Published in final edited form as:

Anesth Analg. 2019 January ; 128(1): 16–18. doi:10.1213/ANE.0000000000003902.

The More You Know: Identifying Factors Associated With Inpatient Mortality Related to Opioid Overdose Can Drive Progress in the Opioid Health Crisis

Andrea L. Nicol, MD, MS*, Douglas A. Colquhoun, MBChB, MSc, MPH†, and Chad M. Brummett, MD†

*Department of Anesthesiology, University of Kansas School of Medicine, Kansas City, Kansas

†Department of Anesthesiology, University of Michigan School of Medicine, Ann Arbor, Michigan.

Although most people in the world may not be aware of every current event at any given time, one that is likely on the radar of just about every American is the opioid epidemic. Seemingly everywhere one turns, whether it be a local radio show, national nightly news program, or an Internet news feed, reports of the opioid epidemic and its impact on society are ever-present and heavily emphasized. During the past quarter century, there has been a dramatic increase in the use of prescription opioids for the treatment of pain. Currently, 1 in every 25 adults in the United States regularly uses prescription opioids.¹ Furthermore, greater health care utilization and its associated costs are linked with prescription opioid use.² Sequelae of prescription opioid use are increased morbidity and mortality due to unintentional overdose, misuse, abuse, the risk of chronic prescription opioid dependence after acute or short-term opioid exposure, and transition into illicit opioid use.^{1,3–7} In the United States alone, the increase in prescription opioid use has followed a similar trajectory of the incidence of overdose due to prescription and illicit opioids.⁸ Sadly, even with this drastic escalation in the use of opioids, there has been no change in the rate or severity of chronic pain conditions.⁹

Opioids—both illicit and prescription—are the main force driving the exponential increase in drug overdose deaths in the United States. The US Department of Health and Human Services has recognized this significant public health problem, and in late 2017, it declared the opioid crisis a national emergency.¹⁰ The president promoted a 5-point strategy that

Address correspondence to Andrea L. Nicol, MD, MS, Department of Anesthesiology, University of Kansas School of Medicine, 3901 Rainbow Blvd, MS 1034, Kansas City, KS 66160. anicol@kumc.edu.

Conflicts of Interest: See Disclosures at the end of the article.

DISCLOSURES

Name: Andrea L. Nicol, MD, MS.

Contribution: This author helped review the literature and prepare the manuscript.

Conflicts of Interest: A. L. Nicol is a consultant for Heron Therapeutics.

Name: Douglas A. Colquhoun, MBChB, MSc, MPH.

Contribution: This author helped review the literature and prepare the manuscript.

Conflicts of Interest: None.

Name: Chad M. Brummett, MD.

Contribution: This author helped review the literature and prepare the manuscript.

Conflicts of Interest: C. M. Brummett is a consultant for Heron Therapeutics and Recro Pharma.

This manuscript was handled by: Honorio T. Benzon, MD.

prioritizes access to opioid use disorder services, availability of opioid-reversing drugs, public health data reporting and collection, and a focus on research and advancing pain management practice. As part of the focus on research, in April 2018, the National Institutes of Health launched the Helping to End Addiction Long-Term initiative—touted as an aggressive transagency effort to speed scientific solutions to stem the national opioid crisis.¹¹ The total budget for fiscal year 2018 for Helping to End Addiction Long Term is \$500 million, of which approximately \$70 million is for focused research on opioid use disorder and how to prevent or reverse overdose. This initiative is very timely: a recent report by the Centers for Disease Control and Prevention showed that opioid drug overdoses killed about 72,000 Americans in 2017, a record number that is reflecting a rise of around 7% from January 2017 to the end of that year.¹² This death toll is higher than the peak yearly death totals from car accidents, gun deaths, and human immuno-deficiency virus (HIV) combined. Recent studies suggest that opioid overdose following discharge after surgery is a relatively rare occurrence that is more common in those using opioids before surgery¹³; however, data regarding the prevalence and trends of inpatient admissions for overdose are lacking.

In this issue of *Anesthesia & Analgesia*, Burton et al¹⁴ present results from their retrospective study utilizing data from the National (Nationwide) Inpatient Sample, a database of the Healthcare Cost and Utilization Project. The National (Nationwide) Inpatient Sample is the largest multistate, all-payor inpatient health care database in the United States. Thus, this database serves to provide those who access it with important deidentified data pertaining to inpatient admissions including demographics, clinical parameters, payment sources, and hospital variables. It approximates a 20% sample of discharges from inpatient admissions in participating hospitals the United States.¹⁵ The authors sought to investigate trends associated with opioid overdose and mortality using this large national database and to report factors that may be associated with inpatient mortality in patients admitted for prescription or illicit opioid overdose. The key word in these previous sentences is “associated” because the cross-sectional data the authors are presenting do not allow for causation to be established. Nonetheless, the authors’ goals with this investigation are meritorious and timely given the current opioid crisis in the United States.

The study affirms that the majority of overdoses requiring hospital admission are for agents that are available as prescribed drugs. While the authors noted rising rates of illicit opioid overdose (classified when the agent involved was heroin) and falling rates of prescription opioid overdose, by the end of the study period (2010–2014), the latter still vastly outnumbered the former. While the study is not able to describe the means of acquisition of the substance—which would be additionally required for a legal definition of prescription versus illicit use—it does continue to add evidence to the contention that prescription opioid use in the community (demonstrated by temporal trends) allows for substantial rates of prescription opioid overdose, regardless of means of acquisition. It is additionally worrisome that the rates of inpatient mortality appeared to be rising in both types of overdose.

Second, a notable finding in the study was the astronomical number of illicit or prescription opioid overdoses in this sample of all hospital activity in a 4-year period of time—more than 584,000 patients. The majority of these admissions were for prescription opioid overdose. Alarming, this sample only includes those who had a hospital admission, and this does not

capture those seen in the emergency department and discharged or those who perhaps expired in the emergency department, during prehospital treatment (eg, via paramedics or first responders), or those who suffered mortality before any treatment. While the present study offers some interesting insights, the factors that may be associated in nonhospital or nonadmission mortality—patients for whom the opportunity to intervene was limited or lost—remain unknown.

Finally, there exists a third troubling inference of this study—that opioid overdose was occurring in the context of other comorbid disease and potentially as a side effect of medical therapy. The median patient had 12 inpatient comorbidities, and half of overdoses in the study occurred in patients more than 50 years of age. While some of these may be attributable to polysubstance use or sequelae from the overdose itself at the time of admission, the authors also found occurrences of other comorbidities such as anemia, hypertension, chronic pain, and solid tumor malignancies, which may relate to general medical conditions for which the patient may be under medical care. Historically, treatment of cancer pain with opioids has been without concern or fear for opioid misuse, yet cancer survivorship is increasing, and new chronic opioid use as a part of cancer care has recently been recognized as a common complication.⁴ Although the increased risk of inpatient mortality associated with prescription opioid overdose compared to illicit opioid overdose in the solid tumor malignancy group cannot be causally inferred given the nature of this database, the data suggest that the risk of prescription opioid over-dose (whether unintentional or intentional) in a group of patients for whom judicious use of opioids is common may warrant further investigation. However, as noted previously, these associations are likely substantially influenced by survivorship bias affecting the study population.

The work by Burton et al¹⁴ once again reminds us that we, as physicians, should be concerned regarding the wide-spread use of these prescription agents in the community. Although opioids have a role in clinical care, the vast over-use in the United States has led to morbidity and mortality. An overwhelming 75% of people who use illicit opioids such as heroin, and presumably fentanyl, began their opioid use disorder with prescription opioids. Therefore, we must continue to reframe and refine our understanding of opioid overdose, especially in light of the worsening trend of illicit use of prescription opioids. Although the increasing rates of the illicit use of prescription opioids muddies the waters in terms of characterizing or defining the overdose as either illicit or prescription, what remains vastly important is a continued clinical and research focus on opioid stewardship. Moreover, recognizing the current climate not only as an opioid epidemic but also as a predicted consequence from another epidemic, one of chronic pain, is important given that more effective and widely accessible chronic pain treatments would heavily impact the utilization and prescribing of opioids. Future avenues of research should focus on basic, translational, and clinical studies on opioid use disorder and addiction and novel therapeutic targets for chronic pain. Furthermore, exploring the impact of comprehensive pain programs (nonpharmacological, pharmacological, interventional, psychological, and complementary care) on opioid use, addiction, and overdoses may provide important data that could influence better coverage for these types of programs for all chronic pain patients, regardless of insurance coverage. Irrespective of our practice settings, we all interact with a public that is at risk for opioid-related harm. We should continue to seek opportunities for minimizing

this in the search for non-opioid-based treatment of pain in our management of overdose and the public policy landscape in which our practice sits.

Acknowledgments

Funding: A.L.N. receives funding from the National Institute of General Medical Sciences of the National Institutes of Health (NIH) (award number K23GM123320). D.A.C. receives funding from the National Institute of General Medical Sciences of NIH (award number T32GM103730). C.M.B. receives funding from the National Institute on Drug Abuse of NIH (award number R01DA042859).

REFERENCES

- Waljee JF, Li L, Brummett CM, Englesbe MJ. Iatrogenic opioid dependence in the United States: are surgeons the gatekeepers? *Ann Surg* 2017;265:728–730. [PubMed: 27429023]
- Ronan MV, Herzig SJ. Hospitalizations related to opioid abuse/dependence and associated serious infections increased sharply, 2002–12. *Health Aff (Millwood)* 2016;35:832–837. [PubMed: 27140989]
- Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers - United States, 2002–2004 and 2008–2010. *Drug Alcohol Depend* 2013;132:95–100. [PubMed: 23410617]
- Lee JS, Hu HM, Edelman AL, et al. New persistent opioid use among patients with cancer after curative-intent surgery. *J Clin Oncol* 2017;35:4042–4049. [PubMed: 29048972]
- Klueh MP, Hu HM, Howard RA, et al. Transitions of care for postoperative opioid prescribing in previously opioid-naïve patients in the USA: a retrospective review. *J Gen Intern Med* 2018;33:1685–1691. [PubMed: 29948809]
- Brummett CM, Waljee JF, Goesling J, et al. New persistent opioid use after minor and major surgical procedures in US adults. *JAMA Surg* 2017;152:e170504. [PubMed: 28403427]
- Bennett KG, Harbaugh CM, Hu HM, et al. Persistent opioid use among children, adolescents, and young adults after common cleft operations. *J Craniofac Surg* 2018;29:1697–1701. [PubMed: 30059422]
- Centers for Disease Control and Prevention (CDC). Unintentional poisoning deaths--United States, 1999–2004. *MMWR Morb Mortal Wkly Rep* 2007;56:93–96. [PubMed: 17287712]
- United Nations Office on Drugs and Crime. World drug report 2014 Available at: http://www.unodc.org/documents/wdr2014/World_Drug_Report_2014_web.pdf. Accessed August 17, 2018.
- Health and Human Services Press Office. HHS acting secretary declares public health emergency to address national opioid crisis Available at: <https://www.hhs.gov/about/news/2017/10/26/hhs-acting-secretary-declares-public-health-emergency-address-national-opioid-crisis.html>. Published October 26, 2017. Accessed September 6, 2018.
- Collins FS, Koroshetz WJ, Volkow ND. Helping to end addiction over the long-term: the research plan for the NIH HEAL initiative. *JAMA* 2018;320:129–130. [PubMed: 29896636]
- Ahmad FB, Rossen LM, Spencer MR, Warner M, Sutton P. Provisional drug overdose death counts Available at: <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm#notes>. Updated September 12, 2018. Accessed September 16, 2018.
- Ladha KS, Gagne JJ, Paterno E, et al. Opioid overdose after surgical discharge. *JAMA* 2018;320:502–504. [PubMed: 30087999]
- Burton BN, Lin TC, Said ET, Gabriel RA. National trends and factors associated with inpatient mortality in adult patients with opioid overdose. *Anesth Analg* 2019;128:152–160. [PubMed: 30198926]
- NIS Overview. Healthcare cost and utilization project (HCUP) Available at: <https://www.hcup-us.ahrq.gov/nisoverview.jsp>. Updated August 13, 2018. Accessed September 19, 2018.