

Today's nonmedical opioid users are not yesterday's patients; implications of data indicating stable rates of nonmedical use and pain reliever use disorder

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According to the narrative underlying current policies aimed at reducing opioid-related deaths, the problem can be traced to a dramatic increase in opioid prescribing that began in the late 1990s. This trend supposedly was fueled by unscrupulous pharmaceutical company representatives who convinced practitioners that opioids posed a low risk of misuse and overdose (although a recent analysis¹ suggests there were probably 30 or more root causes of the crisis). To illustrate this narrative, politicians and journalists have cited examples of patients who accidentally became “hooked” on opioids while taking them for pain, such as teenagers with orthopedic injuries who found the analgesics prescribed for them so alluring that they progressed to lives of drug abuse and addiction.² This narrative drives policies targeting the prescription of opioids to patients in pain, with the goal of reducing the risk of addiction as well as the diversion of prescription opioids to the underground market. These policies include state prescription drug monitoring programs (PDMPs), abuse-deterrent formulations of prescription opioids, prescribing guidelines, and legal restrictions on prescribing for both acute and chronic pain.

Despite these efforts, opioid-related deaths have continued to rise. The US Centers for Disease Control and Prevention (CDC) reported in November 2018 that deaths involving opioids rose by 13% between 2016 and 2017.³ Opioid-related deaths have risen by nearly 500% since 1999.³ The deaths have continued to rise despite the fact that per capita high-dose opioid prescriptions (90 MME or greater) fell by 58% from 2008 to 2017,⁴ while the total volume of opioids dispensed fell by 29% from 2010 to 2017.^{5,6}

The actual components of the opioid-related death toll are as alarming as they are revealing. Since 2010, deaths involving heroin and fentanyl have risen much more dramatically than those involving prescription opioids. The share of opioid-related deaths involving “synthetic opioids other than methadone” rose from 14% in 2010 to 60% in 2017.³ According to the Drug Enforcement Administration, that category consists almost entirely of illicitly produced fentanyl and fentanyl analogs, manufactured in Asia or Mexico and smuggled into the United States, often via mail or private courier.⁷ Based on likely understated CDC data,⁸ fentanyl or heroin was involved in 75% of opioid-related deaths in 2017, up from 28% in 2010.⁹ Just 30% of opioid-related deaths involved prescription analgesics such as hydrocodone and oxycodone in 2017, down

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from 52% in 2010, and roughly 40% of those 2017 cases also involved heroin or fentanyl.⁹ In other words, approximately 18% of total opioid-related deaths in 2017 involved prescription analgesics without heroin or fentanyl. Extrapolation from New Hampshire Department of Justice data suggests that even the 18% figure was grossly overstated (Fallon K, personal communication, December, 2018). Adding other drugs to the analysis of the CDC's data makes the role of prescription opioid analgesics appear even less significant. For instance, 68% of deaths involving prescription opioids in 2017 also involved heroin, fentanyl, cocaine, barbiturates, benzodiazepines, or ethanol. Thus, fewer than 10% of opioid-related deaths involved prescription pain relievers without those other dangerous substances.⁹

These trends suggest that nonmedical opioid users are migrating from prescription drugs to heroin and illicit fentanyl and fentanyl analogs as legally produced prescription opioids become more expensive and difficult to obtain in the underground market. Research suggests that the advent of abuse-deterrent opioids was a significant factor in this shift.¹⁰ There is also some evidence that PDMPs have contributed to the replacement of prescription opioid analgesics with heroin and fentanyl.¹¹

Challenging the standard narrative

It would be reasonable to expect that the increasing prevalence of heroin and illicit fentanyl in drug-related deaths would encourage policymakers to thoughtfully reconsider the relationship between opioid prescribing and deaths involving opioids. The data suggest that the overdose crisis is largely an unintended consequence of drug prohibition. Prohibition provides powerful economic incentives for illicit manufacturers, transporters, and dealers to supply banned substances. Nonmedical users appeared to prefer diverted prescription opioids, perhaps because the doses were reliable or because the fact that they could be legally prescribed for medical purposes created the illusion that they were relatively safe.¹² But as diverted pain pills became more difficult to obtain in recent years, the black market filled the void with cheaper (and more dangerous) heroin and illicit fentanyl.

Yet defenders of the standard narrative believe that the population of nonmedical users consists primarily of patients who were inappropriately prescribed opioids for painful conditions. Based on that premise, they reason that reducing opioid prescribing in conjunction with better drug interdiction and expansion of drug treatment should gradually eliminate the problem. Unfortunately, the data do not support that expectation. Undoubtedly, some patients, when exposed to an opioid

for the treatment of a painful condition, enjoy the psychoactive effects and desire to have that experience again. When presented with an opportunity to use the drug in a nonmedical context – ie, recreationally – they happily indulge. However, this scenario is the exception, not the typical case.

The National Survey on Drug Use and Health (NSDUH) has repeatedly found that <25% of nonmedical prescription opioid users obtain these drugs from a prescriber; the rest obtain them from friends, relatives, or dealers.¹³ In a 2007 study of more than 27,000 OxyContin addicts who entered rehab between 2001 and 2004, Carise et al found that 78% said the drug was never prescribed for them for any medical reason, 86% took the pills to get “high” or get a “buzz”, and 78% had a history of prior treatment for a substance abuse disorder.¹⁴

NSDUH data provide further reason to doubt that the population of nonmedical users is largely made up of former patients. The rate of “past month nonmedical use of pain relievers among people aged 12 or older” was essentially flat in that survey from 2002 through 2014.¹³ The same is true of “pain reliever use disorder in the past year among people aged 12 or older” during that period.¹³ (The wording of the NSDUH questions changed in 2015, and thus the numbers for more recent years are not comparable.) Yet, the volume of opioids prescribed in the United States almost doubled between 2002 and 2014.⁵ Doubling the amount of opioids prescribed does not seem to have had a discernible effect on the rate of nonmedical use or the rate of pain reliever use disorder. Conversely, reducing prescriptions has not reduced opioid-related deaths. To the contrary, it seems to be driving up the death toll by pushing nonmedical users toward deadlier drugs. A more rational approach, based on a more accurate narrative, would emphasize measures aimed at reducing the harms associated with consumption of black-market opioids.

Toward a Truer narrative

In a September 2018 analysis of CDC data going back to the 1970s, Jalal et al found that “death rates from drug overdoses in the U.S. have been on an exponential growth curve that began at least 15 years before the mid-1990s surge in opioid prescribing, suggesting that overdose death rates may continue along this same historical growth trajectory for years to come”.¹⁵ The authors of the article concluded:

The epidemic of drug overdoses in the United States has been inexorably tracking along an exponential growth curve since at least 1979, well before the surge in opioid prescribing in the mid-1990s. Although there have been transient periods of minor acceleration or deceleration, the overall drug overdose mortality rate has regularly returned

to the exponential growth curve. This historical pattern of predictable growth for at least 38 years strongly suggests that the epidemic will continue along this path for several more years. By contrast, the recent historical variability with which some specific drugs have waxed and waned makes predictions about the future role of specific drugs far more uncertain. Indeed, it is possible that in the future, the drug overdose epidemic may be driven by a new or heretofore obscure psychoactive substance.¹⁵

Summing up these findings, NBC News correspondent Maggie Fox observed that the overdose crisis “started before the availability of synthetic opioids, and may have only a little to do with the prescribing habits of doctors or the pushy habits of drug makers”.¹⁶ The shift toward heroin and fentanyl is not just a matter of prescription opioid users switching to other drugs. In recent years, opioid users have become more likely to start with illicit narcotics. In a November 2017 study, Cicero et al found that a third of heroin addicts entering rehab in 2015 initiated opioid use with heroin, up from just 8.7% in 2005.¹⁷

Americans increasingly have been engaging in the non-medical use of licit and illicit drugs since the late 1970s. Some of this drug use may represent self-medication in response to anxiety, depression, alienation, and despair. The rising incidence of drug-related deaths among nonmedical users also indicates that they are facing bigger risks today, probably because potency has become more difficult to predict and possibly because doses have increased and drug mixtures have become more reckless.¹⁸ However, policymakers and the media tend to favor simple explanations and solutions for complex problems, and the opioid overprescribing narrative is no exception. However, as Mencken observed, “There is always a well-known solution to every human problem” that is “neat, plausible, and wrong”.¹⁹ The standard explanation of the overdose crisis is wrong, and the policies it has inspired are not only ineffective, but harmful.

Harmful effects of the standard narrative

Opioid-related deaths continue to rise even as many patients in chronic pain have seen their medication dosages involuntarily reduced or cutoff altogether. Some, in desperation, have sought relief from the black market or even in suicide.^{18,20} Health care providers have criticized the imposition of prescription limitations as a misinterpretation of the opioid prescribing guidelines published by the CDC in 2016, and some have criticized the guidelines themselves as lacking a firm empirical basis.^{21,22} The American Medical Association

has joined the chorus of critics,²³ as have a diverse group of pain and addiction specialists who signed a November 2018 letter in *Pain Medicine* that describes “nonconsensual tapering policies” as a “large-scale humanitarian issue.”²⁴ US Food and Drug Commissioner Scott Gottlieb has acknowledged these concerns and has taken early steps to address them.²⁵

Conclusion

The current overdose crisis is rooted in the intersection of long-term psychosocial and cultural trends with the lucrative opportunities offered by drug prohibition. Ending drug prohibition will not curb the growing tendency to use drugs nonmedically. However, it will potentially reduce the resulting harm. Short of decriminalization, policymakers should abandon one-size-fits-all intrusions into the clinician–patient relationship. As an alternative, they should consider prioritizing harm reduction measures such as expanded access to medication-assisted treatment, needle exchange, and supervised injection facilities, and rescheduling naloxone to make it available as a truly over-the-counter drug.²⁶

Health care in general, and pain and addiction management in particular, are nuanced undertakings. Current public policies aimed at reducing opioid-related deaths ignore such nuance in favor of ham-handed, empirically dubious, and demonstrably harmful dictates. Americans suffering from chronic pain, and those from whom they receive their treatment, deserve medical care managed through better-informed and more even-handed policy.

Disclosure

Dr Singer serves as a consultant to Reed Smith, LLC. Dr Schatman serves as a consultant to Kaleo Pharma. The authors report no other conflicts of interest in this work.

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