectiveness and generally negative biases from the public, patients, criminal justice agencies, and providers.[210] Less than half of all licensed addiction treatment programs offer these medications, and less than half of the eligible patients in those programs receive them.[211]

RECOMMENDATIONS FOR ACTION

7.1 PROVIDE A WAIVER FROM PATIENT CAPS FOR BUPRENORPHINE TREATMENT FOR CLINICS THAT IMPLEMENT EVIDENCE-BASED MODELS OF CARE

Addiction specialist physicians are prohibited under federal law from treating more than 275 patients with buprenorphine.

Rationale: The current cap has no counterpart anywhere in medicine and has led to waiting lists for patients to receive treatment.

Current Status: Lifting these federally imposed caps is an action that the Comprehensive Addiction and Recovery Act (2016) delegated to the Secretary of the Department of Health and Human Services. Additional training of prescribers about opioid agonist treatment should be offered and treatment guidelines, such as the American Society of Addiction Medicine National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use,[212] should be disseminated. Access to buprenorphine treatment across the country should be closely monitored by the federal government. This effort will involve collaboration with Substance Abuse and Mental Health Services Administration and the Drug Enforcement Agency.7.2

7.2 REQUIRE ALL STATE-LICENSED ADDICTION TREATMENT PROGRAMS THAT ADMIT PATIENTS WITH OPIOID-USE DISORDERS TO PERMIT ACCESS TO BUPRENORPHINE OR METHADONE

State-licensed addiction treatment programs should not be permitted to admit patients with an opioid-use disorders unless they permit access to buprenorphine or methadone maintenance. So-called “abstinence only” program policies do not offer evidence-based treatment.

Rationale: Many state-licensed addiction treatment programs do not offer patients access to buprenorphine or methadone maintenance.

Current Status: In 2015, the White House Office of National Drug Control Policy announced that drug court programs will be ineligible to receive future federal funding if they prohibit receipt of buprenorphine and methadone. This effort will involve collaboration with SAMHSA, the Centers for Medicare and Medicaid Services, the White House Office of National Drug Control Policy and state drug and alcohol licensing agencies.

7.3 REQUIRE ALL FEDERALLY QUALIFIED HEALTH CENTERS TO OFFER BUPRENORPHINE

Federally Qualified Health Centers (FQHCs) are safety net providers that primarily provide services typically furnished in an outpatient clinic. They include community health centers, migrant health centers, homeless health centers, and public housing primary care centers as well as outpatient health programs or facilities operated by a tribal organization or by an urban Indian organization. In recent years, an increasing number of FQHCs have been offering buprenorphine[213] and they are one of the few providers that accept Medicaid for office-based buprenorphine treatment. Support and training for high quality treatment can be paired with the expectation that health centers offer this important therapy. Waivers for FQHCs that are structurally unable to meet this requirement should be available.

Rationale: Buprenorphine is an effective treatment for opioid addition, yet access remains limited.

Current Status: The White House Commission on Combating Drug Addiction and the Opioid Crisis called on the Centers for Medicare and Medicaid Services to require all FQHCs to mandate that their staff physicians, physician assistants, and nurse practitioners possess waivers to prescribe buprenorphine.

7.4 ALLOCATE FEDERAL FUNDING TO BUILD TREATMENT CAPACITY IN COMMUNITIES WITH HIGH RATES OF OPIOID ADDICTION AND LIMITED ACCESS TO TREATMENT

To reduce opioid-related overdose deaths, access to buprenorphine and methadone maintenance must be improved. States and counties need federal assistance to develop and expand existing services so that low-threshold treatment is available to all individuals with opioid-use disorders seeking treatment, regardless of their ability to pay for it.

Rationale: Treatment services are disproportionately distributed across communities and do not always reflect need. Using federal resources to identify communities most in need of treatment services and to expand treatment capacity will help to address this disparity.
Current Status: In 2017, $28 million in funding provided by the 21st Century CURES Act was awarded to five grantees to increase access to opioid agonist treatment for opioid-use disorders.

7.5 DEVELOP AND DISSEMINATE A PUBLIC EDUCATION CAMPAIGN ABOUT THE ROLE OF TREATMENT IN ADDRESSING OPIOID ADDICTION

Utilize information from the Department of Health and Human Services and the National Institute on Drug Abuse through the CDC and the White House Office of National Drug Control Policy to educate providers, patients and their families, health plans, state level law enforcement, and policy makers on the nature of opioid addiction as a chronic brain disease, noting that the strongest evidence supports use of maintenance medication with either methadone or buprenorphine. This campaign should also aim to reduce the stigma associated with effective treatment options. A major public education campaign on appropriate treatment that is comprehensive, evidence-based, and follows best practices in health communication is needed and should be evaluated.

Rationale: There is a lack of awareness about the effectiveness of opioid agonist treatment options among providers, patients and their families, health plans, law enforcement, and policy makers, and there is stigma against medication treatment. Both the lack of information and the stigma associated with opioid agonist treatment are barriers to greater use of effective treatment. Opioid agonist treatment is the standard of care for opioid addiction and it should be known as such among providers and the public.

Current Status: Federal health officials from the CDC, National Institutes of Health and the Substance Abuse and Mental Health Services Administration have made public statements supporting opioid agonist treatment. The latter two agencies have also issued materials for health care providers and the public on treatment with buprenorphine. Some health departments, most notably the New York City Department of Health and Mental Hygiene and the Maryland Department of Health, have sponsored efforts to raise awareness and improve access to treatment with buprenorphine and methadone.

7.6 EDUCATE PRESCRIBERS AND PHARMACISTS ABOUT HOW TO PREVENT, IDENTIFY, AND TREAT OPIOID ADDICTION

Develop, evaluate, and disseminate prescriber and pharmacist education to assist in better preventing, identifying, and treating opioid addiction. Training should include both information as well as direct skill development in assessment and treatment of opioid-use disorders. Develop, evaluate, and disseminate information about the standard of care for treatment of opioid addiction to providers who treat patients with opioid-use disorders.

Rationale: Prescribers and pharmacists receive little training on substance use disorders. With improved understanding of the etiology of opioid addiction and its treatment, they may be better able to prevent, recognize, and care for patients suffering from this condition.

Current Status: The American Society of Addiction Medicine and the American Academy of Addiction Psychiatry are currently involved in efforts to improve medical education about substance use disorders. A coordinated national effort to educate prescribers and pharmacists about opioid addiction is not yet underway.

7.7 ESTABLISH ACCESS TO OPIOID AGONIST TREATMENT WITH BUPRENORPHINE AND METHADONE MAINTENANCE IN JAILS AND PRISONS

Rationale: Many people with opioid-use disorders are incarcerated in jails and prisons, but are rarely offered treatment with buprenorphine or methadone. In contrast, use of extended-release naltrexone upon release from jail and prison is becoming more common despite limited evidence of its effectiveness. Opioid agonist treatment with buprenorphine and methadone is an effective intervention in these settings and can reduce incarceration and recidivism.[214,215]

Current Status: Opioid agonist treatment is available at fewer than 40 of the more than 5,000 jails and prisons in the United States.[216] In many criminal justice settings, the only available medication is extended release naltrexone.

7.8 INCENTIVIZE INITIATION OF BUPRENORPHINE IN THE EMERGENCY DEPARTMENT AND DURING HOSPITAL STAYS

Rationale: Opioid-use disorders is more prevalent in patients who present to emergency departments than in the general population.[217] Patients with opioid-use disorders are admitted to hospitals for treatment of opioid overdose, opioid withdrawal, medical problems associated with injection drug use, and other health conditions. Similar to hospital initiated treatment for chronic disorders such as hypertension and diabetes, patients who initiate buprenorphine in hospitals have better outcomes than patients referred for initiation of treatment as an outpatient.[218]

Current Status: Few hospital emergency departments and medical inpatient units offer this standard of care, despite support from the U.S. Surgeon General.[219]

8. IMPROVING NALOXONE ACCESS AND USE

Most evaluations of Overdose Education Naloxone Distribution programs (OEND) report on program implementation; training lay persons to recognize and respond to an overdose event, including the administration of naloxone; and provide information on the number of individuals trained, number of naloxone vials distributed and the number of overdose reversals reported by individuals who were trained (Kerensky 2017).

The settings for OEND evaluations have primarily been in large urban center needle and syringe exchange or harm reduction programs, methadone programs or other opioid-use disorders treatment programs, and have focused on people who inject heroin. Evaluations of programs in New York City, Massachusetts, Los Angeles, San Francisco, Chicago, Rhode Island, Pittsburgh, and Baltimore have been reported in the published literature.[220-221] Because the focus of the evaluations has been on the number of trained individuals and overdose reversals reported, it is not possible to describe the population-level impact of these individual programs. Data from a 2014 survey found that OEND programs in the U.S. had trained and provided naloxone to more than 150,000 individuals between 1996 and 2014, and reported more than 26,000 opioid overdose reversals during this time.[222] Additional evaluations have reported on changes in overdose recognition and response knowledge and/or behaviors as a result of OEND program training.[223-163] Taken together, these data demonstrate that people at high risk for opioid overdose and their friends or family members can successfully be trained to recognize and respond to an overdose, and appropriately administer naloxone in an overdose situation.

The literature examining the broader public health impact of OEND programs is growing. Two identified studies described the Project Lazarus program in North Carolina, which was created in 2008. One component of this program is the co-prescription of naloxone to people at risk for opioid overdose. An initial evaluation of Project Lazarus in Wilkes County, North Carolina, found significant declines in the unintentional drug overdose death rate from a peak of 46.6 deaths per 100,000 population in 2009 to 29.0 deaths per 100,000 in 2010 and 14.4 deaths per 100,000 in 2011.[224,225] However, because Project Lazarus includes overdose prevention components unrelated to naloxone, it is difficult to determine the exact role naloxone played in the reduction of Wilkes County's unintentional drug overdose deaths.

Walley et al., provide an important evaluation examining changes in health outcomes as a result of OEND program implementation. They conducted an interrupted time-series analysis to evaluate the impact of Massachusetts' OEND program on opioid overdose deaths and non-fatal opioid overdose acute care hospital utilization rates from 2002 to 2009. They found that communities that implemented OEND programs during the study time had statistically significant reductions in opioid overdose death rates compared to communities that did not implement OEND programs. Acute care hospital utilizations did not differ between OEND program communities and those that did not implement one.[130]

In recent years, there has been a push to increase naloxone prescribing in the pain management setting and to equip first responders with naloxone. Coffin et al., found among patients prescribed opioids for chronic pain that those who were prescribed naloxone had 47 percent fewer opioid emergency department visits per month in the six months after receiving naloxone and 63 percent fewer visits after one year compared to patients who did not receive naloxone.[226] Rando et al., assessed the impact of a first responder naloxone program in Ohio and found that opioid overdose deaths declined after implementation of the program.[227] There have also been efforts to increase access to naloxone through the use of "standing orders" that allow for an individual to fill a prescription for naloxone based on a pre-approved order from a licensed prescriber.[228]

Based on recent systematic analyses, the available evidence suggests that naloxone is a promising strategy with some evidence of effectiveness in reducing opioid overdose mortality rates.[229] Limitations of the available studies include lack of randomization of distribution methods; lack of generalizability because the data are almost exclusively based on people who inject drugs, primarily heroin; self-reported outcomes; short-term follow-up; significant loss to follow-up; and lack of control over other events occurring simultaneously that could be responsible for effects.[230]

RECOMMENDATIONS FOR ACTION

8.1 PARTNER WITH PRODUCT DEVELOPERS TO DESIGN NALOXONE FORMULATIONS THAT ARE EASIER TO USE BY NON-MEDICAL PERSONNEL AND LESS COSTLY TO DELIVER

Rationale: As the legal landscape changes to allow broader access to naloxone, different populations may prefer different delivery mechanisms for naloxone. Having multiple products that are easy for non-medical personnel to use would likely increase uptake and reduce costs. Price is consistently raised as a concern impacting the sustainability of various OEND programs, and recent reports indicate that the cost of the drug is increasing dramatically.[231,232] Further, the emergence of highly potent illicitly made synthetic opioids such as fentanyl and carfentanil have raised concerns over the need for higher naloxone doses to successfully reverse overdoses – increasing concerns over costs and the effectiveness of current naloxone formulations.

Current Status: An auto-injector formulation of naloxone with audio guidance (Evzio) was approved by the FDA in April 2014. A nasal formulation (Narcan) was approved in 2015. Many formulations, however, remain financially inaccessible.

8.2 WORK WITH INSURERS AND OTHER THIRD-PARTY PAYERS TO ENSURE COVERAGE OF NALOXONE PRODUCTS

Cost remains a significant concern with regard to sustainability of naloxone programs.

Rationale: One approach to sustaining expanded access to naloxone is through coverage by third-party payers.

Current Status: Some states and localities have made progress in gaining coverage for certain naloxone products. However, this has not been accomplished in a systematic way.

8.3 WORK WITH COMMUNITY-BASED OVERDOSE EDUCATION AND NALOXONE DISTRIBUTION PROGRAMS TO IDENTIFY STABLE FUNDING SOURCES TO ENSURE PROGRAM SUSTAINABILITY

Rationale: Some community-based programs have little to no dedicated funding for the purchase and provision of naloxone. These programs provide critical access to naloxone among high-risk populations.

Current Status: The federal government now has multiple grant programs through both the U.S. Department of Health and Human Services and the Department of Justice to expand access to naloxone. However, it is not clear how these funds will impact community-based programs. Other community-based programs have worked with local and state agencies to develop a sustainable funding model and their experience could be informative to other programs across the country.

8.4 ENGAGE WITH THE SCIENTIFIC COMMUNITY TO ASSESS THE RESEARCH NEEDS RELATED TO NALOXONE DISTRIBUTION EVALUATIONS AND IDENTIFY HIGH PRIORITY FUTURE DIRECTIONS FOR NALOXONE-RELATED RESEARCH

Rationale: Naloxone is a promising strategy for reversing overdose and reducing overdose deaths. Rigorous, high-quality research is needed to explore the relative effectiveness of naloxone use in different settings, through different OEND mechanisms (including care and follow-up after overdose reversal events), and on prescription opioid (as opposed to heroin) overdose. With the entree of large scale providers, such as the Veterans Administration into the OEND space, and the expansion of pharmacy-based naloxone via standing orders, opportunities for more robust and definitive evaluations exist.

Current Status: There are several evaluations currently underway. However, available funding to evaluate the various types of programs being implemented is insufficient. The scientific community needs to further engage in a discussion on the various research approaches to evaluate naloxone programs being implemented in a variety of settings.

8.5. ENGAGE WITH THE HEALTH CARE PROFESSIONAL COMMUNITY TO ADVANCE CONSENSUS GUIDELINES ON THE CO-PRESCRIPTION OF NALOXONE

Rationale: There is no consensus on which patients should be co-prescribed or prescribed naloxone in general medical settings. Recent studies show a number of logistical and attitudinal barriers to naloxone co-prescription. However, at least one study demonstrated a positive effect on opioid-related emergency department visits associated with co-prescribing naloxone to patients treated with opioids for chronic pain.[233]

Current Status: Several medical societies have adopted resolutions supporting naloxone co-prescription to patients, and some health systems such as the Veterans Administration have begun implementing campaigns to increase naloxone co-prescription. The CDC, in their Guideline for Prescribing Opioids for Chronic Pain, recommends that clinicians incorporate strategies to mitigate risk into the management plans of patients receiving opioids, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present. However, to date, there is no consensus on the most appropriate patients for naloxone co-prescription.

8.6 ASSESS THE EFFECTS OF STATE LAWS EXPANDING NALOXONE ACCESS TO THE GENERAL PUBLIC

All 50 states and the District of Columbia have made progress in expanding naloxone access to the general public, such as through the use of standing orders from a licensed prescriber.[234] These laws vary and there is a need to assess which types of laws are most effective in achieving beneficial outcomes on the public's health.

Rationale: Administration of naloxone by non-medical personnel has been shown to be both safe and effective for preventing overdose deaths.[235] The current variation in state laws is ripe for evaluations that can provide guidance regarding the most effective policies.

Current Status: All 50 states and the District of Columbia have laws that facilitate naloxone access by non-medical personnel. These laws vary with in the scope of coverage and the circumstances under which they apply.

9. EXPANDING HARM REDUCTION STRATEGIES

Substance-use disorders, and those involving opioids, are increasingly understood as a chronic condition for which effective treatment exists. However, significant barriers to access involving limited investment and inadequate resources, misconceptions about treatment, and stigma limit the current impact of treatment on the opioid epidemic. In addition, treatment entry is not always feasible for people with opioid-use disorders. Harm reduction was borne out of the belief that harms associated with drug use can be reduced while people are actively engaged in drug use. Beginning in the Netherlands in the late 1980s,[236] it took footing in the U.S. in light of the HIV epidemic among people who inject drugs, with advocacy for establishing needle and syringe service programs. In many ways, harm reduction is as much a social movement as guidance for a set of practical policies and programs focused on people who use drugs. In the context of the current opioid crisis, harm reduction schemes such as needle and syringe service programs and naloxone distribution programs are now considered legitimate public health responses and not surrounded by as much controversy as in the past. As some view harm reduction as a permissive attitude toward illicit drug use, some harm reduction approaches such as supervised consumption sites remain controversial as a viable or legitimate approach to addressing opioid-use disorders. Efforts to increase the recognition and use of evidence-based and promising harm reduction strategies are needed.

The Harm Reduction Coalition defines harm reduction as "a set of practical strategies and ideas aimed at reducing negative consequences associated with drug use. Harm reduction is also a movement for social justice built on a belief in, and respect for, the rights of people who use drugs."[237] In the U.S., harm reduction approaches are often traced back to the early days of HIV, when sharing needles and syringes among people who inject drugs was identified as a risk factor in the spread of the disease. In order to prevent transmission of HIV and Hepatitis C, some medical, public health, and substance-use professionals sought interventions to minimize the disease risks associated with injecting drugs. This was part of a larger paradigm shift still underway to frame and address injection drug use as a medical issue.

The most prominent harm reduction scheme is that of needle and syringe service programs, where individuals can receive clean needles and syringes and other "works" (e.g., cottons, cookers) and dispose of used and potentially contaminated equipment. Over the past three decades, numerous evaluations of needle and syringe service programs demonstrate reductions in the transmission of HIV, Hepatitis C, and show increases in treatment seeking among people who inject drugs as well as other positive health outcomes.[238,239,240] Providing access to equipment that is free of life-threatening viruses is a cornerstone of harm reduction and disease prevention efforts for people who inject drugs.

Efforts to provide supervised consumption sites in which sterile needles and syringes are available, and injecting practices can be monitored by medically trained staff have also demonstrated reductions in disease transmission and overdose rates, and increases in treatment uptake. Unlike needle and syringe service programs which have been in place in U.S. cities for decades, sanctioned supervised consumption sites have only existed in communities outside of the U.S., primarily throughout Europe where it is considered a component of a public health response to drug use. There are supervised consumption sites in Vancouver, British Columbia as well as Sydney, Australia. The majority of studies evaluating the impact of supervised consumption sites derive from Vancouver where the program was initiated as a pilot and there was a national legal battle for its continued existence. The overwhelming evidence shows that supervised consumption sites are associated with reductions in overdose,[241] HIV infections,[242] HCV transmission,[243] unsafe injection practices, and fatal and non-fatal overdoses within the facility and in the surrounding area.[244,245,246,247] A survey conducted in Boston, Massachusetts suggests that people who inject drugs, and those who are at high risk for overdose are likely to use supervised consumption sites.[248]

RECOMMENDATIONS FOR ACTION

9.1 ESTABLISH AND EVALUATE SUPERVISED CONSUMPTION SPACES

Establish supervised consumption spaces as a part of a comprehension response to the opioid overdose epidemic, along with evidence collection and evaluation to understand their optimal design and impact. Planning should include medical professionals, people with lived experiences of drug use, case managers, and community-based organizations to ensure programs are designed comprehensively to meet the needs of people who use drugs. Such programs should provide comprehensive services, including injection supervision by medical professionals, sterile injection equipment, and naloxone as well as case management, treatment information and referral support, and primary care services.

Rationale: Supervised consumption spaces are an evidence-based strategy that has been employed outside of the U.S. to reduce opioid overdose, infectious disease transmission, and other injection-related health risks. Supervised consumption spaces also connect people who inject drugs with treatment services, and can decrease addiction rates.[249] A recent review of the peer-

reviewed literature concluded that supervised consumption spaces are associated with reductions in overdose deaths within and in the area surrounding supervised consumption spaces, reductions in injection drug use, and do not increase crime or drug use in the communities where they are located.[250] However, there is insufficient evidence derived from the United States regarding the effects and potential unintended consequences of these spaces since such spaces are not sanctioned in the U.S. Thus, sanctioned programs in the United States, once introduced, should be evaluated.

Current Status: Sanctioned supervised consumption spaces have been in place in more than 100 cities in 10 countries since 1986 when the first site opened in Bern, Switzerland. None of these sites are in the U.S. However, one unsanctioned U.S. space is described in the literature.[251] Several U.S. states and localities are considering policies to establish supervised consumption spaces.

9.2 WORK WITH STATE AND LOCAL STAKEHOLDERS TO ESTABLISH AND SUPPORT NEEDLE AND SYRINGE SERVICE PROGRAMS

Updates to laws at the federal, state, and local levels allow for agencies and organizations in many communities to supply sterile needles and syringes to people who inject drugs, including opioids.[252] Such programs should follow best practices, which include distribution as opposed to any restricted exchange policies which are associated with increased rates of needle and syringe sharing and elevated HIV prevalence. Services are best provided in a comprehensive manner including referrals to drug treatment and other necessary services (e.g., housing, case management). People with lived experiences should be involved with designing and delivering services to enhance the relevancy of these programs.

Rationale: Providing sterile needles and syringes to people who inject drugs has been shown to reduce the spread of HIV, Hepatitis C, and increase uptake of drug treatment among people who inject drugs.[253,254,255,256,257]

Current Status: A 2016 modification to federal law allows for federal funds to be used for programmatic support and services related to needle and syringe service programs, though not for purchasing the needles and syringes themselves.[258] State and local governments and non-government programs can use this policy shift to expand the scope and reach of existing harm reduction efforts. State and local laws vary with regard to the legality of distributing needles, syringes, and other drug-use paraphernalia.[259]

9.3 EVALUATE AND DISSEMINATE THE USE OF TEST KITS FOR FENTANYL IN OPIOIDS

Test kits provide people with information about the content of their drugs.

Rationale: Recent experience has shown the deadly impact that the evolving synthetic opioid market can have. More potent opioids, such as fentanyl, are increasingly common in the U.S., and are often illicitly manufactured to resemble less-potent opioids.[260] Many of those dying from exposure to high potency preparations may have been unaware of the risk.[261,262] Providing people with the means to test their drug supply for adulterants may affect their decisions about which drugs to use or how to use them.

Current Status: Harm reduction organizations in some U.S. communities are using fentanyl test strips as a low threshold method of testing the presence or absence of fentanyl in street-purchased drugs. We are aware of research underway to test the validity and utility of these test strips, and the impact of their use on behavior and overdose. At the time of this writing, there were no peer-reviewed publications of reporting the results of such research.

10. COMBATING STIGMA

Stigma is an attitude, behavior, or condition that is socially discrediting.[263] Both cause and controllability affect stigma. Survey research documents indicators of stigma toward people with opioid-use disorders within both the general public[264] and health care providers.[265] Such attitudes have implications for how interventions to address opioid-use disorders are conceptualized and supported. In studies using varied descriptions of the same person and scenario, framing opioid addiction as the result of irresponsible behavior for which the person with the disorder is to blame results in less supportive reactions to individuals with the associated disorders relative to when addiction is described as the result of environmental and biological influences.[266,267,268] Similarly, when messages emphasize structural barriers to treatment and highlight success stories as opposed to featuring untreated addiction, people are more likely to express support for policies expanding treatment.[269,270,271]

Language to reduce stigma is also important in how people are described. Separating the person from their disorder by avoiding references to people as "substance abusers" and "addicts" and instead describing an individual as "having an opioid-use disorders" can promote a medical frame and emphasize the disease qualities and treatment options available.[272] This change in language is consistent with a trend in appreciating the importance of language in the clinical context and with the more general practice of referring to people as having a particular condition, as opposed to being defined by their condition (e.g., a person has cancer, but is not cancer). McGinty et al provide a detailed review of the literature on these topics that reflects the findings from a consensus process of national experts and includes recommendations for research.[273]

RECOMMENDATIONS FOR ACTION

10.1 UPDATE EMPLOYER HUMAN RESOURCES AND BENEFITS LANGUAGE TO AVOID STIGMATIZING LANGUAGE AND INCLUDE EVIDENCE ABOUT THE EFFECTIVENESS OF TREATMENT FOR OPIOID-USE DISORDERS

Public and private sector employers have human resource policies and benefits packages that include information about substance use disorders and the treatment options available through insurance plans offered. Such materials should reflect current understanding of how best to communicate about opioid-use disorders to avoid stigmatizing language and encourage treatment.

Rationale: The workplace is an important source of information about health care, and can provide information about the medical nature of opioid-use disorders and the effectiveness of treatment in a way that is consistent with the evidence about constructive, non-stigmatizing language. It is also a potential source of support for employees who are grappling with opioid addiction, contemplating treatment, in treatment, or in recovery. Employers have an opportunity to reframe the response to opioid-use disorders within the workplace by using language that is supportive rather than stigmatizing, disseminating information about the effectiveness of treatment and creating an environment where supportive, constructive dialogue can occur.

Current Status: Workplaces offering supported employment and services for people who are in recovery or seeking to treatment for opioid-use disorders provide examples of how to address stigma in the workplace.

10.2 AVOID STIGMATIZING LANGUAGE AND INCLUDE INFORMATION ABOUT THE EFFECTIVENESS OF TREATMENT AND THE STRUCTURAL BARRIERS THAT EXIST TO TREATMENT WHEN COMMUNICATING WITH THE PUBLIC ABOUT OPIOID-USE DISORDERS

Media coverage of the opioid epidemic, and public and private sector initiatives to educate and intervene should avoid stigmatizing language and apply the available evidence when communicating with the public about opioid-use disorders.

Rationale: Messages about the effects of opioid-use disorders on individuals, families, and communities are ubiquitous, as are educational campaigns and interventions designed to reverse the trend. Because how the opioid epidemic is discussed and how people with opioid-use disorders are portrayed affects support for effective interventions, assuring that the language and frames embedded in media reports and interventions are consistent with the available evidence is important to maximizing these efforts.

Current Status: Several professional organizations and groups have written statements and recommendations about what language to use and what language to avoid, including the recent 2017 Associated Press Stylebook.[274] Reports from professional associations and government-led initiatives provide evidence-based guidance for use by the media, professionals, and agencies and organizations that are active in this work.[275,276,277]

10.3 EDUCATE HEALTH CARE PROVIDERS ABOUT THE BENEFITS ASSOCIATED WITH DESTIGMATIZING LANGUAGE

Rationale: Health care providers are key stakeholders in addressing opioid-use disorders. Research documenting the presence of stigma and the use of stigmatizing language among health care providers demonstrates a need for greater awareness about the counter-productive impacts of stigmatizing language, and is an opportunity for intervention.

Current Status: Educational resources are available through several agencies, organizations, and professional associations.[278,279,280]

ENDNOTES

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