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Impact of state policies on opioid prescribing among surgery and injury patients: Controlled interrupted time-series study, North Carolina, 2014–2019

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Abstract

Purpose: Impact of policies limiting opioid prescribing for acute and post-surgical pain among racially minoritized populations are not well understood. We evaluated the impact of two North Carolina (NC) policies on outpatient opioid prescribing among injury and surgical patients by race, ethnicity, age, and sex.

Methods: We conducted controlled and single series interrupted time series using electronic health data from two integrated healthcare systems in NC, among >11 years-old patients having acute injuries and surgery between April 2014 to December 2019. The policy interventions were safe opioid prescribing investigative initiative (SOPI, May 2016) and NC law limiting opioid days'

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supply (STOP Act, January 2018). Outcomes included, proportion of patients receiving index opioid prescription after surgery or injury event, receipt of subsequent opioid prescriptions, days' supply, and milligrams of morphine equivalents (MME).

Results: Of the 621,997 surgical and 864,061 injury patients, 69.4% and 19.7%, respectively, received an index opioid analgesic prescription. There were sustained declines in index opioid prescription among post-surgical patients after SOPI [-2.7% per year ($-4.6, -0.9$)] and STOP act [-4.1% ($-5.9, -2.2$)], but no change among injury patients. Policy-related opioid prescribing declines were larger among black, native American, and Hispanic post-surgical patients than whites and Asians. Index and subsequent opioid days' supply showed sustained declines after SOPI and STOP Act among post-surgical patients. There was no policy impact on MME.

Conclusions: Policies were associated with reductions in opioid prescribing, particularly in post-surgical patients, however, racialized inequities likely reflect implicit and explicit racialized biases in pain management practices.

Plain Language Summary:

In this study, we examined how opioid prescribing patterns in North Carolina (NC) changed in response to two policy initiatives designed to reduce opioid overprescribing: 1) NC safe opioid prescribing initiative (SOPI), an investigative program by the NC medical board (May 2016), and 2) STrengthen Opioid misuse Prevention (STOP) Act, that introduced opioid days' supply limits for acute and post-surgical pain (January 2018)?

We found that the SOPI and STOP Act initiatives resulted in declines in index (first) opioid prescribing rates. Additionally, there were reductions in days' supply of index opioid prescriptions. These reductions in opioid prescribing were part of the intended policy effects. However, there were unintended reductions in subsequent opioid prescribing after the first prescription, including fewer prescriptions and shorter day's supply of subsequent prescriptions related to the STOP act. Further, there were racialized inequities in policy effects, such that opioid prescribing was reduced more among black, native American, and Hispanic pain patients compared to white and Asian patients.

While the findings indicate that the policies attained intended effects in terms of reduced opioid prescribing, there are also unintended effects that may not address continued pain management needs of patients and especially patients who are racially minoritized.

Keywords

opioids; opioid prescribing; policies

Introduction

To curtail the rise in opioid misuse and overdose deaths, policies and guidelines have been implemented to reduce the risk of opioid-involved overdoses.¹ In March 2016, the CDC issued opioid prescribing guidelines for chronic non-cancer pain, which were revised in 2022.^{2,3} The 2016 guidelines influenced many states to codify whole or parts of the guidelines into regulations.⁴ Consequently, the North Carolina (NC) Medical Board enacted the Safe Opioid Prescribing Initiative (SOPI) in April 2016 to investigate, educate, and

potentially discipline high-volume prescribers who have had two or more patients die from opioid overdose.⁵ Since opioids prescribed for long durations or at high doses are associated with opioid use disorder and opioid overdose deaths,^{6–12} in July 2017, the NC legislature passed the STrengthen Opioid misuse Prevention (STOP) Act. The STOP Act, among other mandates, limited index (initial) opioid prescriptions for acute and post-surgical pain to no more than five days and seven days, respectively, beginning January, 2018.¹³

While the regulation of opioid prescribing is understandable given the rise in opioid-related morbidity and mortality in the United States, opioid prescriptions are still a necessary pain management resource for patients. Premature or sudden discontinuation of high-dose opioid prescriptions can have negative consequences and could put patients' safety at risk, such as resorting to unregulated opioids, which could lead to non-medical drug use, opioid use disorder, overdose, and even death.^{10,14–22} Prior studies have also found that racially minoritized populations are under prescribed pain medications leading to unmanaged pain.^{23–27} Opioid limiting policies could therefore have an outsized effect on pain management among racially minoritized people. Therefore, the effects of policies aimed at regulating opioid prescribing need to be evaluated by race and ethnicity, age, and sex.

Accordingly, we evaluated the impacts of SOPI and STOP Act on opioid prescribing and dispensing among acute and post-surgical pain patients who received treatment in two large NC-based integrated healthcare systems, and examined modification of the policy impact by race, ethnicity, age, and sex.

Methods

We used retrospective cohorts of post-surgical and injury patients and conducted controlled and single interrupted time series analyses to examine the immediate and sustained changes in opioid prescribing among injury and surgical pain patients in NC after SOPI in May 2016 and the STOP Act in January 2018. The study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for cohort studies.

Data sources and study populations

We used de-identified electronic health records (EHR) data from two large integrated healthcare systems in NC, the University of North Carolina, and Duke University health systems, from April 2014 to December 2019 using the National Patient-Centered Clinical Research Network Common Data Model.²⁸ Data included patient demographics, inpatient and outpatient encounters, prescribed medications, diagnoses, and procedures. We included all patients >11 years of age who received care for acute injuries or surgical procedures during the study period. Acute injuries were identified using International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) and 10th Revision (ICD-10-CM) codes, while surgical procedures were identified using Current Procedural Terminology (CPT) codes (see Supplementary Tables 1 & 2). We included acute injuries and surgeries treated in any setting, including outpatient, inpatient, emergency, or other specialized settings. Patients with both acute injury and surgical procedures were categorized as surgical pain patients. EHR data was linked with the NC Controlled Substance Reporting

System (CSRS), the state's prescription monitoring program, using a unique encrypted hashing algorithm based on patients' first name (first three characters), last name (first eight characters), sex, date of birth, date of prescription, and provider drug enforcement administration (DEA) license number.²⁹

From the study sample, we identified patients who received an outpatient prescription opioid analgesic temporally proximal to a treated injury or a surgical procedure. An index outpatient opioid prescription for a surgical procedure was defined as the first opioid prescription received between 15 days prior to and 45 days after the surgery. An index outpatient opioid prescription associated with an injury was identified as the first opioid prescription received between the date of injury and 45 days after the injury. A subsequent opioid prescription was defined as any additional opioid prescriptions after the index prescription which could be during or beyond the 45 days from the injury or surgery event unless it was 90 days after the last day of the previous index or subsequent prescription. A new index prescription for a different injury or surgery event had to be at least 90 days apart from the last day from the previous index or subsequent opioid prescription.

Outcomes

We examined the following opioid prescribing and dispensing outcomes: 1) proportion of patients receiving an index opioid prescription; 2) rate of index opioid prescriptions per 100 person-months; 3) rate of subsequent opioid prescriptions per 100 person-months; 4) days' supply for dispensed index opioid prescriptions; 5) days' supply for dispensed subsequent opioid prescriptions; 6) daily morphine milligram equivalents (MME) for dispensed index opioid prescriptions; and 7) daily MMEs for dispensed subsequent opioid prescriptions. All outcomes were stratified by injury or surgery pain.

The proportion of patients receiving an index opioid prescription and rates of index and subsequent monthly opioid prescriptions were examined using EHR data. The denominators for these outcomes were the monthly number of patients diagnosed with injury and surgery pain at the two healthcare systems, representing the population "at risk" of receiving an opioid prescription. Monthly rates per 100 person-months (PM) were calculated from April 2014 to December 2019 to create a time series with 69 time points.

The days' supply and MME outcomes were examined for the prescriptions that were linked with the NC CSRS data representing dispensed prescriptions only. Daily MME were calculated by dividing the total MME dispensed in a prescription by the days' supply.³⁰ We summed MME across overlapping prescriptions during the period of overlap. The prescription days' supply and daily MME were averaged over the number of days with any supply during a calendar month to create outcome time-series for dispensed opioids.

Exposures (policy interventions)

We assessed the impact of two NC policies, SOPI and the STOP Act. SOPI was announced in April 2016 and launched in May 2016. This action sent letters to all licensed NC clinicians informing them of the initiative to proactively investigate those who prescribed high doses and high volume of opioids to the majority of their patients, or who had two or more patients die from an opioid overdose.³¹ In July 2017, the STOP Act was implemented.

It required 1) a license physician to review opioid prescriptions prescribed by physician assistants and nurse practitioners (beginning July 1, 2017), 2) restricting the maximum days' supply of an initial prescription for acute (five days) or post-surgical (seven days) pain (starting January 1, 2018), and 3) prescribers to review the CSRS before prescribing a schedule II or III opioid or narcotic medication. The third mandate was not enforced during the study period. We used January 2018 as the first month for STOP Act intervention.

Control

Benzodiazepine prescriptions among the pain patients from April 2014 through December 2019 were utilized as a control. Because the 2016 CDC guidelines advised extreme caution when co-prescribing opioids and benzodiazepines, changes in benzodiazepine prescribing could address confounding bias due to other policy interventions like the CDC guidelines.² The proportion of index benzodiazepine prescriptions and index monthly prescription rates were calculated in the same manner as the opioid prescribing outcomes. The resulting benzodiazepine prescribing time-series were used as a control.

Covariates:

Self-reported race was categorized as American native, Asian, black, and white. Self-reported ethnicity was classified as Hispanic or non-Hispanic of any race. Due to small sample resulting in unstable time series, multiracial groups were excluded. Continuous age from EHR data was categorized as <36, 36–65, and >65 years of age. Sex was categorized as male or female.

Statistical Analyses

We conducted controlled interrupted time series (CITS) analyses using an autoregressive integrated moving average (ARIMA) model^{32–35} with two policy inflection time points to examine immediate and sustained trend changes in index and subsequent opioid prescribing after the two policy interventions, relative to benzodiazepine prescriptions (control). We conducted single-series ITS analyses to examine policy impact on days' supply and MME of dispensed index and subsequent opioid prescriptions. See supplementary materials for CITS and single-series ITS model specifications. The monthly time series from April 2014 to December 2019 (69 time points, was divided into three periods: pre-SOPI (25 time points), post-SOPI/ pre-STOP act (20 time points), and post-STOP act (24 time points). Each period of time series is compared with the prior period.

To examine effect measure modification of the policy impact on opioid prescribing, we stratified the analyses by race, ethnicity, age, and sex. We annualized the sustained trend change estimates by multiplying by 12 to present annual sustained policy effects.

Compliance with Ethics Guidelines

This study was approved by the Institutional Review Boards at the University of North Carolina at Chapel Hill and the Duke University Health System.

Results

Between April 2014 and December 2019, 621,997 surgical patients and 864,061 patients with acute injuries received treatment within two large integrated healthcare systems. Of those, 69.4% surgical patients and 19.7% acute injury patients received an index opioid prescription for pain control (Table 1). Overall prescribing proportions, rates, MMEs, and days' supply by pre- and post-policy time periods are presented in Supplemental Table 3.

Surgery pain patients

Index opioid prescriptions and prescribing rates: Compared to benzodiazepine prescribing trends, there was an immediate 3.2% increase (95% confidence interval [CI]: 1.4, 5.1) in the proportion of patients receiving an index opioid prescription in the month following SOPI implementation (Table 2; Figure 1A), and an immediate increase of 9.2 new opioid prescriptions per 100 person-months (95% CI: 5.2, 13.1) (Table 2; Figure 1B). Thereafter, the index opioid prescription proportion trend decreased by -2.7% (95% CI: -4.5, -0.9) per year (annualized estimate), and the index opioid prescribing rate trends decreased by -3.8 (95% CI: -7.5, -0.05) new prescriptions per 100 person-years, relative to benzodiazepines, in the 25 months post-SOPI (Table 2; Figure 1A). After the STOP Act, there was a notable decrease of -4.1% (95% CI: -5.9, -2.2) per year in the trend of patients receiving index opioid prescriptions, relative to benzodiazepines (Table 2).

Subsequent opioid prescribing rates: Subsequent opioid prescribing rates were increasing pre-SOPI (Supplementary Table 4; Figure 2A). However, after SOPI, there was a -12.5% per year (-14.9, -10.2) sustained decline in subsequent opioid prescribing rates. Thereafter, there was -1.9% (-4.4%, 0.5%) immediate decline post-STOP Act, but no additional trend changes.

Dispensed index and subsequent days' supply: After SOPI, there was a sustained decline of -0.77 days' supply per year (-0.97, -0.56) in dispensed index opioid prescriptions (Supplementary Table 4; Figure 2B). Then, there was an immediate decrease in days' supply of -0.70 days (-0.91, -0.48) post-STOP Act, followed by a sustained decline of -0.32 days per year (-0.5, -0.1) (Supplementary Table 4). For subsequent opioid prescriptions days' supply, there was a sustained decline of -1.10 days per year (-1.34, -0.85) post-SOPI, followed by an immediate and sustained decline of -0.80 days (-1.10, -0.53), and -0.28 days per year (-0.45, -0.02), post-STOP Act.

Injury pain patients

Index opioid prescriptions and prescribing rates: The proportion of patients receiving index opioid prescriptions and the index opioid prescription rate among injury patients were decreasing throughout the study period. Compared to benzodiazepines, there was an immediate 2.1% new prescriptions (1.3, 2.9) increase in the proportion of index opioid prescriptions (Table 2; Figure 1A), and an immediate increase of 2.6 new prescriptions per 100 person-months (1.4, 3.9) post-SOPI (Table 2; Figure 1B). Thereafter, there were minimal relative trend changes. After the STOP Act, the declining trend in the

proportion of patients receiving an index opioid prescription and index opioid prescribing rates slowed but continued to decline (Table 2; Figure 1).

Subsequent opioid prescribing rates: Subsequent opioid prescribing rates were increasing pre-SOPI (Supplementary Table 4; Figure 2A). Post-SOPI, there was a 0.89% (−1.74, −0.03) immediate decline, followed by a 1.0% per year (−1.8, −0.2) sustained decline. Post-STOP Act, there was a 1% (−1.8%, −0.1%) immediate decline, but no sustained changes.

Dispensed index and subsequent day's supply: The mean index days' supply among injury patients was increasing pre-SOPI (Supplementary Table 4, Figure 2B). Post-SOPI, there was 0.54 days per year (−0.88, −0.20) sustained decline. Post-STOP Act, the index days' supply decreased immediately by 0.71 days (−1.06, −0.36), with no sustained changes (Supplementary Table 4). Subsequent days' supply trends had sustained decline of 1.21 days per year (−2.04, −0.37) post-SOPI, and then additional sustained decline of 1.38 days per year (−2.23, −0.53) post-STOP Act.

Dispensed index and subsequent MME results for both surgery and injury patients are presented in the supplemental materials.

Racial and ethnic inequities: Among both surgery and injury patients, black Americans were more likely to receive an opioid prescription, and more commonly from an emergency department (ED) visit, compared to white, Asian, and native American patients who commonly received their opioid prescriptions from outpatient care (Supplementary Table 5–6, Supplementary Figures 3–4). Post-SOPI and STOP Act, black and native American patients experienced the greatest reductions in index and subsequent opioid prescribing for post-surgical pain, while white and Asian Americans experienced the smallest reductions (Table 3). For injury pain, the largest policy-related reductions were experienced by white patients relative to all racially minoritized groups (Table 3). While non-Hispanic patients experienced greater policy-related sustained decline in post-surgical opioid prescribing, Hispanic patients experienced a greater policy-related immediate declines in post-surgical opioid prescribing (Supplementary Table 7).

Age and sex-based disparities: Post-SOPI, surgical patients >65 years experienced the greatest sustained decline in opioid prescribing, followed by the 36–65 years age group, while those <36 years experienced sustained increases. However, post-STOP Act, those <36 years experienced greatest declines in post-surgical opioid prescribing (Supplementary Table 7). This policy-age interaction reversed for injury patients (Supplementary Table 8).

Lastly, post-STOP act, females experienced greater declines than males in receiving an index opioid prescription for both post-surgical (sustained change) and injury (immediate change) pain.

Discussion

We found that the two NC opioid prescribing policies, SOPI and STOP Act, led to sustained declines in index and subsequent opioid prescribing rates among patients with post-surgical pain at two large integrated healthcare systems in NC. These effects may be due to policy-concordant changes in provider opioid prescribing practice but may also be due to potentially chilling influence of the policies.^{36,37} While the mandate to reduce days' supply for index post-surgical and injury opioid prescriptions was implemented with the STOP Act, these changes were already occurring after SOPI. Per the STOP Act, the days' supply changes were meant to impact index opioid prescriptions only; however, there was a greater policy impact on subsequent prescriptions than index prescriptions for both surgical and injury pain patients. The changes in subsequent days' supply may be related to the reduction index days' supply as prior studies have shown that higher days' supply of first opioid prescriptions result in more subsequent prescriptions and long-term use.³⁸ However, these changes may also reflect clinician's unwillingness to prescribe as prior qualitative research suggests.³²

Our results are comparable to our prior studies of privately insured NC patients, which showed overall decreases in opioid prescribing in acute, post-surgical, and chronic pain patients after SOPI and STOP Act.^{39,40} However, those studies were not generalizable to publicly insured and uninsured patients nor could we previously examine policy-related disparate effects by race and ethnicity.^{39,40} Furthermore, this study separates index and subsequent opioid prescriptions to examine potential unintended consequences for patients who may need additional pain management after the index prescription. This study also has greater follow-up after the STOP Act allowing a better examination of sustained policy effects.

While statewide policies to reduce opioid prescribing seem appealing to reduce opioid-related harms, racialized inequities in policy effects, and thereby pain management, are concerning. Contrary to prior research, we found that black patients with injury and surgery pain were prescribed more opioids than all other racialized groups.²⁴ However, most of the black patients who received opioid prescriptions presented in the ED, suggesting potentially higher levels of clinical complications and pain and therefore more opioid prescriptions.³⁵ Racially minoritized patients are known to access ED more frequently than white patients due to barriers in accessing outpatient care, with greater complications due to barriers to accessing primary care.⁴¹ We found black and native American post-surgical patients experienced a greater SOPI and STOP Act-related reductions in opioid prescribing than white patients. Prior studies have consistently found that healthcare providers exhibit racial prejudice against black and racially minoritized people regarding substance use disorders.^{42–44} Racialized healthcare inequities in patient care and inbuilt algorithmic biases toward racially minoritized patients are widely documented, and our study adds to the growing literature.⁴⁵ Policy modifications to ensure equitable opioid prescribing practices and mitigating racialized inequities are needed.

SOPI-related reduction in prescribing were greatest among 65 years and older patients, while STOP Act led to greatest declines in those 35 years and younger. This may be because

pre-SOPI, the patients >65 years old received most opioid prescriptions and therefore may have been the first to experience cuts.⁴⁶ It is unclear if the greater opioid prescribing reductions experienced by females compared to males represent a systemic bias or because of specific changes in certain practices like opioid prescribing during labor and other female-specific surgical procedures.^{47–49}

Limitations:

First, our study evaluated NC-specific policies. However, our results, along with research from other states, can inform policy in jurisdictions considering similar policies.^{50,51} Second, the two integrated healthcare systems we used do not offer healthcare to all NC residents. However, both institutions offer care in all 100 NC counties and the EHR data include public, private, and uninsured patients, which offers good generalizability. Finally, although our data represents opioid prescribing and dispensing trends, this may not be the same as consumption or non-medical use of prescription opioids, which cannot be measured in this study.

Conclusions

We found that two NC-based opioid prescribing policies resulted in intended and unintended changes in opioid prescribing practices for acute injury and post-surgical pain patients. There were concerning racialized inequities in policy effects, such that black, Hispanic, and native American patients experienced the greatest post-surgical opioid prescribing declines than whites and Asians. This may reflect implicit and explicit racialized bias in pain management practices that may be driven by racial stereotyping rather than clinical evidence. Healthcare interventions that can mitigate prescriber biases are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Abuse NI on D. Overdose Death Rates. National Institute on Drug Abuse. January 20, 2022. Accessed November 9, 2022. <https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates>
2. Dowell D, Haegerich T, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep. 2016;65(1):1–49. doi:10.15585/mmwr.rr6501e1er

3. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain - United States, 2022. *MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep*. 2022;71(3):1–95. doi:10.15585/mmwr.rr7103a1
4. Center for Public Health Law Research Staff. PDAPS - State Laws Limiting Prescriptions for Opioid Analgesics. PDAPS (Prescription Drug Abuse Policy System). December 31, 2019. Accessed July 24, 2023. <https://pdaps.org/datasets/opioid-analgesics-prescribing-limits>
5. North Carolina Medical Board Annual Report. Published online 2016. Accessed May 30, 2022. https://www.ncmedboard.org/images/uploads/disciplinary_reports/2016_Annual_Report1.pdf.
6. Heins SE. Prescription Opioids: A Continuing Contributor to the Epidemic. *Am J Public Health*. 2019;109(9):1166–1167. doi:10.2105/AJPH.2019.305253 [PubMed: 31390249]
7. Edlund MJ, Martin BC, Russo JE, Devries A, Braden JB, Sullivan MD. The Role of Opioid Prescription in Incident Opioid Abuse and Dependence Among Individuals with Chronic Non-Cancer Pain: The Role of Opioid Prescription. *Clin J Pain*. 2014;30(7):557–564. doi:10.1097/AJP.0000000000000021 [PubMed: 24281273]
8. Turner BJ, Liang Y. Drug Overdose in a Retrospective Cohort with Non-Cancer Pain Treated with Opioids, Antidepressants, and/or Sedative-Hypnotics: Interactions with Mental Health Disorders. *J Gen Intern Med*. 2015;30(8):1081–1096. doi:10.1007/s11606-015-3199-4 [PubMed: 25650263]
9. Zedler B, Xie L, Wang L, et al. Risk factors for serious prescription opioid-related toxicity or overdose among Veterans Health Administration patients. *Pain Med Malden Mass*. 2014;15(11):1911–1929. doi:10.1111/pme.12480
10. Bohnert ASB, Ilgen MA. Understanding Links among Opioid Use, Overdose, and Suicide. *N Engl J Med*. 2019;380(1):71–79. doi:10.1056/NEJMr1802148 [PubMed: 30601750]
11. Dasgupta N, Funk MJ, Proescholdbell S, Hirsch A, Ribisl KM, Marshall S. Cohort Study of the Impact of High-Dose Opioid Analgesics on Overdose Mortality. *Pain Med Malden Mass*. 2016;17(1):85–98. doi:10.1111/pme.12907
12. Harbaugh CM, Nalliah RP, Hu HM, Englesbe MJ, Waljee JF, Brummett CM. Persistent Opioid Use After Wisdom Tooth Extraction. *JAMA*. 2018;320(5):504–506. doi:10.1001/jama.2018.9023 [PubMed: 30088000]
13. The Strengthen Opioid Misuse Prevention (STOP) Act of 2017. Published online 2017. Accessed May 30, 2022. https://www.ncmedboard.org/images/uploads/article_images/The_STOP_Act_summary-OnLetterhead.pdf
14. 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 [PubMed: 31018066]
15. 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 [PubMed: 32927194]
16. 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 [PubMed: 32365132]
17. Hartung DM, Johnston KA, Hallvik S, et al. Prescription Opioid Dispensing Patterns Prior to Heroin Overdose in a State Medicaid Program: a Case-Control Study. *J Gen Intern Med*. 2020;35(11):3188–3196. doi:10.1007/s11606-020-06192-4 [PubMed: 32935311]
18. Muzzio K, Chandler M, Painter JT, Dragic L. Characterizing Patients after Opioid Taper in a VA Medical Center. *J Pain Palliat Care Pharmacother*. 2021;35(2):84–90. doi:10.1080/15360288.2021.1900492 [PubMed: 33956566]
19. Perez HR, Buonora M, Cunningham CO, Heo M, Starrels JL. Opioid Taper Is Associated with Subsequent Termination of Care: a Retrospective Cohort Study. *J Gen Intern Med*. 2020;35(1):36–42. doi:10.1007/s11606-019-05227-9 [PubMed: 31428983]
20. Ranapurwala SI, Ringwalt CL, Pence BW, et al. State Medical Board Policy and Opioid Prescribing: A Controlled Interrupted Time Series. *Am J Prev Med*. 2021;60(3):343–351. doi:10.1016/j.amepre.2020.09.015 [PubMed: 33309449]
21. CDC Advises Against Misapplication of the Guideline for Prescribing Opioids for Chronic Pain. Published online 2019. Accessed May 29, 2022. <https://www.cdc.gov/media/releases/2019/s0424-advises-misapplication-guideline-prescribing-opioids.html>

22. May T, Holloway K, Buhociu M, Hills R. Not what the doctor ordered: Motivations for nonmedical prescription drug use among people who use illegal drugs. *Int J Drug Policy*. 2020;82:102823. doi:10.1016/j.drugpo.2020.102823 [PubMed: 32585584]
23. Townsend TN, Bohnert ASB, Lagisetty P, Haffajee RL. Did prescribing laws disproportionately affect opioid dispensing to Black patients? *Health Serv Res*. 2022;57(3):482–496. doi:10.1111/1475-6773.13968 [PubMed: 35243639]
24. Ly DP. Association of Patient Race and Ethnicity With Differences in Opioid Prescribing by Primary Care Physicians for Older Adults With New Low Back Pain. *JAMA Health Forum*. 2021;2(9):e212333. doi:10.1001/jamahealthforum.2021.2333 [PubMed: 35977182]
25. Zhang S, Silverman A, Suen SC, Andrews C, Chen BK. Differential patterns of opioid misuse between younger and older adults - a retrospective observational study using data from South Carolina's prescription drug monitoring program. *Am J Drug Alcohol Abuse*. 2022;48(5):618–628. doi:10.1080/00952990.2022.2124380 [PubMed: 36194086]
26. Ringwalt C, Roberts AW, Gugelmann H, Skinner AC. Racial Disparities Across Provider Specialties in Opioid Prescriptions Dispensed to Medicaid Beneficiaries with Chronic Noncancer Pain. *Pain Med*. 2015;16(4):633–640. doi:10.1111/pme.12555 [PubMed: 25287703]
27. Morden NE, Chyn D, Wood A, Meara E. Racial Inequality in Prescription Opioid Receipt — Role of Individual Health Systems. *N Engl J Med*. 2021;385(4):342–351. doi:10.1056/NEJMSa2034159 [PubMed: 34289277]
28. Klann JG, Abend A, Raghavan VA, Mandl KD, Murphy SN. Data interchange using i2b2. *J Am Med Inform Assoc*. 2016;23(5):909–915. doi:10.1093/jamia/ocv188 [PubMed: 26911824]
29. University of North Carolina at Chapel Hill. DAREL. Published online July 22, 2020. Accessed August 15, 2023. <https://github.com/NCtraCSIDSci/darel>
30. Dasgupta N, Wang Y, Bae J, et al. Inches, Centimeters, and Yards: Overlooked Definition Choices Inhibit Interpretation of Morphine Equivalence. *Clin J Pain*. 2021;37(8). https://journals.lww.com/clinicalpain/Fulltext/2021/08000/Inches,_Centimeters,_and_Yards__Overlooked.1.aspx
31. Annual Reports. Accessed April 11, 2022. <https://www.ncmedboard.org/about-the-board/annual-reports>
32. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int J Epidemiol*. 2017;46(1):348–355. doi:10.1093/ije/dyw098 [PubMed: 27283160]
33. Lopez Bernal J, Cummins S, Gasparrini A. The use of controls in interrupted time series studies of public health interventions. *Int J Epidemiol*. 2018;47(6):2082–2093. doi:10.1093/ije/dyy135 [PubMed: 29982445]
34. Crifasi CK, Ward JA, Fitch KV, Ranapurwala SI. The State of Firearm Policy Research in the United States. *Am J Epidemiol*. Published online October 1, 2024;kwae298. doi:10.1093/aje/kwae298 [PubMed: 39358998]
35. Linden A Using randomization tests to assess treatment effects in multiple-group interrupted time series analysis. *J Eval Clin Pract*. 2019;25(1):5–10. doi:10.1111/jep.12995 [PubMed: 30003627]
36. Wee Jun Yan I, Lim Tian Ying B, Brennan F. Public Policy: An Analgesia for Opioid Diversion. *J Pain Palliat Care Pharmacother*. 2018;32(2–3):178–191. doi:10.1080/15360288.2018.1546788 [PubMed: 30676178]
37. Joniak-Grant E, Blackburn NA, Dasgupta N, et al. “Cookbook medicine”: Exploring the impact of opioid prescribing limits legislation on clinical practice and patient experiences. *SSM - Qual Res Health*. 2023;3:100273. doi:10.1016/j.ssmqr.2023.100273
38. Young JC, Dasgupta N, Chidgey BA, et al. Impacts of Initial Prescription Length and Prescribing Limits on Risk of Prolonged Postsurgical Opioid Use. *Med Care*. 2022;60(1). https://journals.lww.com/lww-medicalcare/Fulltext/2022/01000/Impacts_of_Initial_Prescription_Length_and.11.aspx
39. Maierhofer CN, Ranapurwala SI, DiPrete BL, et al. Association Between Statewide Opioid Prescribing Interventions and Opioid Prescribing Patterns in North Carolina, 2006–2018. *Pain Med*. 2021;22(12):2931–2940. doi:10.1093/pm/pnab181 [PubMed: 34175958]
40. Maierhofer CN, Ranapurwala SI, DiPrete BL, et al. Intended and unintended consequences: Changes in opioid prescribing practices for postsurgical, acute, and chronic pain indications

following two policies in North Carolina, 2012–2018 – Controlled and single-series interrupted time series analyses. *Drug Alcohol Depend* 242:109727. 2023;242. <https://stacks.cdc.gov/view/cdc/123200>

41. CDCMMWR. QuickStats: Percentage of Emergency Department Visits with Medicaid as the Primary Expected Source of Payment Among Persons Aged <65 Years, by Race and Ethnicity — National Hospital Ambulatory Medical Care Survey, United States, 2011–2021. *MMWR Morb Mortal Wkly Rep*. 2023;72. doi:10.15585/mmwr.mm7231a6
42. Ghonasgi R, Paschke ME, Winograd RP, Wright C, Selph E, Banks DE. The intersection of substance use stigma and anti-Black racial stigma: A scoping review. *Int J Drug Policy*. 2024;133:104612. doi:10.1016/j.drugpo.2024.104612 [PubMed: 39369573]
43. Crusto CA, Kaufman JS, Harvanek ZM, Nelson C, Forray A. Perceptions of Care and Perceived Discrimination: A Qualitative Assessment of Adults Living with Sickle Cell Disease. *J Racial Ethn Health Disparities*. Published online September 3, 2024. doi:10.1007/s40615-024-02153-3
44. Moskowitz D, Thom DH, Guzman D, Penko J, Miaskowski C, Kushel M. Is Primary Care Providers' Trust in Socially Marginalized Patients Affected by Race? *J Gen Intern Med*. 2011;26(8):846–851. doi:10.1007/s11606-011-1672-2 [PubMed: 21394422]
45. Vyas Darshali A, Eisenstein Leo G, Jones David S Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms. *N Engl J Med*. 2020;383(9):874–882. doi:10.1056/NEJMms2004740 [PubMed: 32853499]
46. Shiue KY. Prescription Opioid Use: An Assessment of Social Factors and Birth Cohort Trends. Ph.D. The University of North Carolina at Chapel Hill; 2023. Accessed August 15, 2023. <https://www.proquest.com/docview/2816727307/abstract/35CDD5FC212A44E2PQ/1>
47. Ballard K, Lowton K, Wright J. What's the delay? A qualitative study of women's experiences of reaching a diagnosis of endometriosis. *Fertil Steril*. 2006;86(5):1296–1301. doi:10.1016/j.fertnstert.2006.04.054 [PubMed: 17070183]
48. Coleman C, Lennon RP, Robinson JM, Tuan WJ, Sehgal N, Zgierska AE. Provider and patient sex disparities in opioid prescribing and patient outcomes. *J Opioid Manag*. 2022;18(5):435–445. doi:10.5055/jom.2022.0737 [PubMed: 36226783]
49. Escorial M, Muriel J, Margarit C, Agulló L, Morales D, Peiró Peiró AM. Sex-Differences in Pain and Opioid Use Disorder Management: A Cross-Sectional Real-World Study. *Biomedicines*. 2022;10(9):2302. doi:10.3390/biomedicines10092302 [PubMed: 36140403]
50. Hincapie-Castillo JM, Goodin A, Possinger MC, Usmani SA, Vouri SM. Changes in Opioid Use After Florida's Restriction Law for Acute Pain Prescriptions. *JAMA Netw Open*. 2020;3(2):e200234–e200234. doi:10.1001/jamanetworkopen.2020.0234 [PubMed: 32108887]
51. Sun EC, Rishel CA, Waljee JF, Brummett CM, Jena AB. Association Between State Limits on Opioid Prescribing and the Incidence of Persistent Postoperative Opioid Use Among Surgical Patients. *Ann Surg*. 2023;277(4):e759–e765. doi:10.1097/sla.0000000000005283 [PubMed: 35129496]

Key Points:

- The two NC-based opioid prescribing policies resulted in intended and unintended changes in opioid prescribing practices for acute injury and post-surgical pain patients.
- However, black, Hispanic, and native American patients experienced the greatest declines in post-surgical opioid prescribing compared to white and Asian patients.
- The racialized inequities likely reflect implicit and explicit racialized biases in pain management practices, likely driven by racial stereotyping rather than clinical evidence.
- Unintended effects on opioid prescribing, specifically fewer second prescriptions and smaller days' supply of second prescriptions may reflect either secondary effects of reductions in index prescribing or clinician's unwillingness to prescribe subsequent prescriptions.
- While the two policies reduced overall opioid prescribing practices, racialized inequities and unintended effects on patients with legitimate pain needs were concerning.

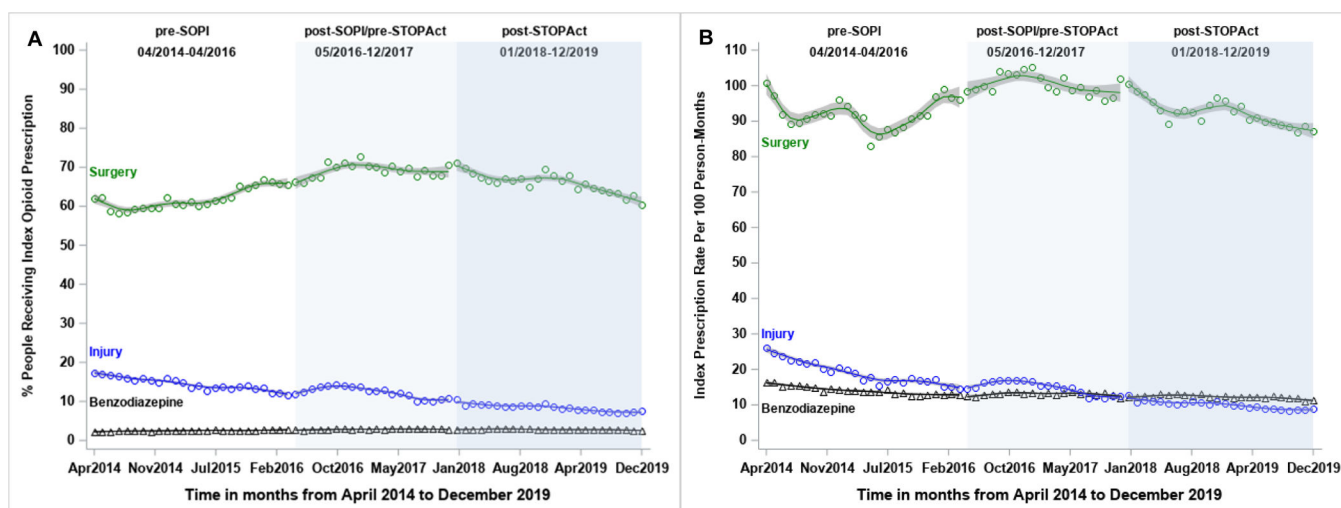


Figure 1 (A-B).

Association of SOPI and STOP Act with index opioid prescription proportion (A) and index opioid prescribing rate (B) in NC using controlled interrupted time series analyses: 2014–2019. PM, Person-Months; NC, North Carolina; SOPI, Safe Opioid Prescribing Initiative; STOP Act, Strengthen Opioid Misuse Prevention Act.

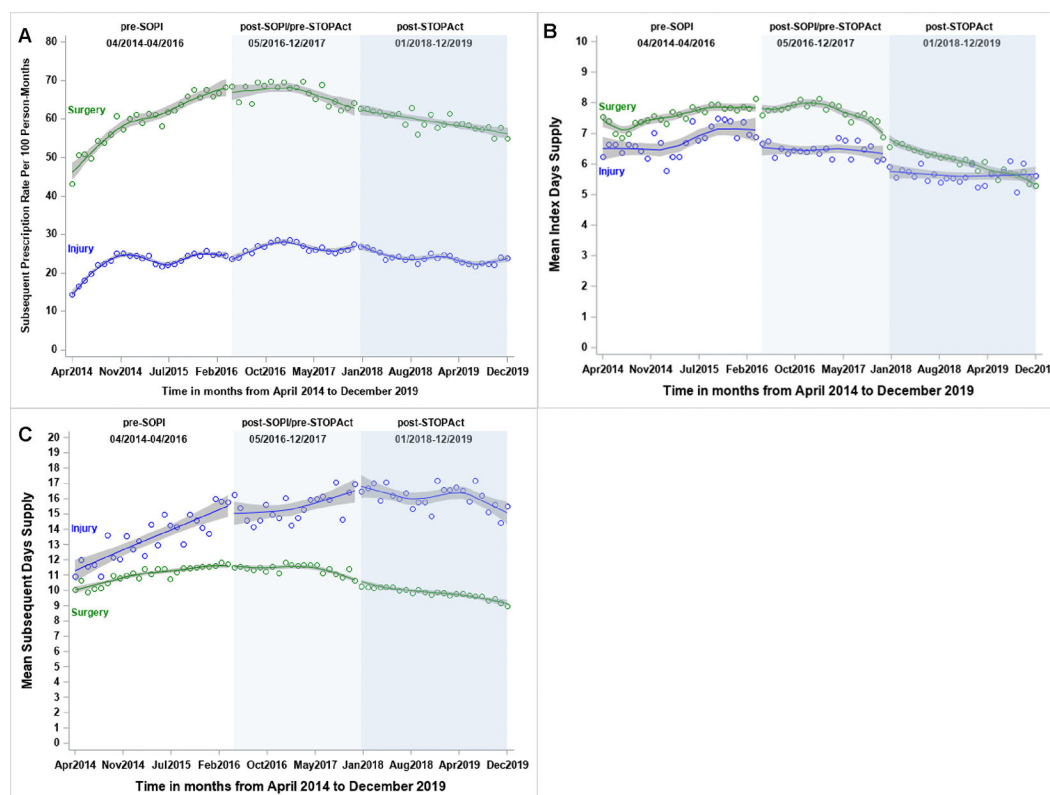


Figure 2(A-C).

Association of SOPI and STOP Act with (A) subsequent opioid prescribing rate, (B) mean index days' supply, and (C) mean subsequent days' supply in NC using single interrupted time series analyses: 2014–2019. PM, Person-Months; NC, North Carolina; SOPI, Safe Opioid Prescribing Initiative; STOP Act, Strengthen Opioid Misuse Prevention Act.

Table 1.

Patients receiving care for surgery and injury pain at two integrated healthcare systems in North Carolina, 2014–2019.

	Site 1		Site 2		Total	
	Surgery	Acute Injury	Surgery	Acute Injury	Surgery	Acute Injury
Total Patients	345,952	491,672	276,045	372,389	621,997	864,061
Patients received index opioid Rx	217,871	96,346	214,095	73,948	431,966	170,294
% Received index opioid Rx^a	62.98%	19.60%	77.56%	19.86%	69.45%	19.71%
Patients received subsequent opioid Rx	110,041	29,775	140,097	24,474	250,138	54,249
% Received subsequent opioid Rx^c	50.51%	30.90%	65.44%	33.10%	57.91%	31.86%

Abbreviations: Rx – prescription; % – percent

^a – number of patients who received an index opioid Rx divided by total patients

^b – number of index opioid Rxs divided by the number of patients who received an index opioid Rx

^c – number of patients who received a subsequent opioid Rx divided by the number of patients who received an index opioid Rx

^d – number of subsequent opioid Rxs divided by the number of patients who received subsequent opioid Rx

Table 2. Control Interrupted Time Series Results of Opioid Use for surgery and injury based on two policy implementations in North Carolina compared to benzodiazepine prescriptions from April 2014 through December 2019

Categories	Rates (95% CI)				
	Immediate absolute change post-SOPI	Post-SOPI sustained trend change	Immediate change post-STOP act	Post-STOP act sustained trend change	
	β_8	β_9^*	β_{10}	β_{11}^*	
Surgery					
% Patients receiving index opioid Rx	3.25 (1.33, 5.16)	-2.74 (-4.55, -0.93)	0.12 (-1.79, 2.03)	-4.07 (-5.92, -2.22)	
Index Rx Rate per 100 person-months	9.20 (5.27, 13.14)	-3.77 (-7.49, -0.05)	-1.01 (-4.92, 2.91)	-2.34 (-6.14, 1.46)	
Injury					
% Patients receiving index opioid Rx	2.11 (1.32, 2.90)	0.30 (-0.45, 1.05)	-0.77 (-1.56, 0.02)	1.06 (0.30, 1.83)	
Index Rx Rate per 100 person-months	2.63 (1.35, 3.90)	0.32 (-0.89, 1.52)	-0.50 (-1.77, 0.77)	1.83 (0.60, 3.06)	

* - annualized estimates, calculated by multiplying monthly trend change estimates to 12.

Table 3.

Association of two policies on prescribing behaviors for prescription opioid patients for surgery and injury pain by race in North Carolina from April 2014 through December 2019

Categories	pre-SOPI		post-SOPI		post-STOP	
	Trend (95% CI)	Absolute Immediate change (95% CI)	Sustained trend change (95% CI)	Absolute immediate change (95% CI)	Sustained trend change (95% CI)	
β1* 						

Categories	pre-SOPI		post-SOPI		post-STOP	
	Trend (95% CI)	Absolute Immediate change (95% CI)	Sustained trend change (95% CI)	Absolute immediate change (95% CI)	Sustained trend change (95% CI)	
	β_1^*	β_2	β_3^*	β_4	β_5^*	
Black	-8.80 (-9.77, -7.83)	4.66 (2.88, 6.43)	4.67 (3.00, 6.35)	-1.10 (-2.87, 0.66)	2.16 (0.45, 3.87)	
White	-3.91 (-4.57, -3.26)	3.63 (2.43, 4.82)	1.47 (0.34, 2.60)	-0.66 (-1.85, 0.53)	0.99 (-0.17, 2.14)	
Injury: Subsequent opioid Rx rate ^a						
American Native	0.11 (-1.59, 1.82)	3.36 (0.26, 6.47)	-1.22 (-4.16, 1.71)	2.74 (-5.84, 0.35)	-0.70 (-3.70, 2.30)	
Asian	-0.26 (-0.79, 0.27)	0.07 (-0.89, 1.03)	-0.11 (-1.02, 0.80)	0.65 (-0.33, 1.63)	-0.72 (-1.70, 0.26)	
Black	-0.35 (-0.85, 0.15)	-0.90 (-1.81, 0.01)	-0.75 (-1.61, 0.11)	-0.92 (-1.83, -0.01)	0.09 (-0.79, 0.97)	
White	0.99 (0.48, 1.49)	-0.56 (-1.48, 0.35)	-0.89 (-1.76, -0.02)	-1.06 (-1.97, -0.15)	-0.93 (-1.81, -0.04)	

Note. SOPI=Safe Opioid Prescribing Initiative; STOP Act=Strengthen Opioid Misuse Prevention Act; CI=confidence interval.

^aPrescribing rates per 100 insured person-months; trends calculated per 100 per year.

* - annualized estimates, calculated by multiplying monthly trend change estimates to 12.