JAMA Network Open

Editorial

New Data on Opioid Dose Reduction—Implications for Patient Safety

Stefan G. Kertesz, MD; Allyson L. Varley, PhD

+ Related article

Author affiliations and article information are listed at the end of this article.

In the US, prescribing of opioids for pain reached its peak in 2011 to 2012. By 2020, prescribing per capita had decreased to levels last seen in 1993.[1] Whether that reversal delivered some mitigation to an escalating North American tragedy of drug-related deaths remains a matter of anxious debate. Few, however, would contest the view that this ongoing reversal bears with unique intimacy on the 8 to 10 million US individuals who receive prescribed opioids on a long-term basis, or who may yet need them.[1] New research on prescription opioid dose reduction should cause us to look upon their situation with fresh eyes, and with concern.

Reductions and stoppages in these patients' prescription regimens are likely to reflect varied motivations and understandings among physicians and other professionals who care for them. Some may reduce doses out of a belief that the dose reductions confer safety and well-being, a perspective reinforced by studies in which voluntary tapers are achievable or even salutary for some patients. However, it is likely that many clinicians are reacting to a fraught public discourse and to external pressures as well, including measures that rate the quality of their work. According to a metric issued by the National Committee for Quality Assurance and taken up by most payers, patients taking a daily dose more than the equivalent of 90 mg of morphine count as receiving poor care, regardless of their prior dose history.[2] Such measures do incentivize either reduction or termination of the care relationship. Unsurprisingly, dose reductions and stoppage have become more common in recent years.[3]

Some retrospective studies found an association between dose reduction and poor outcomes, such as death by overdose, suicide, or mental health crisis, after comparing patients who underwent such reductions and others who did not. One limitation to such reports is that people who underwent reduction could have differed in important ways from those who did not. Differences in their risk could have spurred both the dose reduction and the outcome. For example, a patient with volatile behavior may be at risk for suicide, and that same volatile behavior could spur clinicians to alter prescriptions. Some may suggest that the dose reduction did not cause a subsequent suicide. If existing studies are confounded in this way, they render an unduly pessimistic portrait of the risk of harm resulting from prescription opioid reduction.

The new study by Fenton et al[4] addresses these challenges with 2 methodological innovations. First, they apply an exposure-crossover design, in which each person serves as their own control in the assessment of event frequencies before and after the dose reduction. Second, they attempt to mitigate time-limited volatility in the period before and after dose reduction by focusing on outcomes occurring a full year after the taper was initiated (which they term postinduction).

The article by Fenton et al[4] reports on 19 377 commercially insured and Medicare Advantage enrollees who underwent tapering (2008-2017) after a 12-month period of stable doses. Taper was operationalized as a 15% or more reduction in mean daily dose. The exposure-crossover method applies conditional regression models to compare periods after taper (12-24 months) with periods before in the same population, adjusting for clinical covariates such as drug- and alcohol-related diagnoses and demographic characteristics.

Fenton et al[4] also report adverse outcomes. Compared with the period before dose reduction, the incidence of hospital or emergency department encounters for drug overdose or withdrawal was elevated by 57% (adjusted incident rate ratio, 1.57), in relative terms, and by 52% (adjusted incident rate ratio, 1.52) for mental health crisis in the 12 to 24 months following reduction.[4] The elevations in observed risk were greater for patients whose baseline opioid dose was greater than the equivalent

of 300 mg of morphine daily.[4] Supplementary analyses comparing tapered patients with those not tapered were concordant: patients at stable dose remained at lowest risk, compared with patients whose doses were lower or higher.

By our count, this is the tenth retrospective comparative study to document an adverse association between opioid dose reduction and patient safety,[5-13] although a gain in safety was shown in one other study.[14] We caution that the article by Fenton et al,[4] despite its strengths, still cannot fully resolve potential bias from unmeasured factors, because many aspects of the clinical story remain outside of the researchers' database. Evidence derived from retrospective analysis demands our caution. For that reason, it is deeply regrettable that such caution was absent when many health systems, government agencies, and payers incentivized dose reduction on the basis of retrospective data that were subject to all the same limitations, and many more.[15]

How should clinicians and health systems respond today, in light of these evolving, cautionary findings on opioid dose reduction? Our view is that opioid dose reduction is likely to offer benefit for some, while harming others. The harms may include worsening pain, distress, or death. Given this uncertain balance of harm and benefit, it would be wise for health systems to stop promoting this change to care. A policy of tapering all patients to doses lower than a specified threshold cannot be supported from available evidence. Quality metrics that incentivize these policies, such as the High Dose Opioid criterion promulgated by the National Committee for Quality Assurance,[2] are overdue for retirement. Indeed, experts who assisted the Centers for Disease Control and Prevention's 2016 guideline urged that it not be adopted in the first place.[16]

What about individual care decisions? If an elective change to care involves both potential benefit and risk of serious harm, including loss of life, the longstanding norms of ethical medical care call for informed consent. We see no reason to set these norms aside when discussing dose reductions.

Clinicians will observe that, in some instances, consent will not be forthcoming, despite compelling evidence of harm resulting from prescription opioid therapy. To our view, a lack of consent does not compel a prescribing clinician to continue a treatment that they believe is actively harming that patient. However, that same clinician should proceed with reductions only after (1) documenting evidence of harm, (2) offering a plan to mitigate harm from the reduction, and (3) telling the patient what criteria will be used to decide whether the taper has failed or succeeded. When tapers fail, as many do, then clinicians must be open to reversing them. For this reason, the long-standing adage that opioid tapers must not be reversed, most recently cited in a draft revision to the Centers for Disease Control and Prevention's opioid prescribing guideline,[16] has been worn thin by studies such as this one and the many that precede it. To our view, that adage is not tethered to clear and compelling evidence. It should be set aside.

Finally, whenever consent is sought, it should be in the context of a serious conversation grounded in mutual respect, rather than an attempt to convince the patient to embrace something they do not really believe in. This is because patients—it has been overlooked far too often—are the moral equals of the people writing the prescriptions.

ARTICLE INFORMATION

Published: June 13, 2022. doi:10.1001/jamanetworkopen.2022.16733

Corresponding Author: Stefan G. Kertesz, MD, Division of Preventive Medicine, University of Alabama at Birmingham, 1720 Second Ave S, MT608, Birmingham, AL 35294 (skertesz@uabmc.edu).

Author Affiliations: Birmingham VA Health Care System, Birmingham, Alabama (Kertesz, Varley); Division of Preventive Medicine, University of Alabama at Birmingham, Birmingham (Kertesz, Varley).

Conflict of Interest Disclosures: Dr Kertesz reported holding stock in Zimmer Biomet and Thermo Fisher and receiving royalties from UpToDate (Wolters-Kluwer). He also held stock in CVS Caremark, in 2020 only. Dr Varley reported being employed part time with Heart Rhythm Clinical and Research Solutions, LLC, and 3PH Alliance, Inc.

Disclaimer: The opinions in this article are those of the authors alone and do not represent formal positions of the US Department of Veterans Affairs or any other government agency.

REFERENCES

1. Woods C. Prescription opioid utilization patterns in the U.S. FDA public workshop on opioid prescriber education. October 13, 2021. Accessed January 29, 2022. https://healthpolicy.duke.edu/sites/default/files/2021-10/Opioid%20Prescriber%20Education%20Workshop%20Slide%20Deck.pdf

2. National Committee for Quality Assurance. HEDIS and performance measurement. Accessed May 12, 2022. https://www.ncqa.org/hedis/

3. Neprash HT, Gaye M, Barnett ML. Abrupt discontinuation of long-term opioid therapy among Medicare beneficiaries, 2012-2017. *J Gen Intern Med*. 2021;36(6):1576-1583. doi:10.1007/s11606-020-06402-z

4. Fenton JJ, Magnan E, Tseregounis IE, Xing G, Agnoli AL, Tancredi DJ. Long-term risk of overdose or mental health crisis after opioid dose tapering. *JAMA Netw Open*. 2022;5(6):e2216726. doi:10.1001/jamanetworkopen.2022.16726

5. Oliva EM, Bowe T, Manhapra A, et al. Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation. *BMJ*. 2020;368:m283. doi:10.1136/bmj.m283

6. Hallvik SE, El Ibrahimi S, Johnston K, et al. Patient outcomes after opioid dose reduction among patients with chronic opioid therapy. *Pain*. 2022;163(1):83-90. doi:10.1097/j.pain.0000000000002298

7. James JR, Scott JM, Klein JW, et al. Mortality after discontinuation of primary care-based chronic opioid therapy for pain: a retrospective cohort study. *J Gen Intern Med*. 2019;34(12):2749-2755. doi:10.1007/s11606-019-05301-2

8. Coffin PO, Rowe C, Oman N, et al. Illicit opioid use following changes in opioids prescribed for chronic non-cancer pain. *PLoS One*. 2020;15(5):e0232538. doi:10.1371/journal.pone.0232538

9. Mark TL, Parish W. Opioid medication discontinuation and risk of adverse opioid-related health care events. *J Subst Abuse Treat*. 2019;103:58-63. doi:10.1016/j.jsat.2019.05.001

10. Binswanger IA, Glanz JM, Faul M, et al. The association between opioid discontinuation and heroin use: a nested case-control study. *Drug Alcohol Depend*. 2020;217:108248. doi:10.1016/j.drugalcdep.2020.108248

11. Glanz JM, Binswanger IA, Shetterly SM, Narwaney KJ, Xu S. Association between opioid dose variability and opioid overdose among adults prescribed long-term opioid therapy. *JAMA Netw Open*. 2019;2(4):e192613. doi:10.1001/jamanetworkopen.2019.2613

12. Agnoli A, Xing G, Tancredi DJ, Magnan E, Jerant A, Fenton JJ. Association of dose tapering with overdose or mental health crisis among patients prescribed long-term opioids. *JAMA*. 2021;326(5):411-419. doi:10.1001/jama.2021.11013

13. DiPrete BL, Ranapurwala SI, Maierhofer CN, et al. Association of opioid dose reduction with opioid overdose and opioid use disorder among patients receiving high-dose, long-term opioid therapy in North Carolina. *JAMA Netw Open*. 2022;5(4):e229191. doi:10.1001/jamanetworkopen.2022.9191

14. Hayes CJ, Krebs EE, Li C, Brown J, Hudson T, Martin BC. Association between discontinuing chronic opioid therapy and newly diagnosed substance use disorders, accidents, self-inflicted injuries and drug overdoses within the prescribers' health care system: a retrospective cohort study. *Addiction*. 2022;117(4):946-968. doi:10.1111/add.15689

15. Dowell D, Haegerich T, Chou R. No shortcuts to safer opioid prescribing. *N Engl J Med*. 2019;380(24):2285-2287. doi:10.1056/NEJMp1904190

16. Kertesz SG. An opioid quality metric based on dose alone? 80 professionals respond to NCQA. March 22, 2017. Accessed April 5, 2022. https://stefankertesz.medium.com/an-opioid-quality-metric-based-on-dose-alone-80-professionals-respond-to-ncqa-6f9fbaa2338