At this writing, opioids are the most commonly prescribed class of medication in the United States (1). Prescription of some opioids, such as methadone, has increased more than 800% in the past 10 years (2). This increase in opioid prescribing has caused an increase in overdoses and deaths. Opioid overdose is among the most common causes of death nationwide (3). The increase in deaths due to prescription opioids is a major public health priority and not just a concern for individual physicians and their patients.

It is easy to blame the growing epidemic of opioid overdose and death on manipulative patients who misrepresent pain symptoms to obtain drugs to abuse or sell. A recent report (4) on overdose deaths in West Virginia found that 51% occurred in persons who had never actually been prescribed an opioid (that is, prescription diversion) and that another 20% occurred in persons who had received prescriptions from 5 or more physicians (that is, “doctor shopping”). In an accompanying editorial (5), we acknowledged the role of the patient in adverse events from opioids but also suggested opportunities for physicians to stem the rise in prescription opioid deaths.

In this issue, Dunn and colleagues (6) identify a potential role for physicians in reducing prescription opioid overdose and death. The authors examined stably insured patients with a range of noncancer pain diagnoses in the Group Health Cooperative network in Washington. Doctor shopping with multiple opioid prescriptions was probably minimal in this setting, which had a systemwide electronic health record. Patients most likely to seek drugs from multiple physicians probably left the system, as did one third of the study sample during the 4-year follow-up. Yet, even in this closed system, the rates of documented serious overdose incidents and deaths were substantial (117 and 17 per 100 000 person-years, respectively). True rates were probably even higher because of inevitable gaps in the reporting of these events.

A disturbing observation from Dunn and colleagues’ study was that many overdose incidents might have been averted by changes in prescriber practices. First, the raw data (unadjusted) revealed more overdoses in patients who were diagnosed with depression or substance abuse or who were concurrently prescribed sedative-hypnotics (for example, benzodiazepines). It is unknown whether these patients were first treated, as they should have been, with alternative nonopioid pharmacologic and nonpharmacologic approaches (for example, physical therapy) to manage chronic pain. Regardless, depression, substance use, and benzodiazepine use are all well-known risks for adverse events from opioids (7); therefore, these persons require substantial education and close oversight if opioids are prescribed.

The authors did not evaluate other risk factors for opioid misuse, including history of illicit drug use (because it is infrequently entered as a diagnosis). When alcohol use is recorded, it is located in the social history, where it rarely affects prescribing (8). Substance abuse screening and brief intervention protocols have been shown to reduce substance use–related problems (9) but have not been widely incorporated into physician practice (10). Physicians may fear finding an addiction, which many are unprepared to treat (11). But brief screening discussions about substance use—not just addiction—are needed to reduce opioid overdose as well as other drug–alcohol or drug–drug interactions.

A unique contribution of this study is the examination of the relationship between overdose events and the timing and morphine-equivalent dose of the prescribed drug. As expected, the authors found that risk for an adverse event was greatest shortly after the initial opioid prescription or after a refill. These data reinforce the importance of closely monitoring patients who are prescribed opioids. The authors also report a dose–response relationship between higher morphine-equivalent doses and risk for opioid-related overdose. Although the highest dose of opioids (≥100-mg morphine equivalents) was received during only 2% of the follow-up, the associated annual overdose rate was very high during that period: 1791 per 100 000 person-years. Low doses rarely resulted in adverse events. Prescribing opioids at high doses is both dangerous and questionable for indications other than methadone treatment of opioid dependence.

Opioid therapy can be monitored by making an opioid agreement with the patient when therapy is initiated. The agreement is updated whenever therapy is modified. Typically, these agreements not only set out the responsibilities of both patient and provider when these drugs are used but also make clear the potential dangers of using these drugs other than as prescribed. Dunn and colleagues’ findings reinforce the importance of goal-directed opioid therapy, in which continued or increased doses of opioid therapy should be contingent on clear improvements in function and quality of life (for example, resuming more normal activities) (7). Long-term opioid therapy carries too many risks to justify use without improvements in health status.

Of note, the patients in Dunn and colleagues’ study received prescriptions primarily for short-acting opioids, namely hydrocodone and oxycodone. Although not specified, these drugs were probably in formulations with acet-
aminophen. Not only are short-acting opioids associated with greater risk for tolerance and dependence (12), a recent panel of the U.S. Food and Drug Administration (13) recommended that these combination drugs be removed because of acetaminophen-related hepatotoxicity. Acetaminophen poisoning was not examined in this study but represents yet another risk that patients and physicians should seek to reduce.

Finally, Dunn and colleagues’ findings strengthen the argument for an easy-to-use, real-time, prescription-drug monitoring program in which physicians can track all opioid prescriptions for a patient. Two promising systems, one designed by the Department of Health and Human Services and one by the Department of Justice, are in testing now. However, neither is fully satisfactory. To be successful, the program needs to be readily accessible for all health care clinical information systems, including pharmacies. The White House Office of National Drug Control Policy and other federal agencies are actively collaborating on development of this key resource to help physicians reduce patient abuse of prescriptions (for example, doctor shopping) and adverse drug interactions.

It is easy to suggest time-consuming, unreimbursed approaches to improve the safety of opioid prescribing without specifying how they can be incorporated into already overburdened clinical settings. Frankly, we do not know how to increase clinical diligence without additional work, time, or money, although technology can facilitate some of these suggested practice changes. The threat to patient safety is too great to allow current pain management and opioid-prescribing practices to remain as they are. Dunn and colleagues’ data show the need to assess the risk for opioid misuse, provide close oversight, dose judiciously, and continually reevaluate the benefit of these potentially risky drugs. Smarter, more responsible practices are the only hope to avoid tragic, avoidable deaths.

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