The National Opioid Epidemic: Local, State, and National Responses

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After falls, the leading cause of accidental death in 2013 among all Wisconsin residents was drug overdoses. That year, prescription opioids such as oxycodone, hydrocodone, and methadone were involved in 45% of these overdoses.[1] Nationally, overdoses are the number one cause of unintentional injury deaths among 25 to 65 year olds.[2]

Prescription opioids were developed to treat the pain associated with terminal conditions like cancer, end-of-life pain, and severe acute pain following surgery. In the 1990s, the concept of pain as the "fifth vital sign" was developed by the Veterans Affair Hospital System with the thought that pain was undertreated. The American Pain Society quickly adopted and propagated this view, resulting in professional and consumer groups advocating for increased use of opioids for management of chronic, nonterminal pain. Coincidently, in 1996, Purdue Pharmaceuticals released OxyContin, an extended release form of oxycodone, that was touted in an aggressive marketing campaign as having less abuse potential than short-acting opioids. In 2000, the Joint Commission for Accreditation of Hospital Organizations' Ambulatory Care Division launched a campaign in partnership with Purdue Pharmaceuticals advocating patients' right to effective pain assessment, thus perpetuating the treatment of pain as a vital sign. The addiction and abuse potential soon became clear as this original OxyContin could be chewed, crushed, snorted, or injected, producing a high similar to heroin. This is of concern because 1 in 4 patients prescribed prescription painkillers will transition to long-term use.[3] In the United States, the number of prescriptions written for opioids increased by 300% between 1991 and 2009.[4] In 2007, Purdue Pharmaceuticals pleaded guilty to misleading marketing regarding the abuse and addiction potential of OxyContin, resulting in a $634.5 million fine.[5]

Evidence supporting the efficacy of long-term opioid use over nonopioid therapy for chronic pain treatment is poor outside of the setting of end-of-life care and must be weighed carefully against the substantial risks.[6] Studies suggest that opioids for chronic pain actually may increase pain and decrease functional status by potentiating pain perception.[7] Chronic opioid therapy is associated with an increased risk of myocardial infarction; heart failure; respiratory depression; opioid-associated androgen deficiency; osteoporosis; fractures secondary to increased falls; immunosuppression; opiate-induced hyperalgesia, addiction, and misuse; fatal and nonfatal overdose; and all-cause mortality.[8] Risk for overdose clearly increases in a dose-response manner with markedly greater risk at doses of 90 or more morphine milligram equivalents (MME) per day.[6]

Prior to initiating opioids, other pharmacologic options should be considered. Nonopioid pharmacologic options include acetaminophen, NSAIDs, Cox-2 inhibitors, duloxetine (particularly for chronic pain related to fibromyalgia or coincident with depression), gabapentin (particularly for neuropathic pain), other antidepressants, eg, tricyclics and topical analgesics.[9] Nonpharmacologic modalities include physical therapy, massage, manipulation, physical activity and weight loss, cognitive behavioral therapy, and treatment of comorbid mental illness.[9]

The 2016 Centers for Disease Control and Prevention (CDC) Guideline[6] is consistent with contemporary review papers along with platforms from the American Medical Association (AMA), American College of Physicians (ACP), and the Wisconsin Medical Society. We strongly support the CDC guideline: providing direction for clinicians, recommendations for health systems and legislatures, and awareness of the issues nationally. The guideline provides practicing clinicians a structure for safe prescribing of opioids and guidance with patient discussions. (See Box 1.)

We also strongly support and advocate for the dissemination of the 2016 Wisconsin Medical Examining Board (MEB) Opioid Prescribing Guideline.[10] This guideline closely follows the CDC guideline for evidence-based best practices and adds specific recommendations to indications, dosing, follow-up, discontinuing opioids with specific tapering regimens, and assessing risk and mitigating harms of opioid use. (See Box 2.)

Additionally, we applaud the Food and Drug Administration (FDA) for its proactive response to prescription opioid abuse.[11] The FDA supports development of abuse-deterrent formulations of opioids, expanding availability of lifesaving reversal agents like naloxone and prioritizing approval of nonopioids for pain. Manufacturers of long-acting opioids are now required to have stricter labeling, post-market safety and outcomes research, and funding of voluntary continuing medical education for prescribers referred to as Risk Evaluation and Mitigation Strategy (REMS).

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Box 1. Summary of Centers for Disease Control and Prevention Guideline

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Opioid therapy should be considered only if the expected benefits in both pain and functional improvement are anticipated to outweigh risks to the patient. Additionally, if opioids are used, they should be combined with nonpharmacologic therapy.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals which include both pain control and functional improvement.
3. Clinicians should discuss with patients known risks and realistic benefits of opioid therapy.
4. When starting opioid therapy, clinicians should prescribe immediate-release opioids instead of extended-release opioids. Methadone is not the first choice for a long-acting opioid and should be only used by clinicians with special expertise.
5. When opioids are started, clinicians should use the lowest effective dosage. Clinicians should carefully assess individual risks/benefits when considering dosages of 50 morphine milligram equivalents (MME) or more per day, and must carefully justify a decision to prescribe 90 MME or more per day.
6. For acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and in no greater quantity than the expected length of severe pain requiring opioids, a duration of 3 days in most cases while more than 7 days will rarely be needed.
7. Benefits and harms of opioid therapy should be reviewed with patients within 1 to 4 weeks of starting therapy or escalating dose, and at least every 3 months thereafter.
8. Clinicians should incorporate strategies to mitigate opioid risk into the management plan, including offering naloxone when factors are present that increase risk for opioid overdose. Providers should avoid prescribing opioids to patients with moderate to severe sleep apnea due to increased risk for overdose. Other patient populations requiring closer monitoring include patients with renal or hepatic impairment, over age 65, with mental health conditions, and with a history of substance abuse. Additionally, caution should be exercised in patients with a history of prior nonfatal overdose. Secure storage is essential to help prevent diversion or overdose risk posed to household members, particularly children and young adults.
9. Clinicians should review prescription drug monitoring programs at the initiation of opiate therapy and at least every 3 months thereafter to determine if high drug dosages, dangerous combinations of prescriptions, or multiple prescribers place the patient at increased risk.
10. Clinicians should consider using urine drug testing at initiation of opioid therapy and at least annually thereafter.
11. Clinicians should avoid concurrent benzodiazepine use whenever possible due to increased risk for overdose.
12. Clinicians should monitor patients for opioid use disorder, such as addiction or dependence, and offer or arrange for evidence-based treatment. This may include medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies.

Adapted from 2016 CDC Guideline.[6]

To help limit the substantial risks of addiction, overdose, and death from chronic opioid therapy, we advocate for the following measures and also make special note of measures already addressed in Wisconsin.

1. ***Required use of Wisconsin's enhanced Prescription Drug Monitoring Program (ePDMP) by prescribing clinicians.*** As of April 2017, Wisconsin state law requires prescribers to review the ePDMP before prescribing any controlled substance for greater than a 3-day supply.[10] Prescribers will require education on the optimal use of the state ePDMP (offered by the Wisconsin Medical Society as one of its opioid prescribing webinars).[12] We advocate for the development of a national prescription drug monitoring program to track cross border and interstate prescriptions in an effort to avoid multiple providers/pharmacies, high opioid dosages, and dangerous combinations such as concomitant benzodiazepine use.
2. ***Mandatory physician-patient narcotic contracts with initiation of long-term opioids.*** The contracts should outline appropriate behavior, refill protocols including warnings for early or lost refills, agreement to limit refills to a single clinician and a single pharmacy, and warnings against using medications not prescribed or illicit drugs. Consequences for contract violations should be clearly outlined. Although this recommendation is not evidence-based, both the CDC and the Wisconsin MEB urge the use of narcotic contracts to detail and document the risks for adverse effects and to outline required patient behaviors to limit these risks.
3. ***Periodic urine drug screens, at least once a year, also should be mandatory and used to identify situations of drug divergence and abuse.*** This also may be beneficial in early identification of patients who are at risk of polypharmacy overdose. Additionally, we encourage the development of urine drug screen standardization at the national level.
4. ***Prescriber education about the appropriate use and risks of opioid therapy is much needed as most US clinicians have not received such formal training.*** The Drug Enforcement Administration Office of Diversion Control should mandate opioid education programs in order to renew licenses for those clinicians prescribing scheduled drugs. More than 60 US medical schools, including the University of Wisconsin School of Medicine and Public Health, now require education consistent with the 2016 CDC Guideline.[13] The American Medical Association and other national organizations have developed online self-education programs for the safe prescribing of opioids. The Wisconsin MEB now requires that all DEA licensees complete an approved 2-hour course on its guideline from the course's approval date through the calendar year of 2017 and again during 2018-2019.[14] A Wisconsin Medical Society opioid prescribing webinar satisfies this requirement.
5. ***Medical systems, health plans, and insurers should play an increased role by closely monitoring opiate prescriptions for possible abuse, misuse, and unsafe prescribing practices.*** Organizations should develop and mandate medical informatics systems to promote safe prescribing. Ideally, local health care systems should be proactive about identifying additional targeted educational opportunities for practitioners prescribing outside standard parameters as outlined by new guidelines. We also call for prescription plans to end financial incentives for 90-day supplies of opioids, as this practice significantly increases the risk for overdose and is not conducive to tapering.[15]

Box 2. Summary of Wisconsin Medical Examining Board Opioid Prescribing Guideline

1. Assess pain to see if intensity matches causative factors and if the pain can be addressed with nonopioid therapy.
2. Start with the lowest possible effective dosage of immediate-release opioids for the shortest possible duration and the fewest number of pills. In most cases, less than 3 days and rarely more than 5 days are needed.
3. Attempt to identify the cause of pain; opioids should not be prescribed unless the underlying medical condition would reasonably be expected to cause pain severe enough to warrant opioid treatment.
4. Opioids should not be the first choice for treatment. Evidence for opioids in acute pain is weak and for chronic pain evidence is poor. There is no high-quality evidence to support the efficacy of opioids longer than 6 months in duration. Despite this fact, it is acceptable, although not preferable, to continue patients on chronic opioid therapy started prior to the Guideline release if they have not shown evidence of aberrant behavior.
5. Patients should not receive opioids from multiple providers/pharmacies.
6. Providers should avoid the use of intravenous or intramuscular opioids for exacerbations of chronic non-cancer pain in acute care settings.
7. Providers are encouraged to review the prescription Drug Monitoring Program (PDMP) prior to prescribing. After April 2017, review of the PDMP will be mandatory for prescribing opioids for greater than 3 days duration.
8. Pain from acute trauma or chronic inflammation can often be managed with non-opioids prior to surgery. Surgery outcomes are improved without opioids prior to surgery, ie, less surgical complications and improved patient satisfaction.
9. Avoid coprescribing benzodiazepines as the combination triples the already high annual mortality rates from overdose.
10. Oxycodone use is discouraged due to increased abuse and addiction potential compared to other opioids.
11. Patients presenting for chronic pain treatment, in addition to targeted history and physical exam, should be evaluated for conditions which may affect therapy such as:
    - Coexisting illnesses, ie, respiratory disease, sleep apnea, renal insufficiency.
    - Personal or family history of substance abuse.
    - History of psychiatric disorders associated with opioid abuse, eg, bipolar, attention deficit hyperactivity disorder, borderline personality disorder, uncontrolled depression.
12. Prior to starting opioids, objective symptomatic and functional goals should be established, with a plan for discontinuation if not met.
13. Risk/benefit ratio should be assessed continually. If evidence of increased risk develops, opioids should be weaned or discontinued with treatment for withdrawal. Components of ongoing risk assessment include review of the PDMP, periodic urine drug testing, periodic pill counts, and violations of the opioid agreement.
14. All patients on chronic opioid therapy should have informed consent agreements, which should detail specifically possible significant adverse effects including addiction, overdose, and death. The agreement also should outline required patient behaviors to ensure that they remain safe.
15. Initial dose titration should start with short-acting opioids.
16. Opioids should be prescribed in the lowest effective dose for the shortest possible duration. Caution should be noted for dosages above 50 MME and, given no evidence to support dosages over 90 MMEs along with dramatically increased risks for overdose and death, appropriate justification for use should be carefully documented in the chart.
17. The use of methadone is not encouraged unless the prescriber has extensive training or experience in its use. Methadone has variable metabolism, multiple drug interactions, and can have a potent effect on prolonging the QTc, increasing the risk for fatal arrhythmias.
18. Prescribing of opioids is strongly discouraged for patients abusing illicit drugs, as these patients are at extremely high risk for abuse, overdose, and death.
19. During initial opioid titration, patients should be re-evaluated every 1 to 4 weeks and during chronic therapy, at least every 3 months.
20. Practitioners should consider co-prescribing naloxone for patients at high risk for overdose as evidenced by aberrant behaviors, dosages over 50 MME per day, clinical depression, and history of overdose, which alone is a relative contraindication to chronic opioid therapy. Family members can be prescribed naloxone for use with the patient.
21. All prescribing practitioners are expected to provide care for potential complications of the treatments they provide, including opioid use disorder, by either directly providing medication-assisted treatment or referral to an addiction treatment center that is willing to accept the patient.
22. Discontinuing Opioid Therapy: Consider tapering or discontinuing if circumstances warrant.
    If lack of efficacy is determined, opioid weaning can be performed by tapering the MED by 10% weekly and then discontinued when tapered to 5mg to 10mg MED.
    - If evidence of increased risk develops, opioid weaning can be performed by tapering the MED by 25% weekly and then discontinued when tapered to 5 mg to 10mg MED.
    - If evidence of imminent danger (addiction, overdose) or diversion, opioids should be discontinued immediately and the patient should be treated for withdrawal. Exceptions requiring slower taper include patients with unstable angina and pregnant patients, as withdrawal may precipitate angina and preterm labor, respectively.
    - Prescription of clonidine 0.2mg by mouth (po) twice a day or tizanidine 2mg po 3 times a day can be provided to patients complaining of opioid withdrawal related symptoms.

Adapted from the 2016 Wisconsin Medical Examining Board Opioid Prescribing Guideline. [14]

6. ***Targeted public education and awareness of the many potential harms of opioid treatment should be strengthened for high-risk groups, teenagers, and parents of teenagers.*** A recent CDC survey found that 1 in 5 high school students had taken a prescription drug without a prescription. Community outreach is necessary to curb the epidemic by education and cultural change. In fiscal year 2015, the CDC committed $20 million to launch safe opioid prescribing programs in 16 states. The AMA, ACP, and many other national organizations have developed public education and physician education campaigns. At the state level, in 2016 the Wisconsin Attorney General launched a campaign called "A Dose of Reality" to educate the public regarding the dangers of prescription painkiller misuse.

7. ***When opioid prescriptions are justified, care must be taken to ensure that prescriptions are not diverted, intentionally or otherwise.*** According to the National Survey on Drug Use and Health, over 67.6% of people who reported nonmedical use of prescription drugs obtained their supplies from friends or relatives.[16] Patients must be educated regarding the importance of locking up prescriptions

and making sure they are not being diverted by theft or by family members.[12] Prescribers must be educated to prescribe the lowest effective dose of short-acting opioids for a period no greater than that which would be expected for the severity of pain: "3 days or less will often be sufficient; more than 7 days will rarely be needed."[6]

8. ***Legislation for closer monitoring and tighter regulation of opiate prescribing, both at the state and federal level, is essential.*** Tighter oversight by regulatory agencies like the DEA could make clinicians, health care systems, and insurance carriers more accountable for prescribing patterns. In 2016, the AMA organized a task force to reduce opioid abuse and is working at the federal and state levels to address the prescription drug abuse and diversion crisis. In addition, the Wisconsin Legislature has passed 17 bills known as the Heroin, Opioid Prevention and Education (HOPE) Agenda aimed at prevention and treatment of the growing heroin and prescription drug epidemic.
9. ***Harm reduction strategies should be implemented at the local, state, and national levels.*** Practitioners should consider prescribing naloxone for patients at higher risk for overdose and those on opioid doses over 50 MMEs/day as recommended by the MEB Guideline. Furthermore, in August 2016, Wisconsin passed the first of the HOPE bills, which provides standing orders for pharmacies to dispense naloxone, without a prescription, to any person in a position to assist an individual at risk for opioid-related drug overdose. Many local police departments and pharmacies nationally are installing safe medication disposal units, providing a necessary outlet to properly dispose of unused medication.[13]
10. ***Lastly, and perhaps most importantly, increased availability, access, funding, and support for behavioral health, substance abuse, and addiction services is paramount.*** Prescribers should be able to provide medication-assisted treatment or refer patients to local addiction treatment centers.[10] Yet, sadly, affordable and timely access to treatment centers is one of the biggest barriers to long-term success in combating the opioid epidemic. Local, state, and federal resources should be allocated to lifesaving, quality addiction treatment centers and improved access to behavioral health clinicians to treat mental illness comorbidities and support healthy decisions. Complementary, psychological, and multidisciplinary therapies also are effective for chronic pain, but often cost is a barrier for patients.[6] In response, a federal task force was created in March 2016 to implement federal parity protections intended to ensure that health plans' coverage of mental health and substance abuse disorder benefits are comparable to coverage of medical and surgical benefits.[13] At the state level, guaranteed coverage also could be driven by requiring all insurers—including public options—to cover the costs of substance abuse treatment, including medication-assisted treatment, multidisciplinary treatment teams, mental health services, and recovery support.[17]

Advancing the understanding of the prescription drug epidemic through ongoing education and community outreach needs to occur at the office, health system, state, and national levels. We are very encouraged by physician education at the office level, new opiate prescribing policies, and electronic databases at the health system level; new legislation (HOPE Agenda bills), new prescribing guidelines (the MEB Opioid Prescribing Guideline), prescriber education (the Wisconsin Medical Society opioid prescribing webinars), and public education (Dose of Reality) at the state level; new federal funding to support expanding access to treatment along with parity protections, the CDC 2016 opioid prescribing guideline, and national organization involvement in public and physician education at the national level. The wheels of change have been set in motion, but success will require a cultural sea change.

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