An Examination of Trends in Low-Value Opioid Prescribing for Acute Low Back Pain in Rural vs. Non-Rural Virginia

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ACADEMIC ABSTRACT

Background: The Centers for Disease Control and Prevention (CDC) recommends against the use of prescription opioids for most types of acute pain. Despite these recommendations, some evidence suggests that opioid prescribing for acute low back pain (LBP) - among the most common acute pain complaints - persists. This study evaluated trends in low-value opioid prescribing for acute LBP among patients residing in rural versus non-rural areas of Virginia during 2019-2021 and evaluated the influence of the COVID-19 pandemic timeframe on prescribing rates.

Methods: In this retrospective cohort study, we examined insurance claims from the Virginia All-Payer Claims Database for adults continuously enrolled in Medicaid, Medicare Advantage, or commercial plans from 2019 to 2021. We used the Milliman MedInsight Health Waste Calculator to identify low-value claims and calculated annual and bi-monthly prescribing incidence rates per 1000 patients. Heterogeneous difference-in-differences models generated incidence rate ratios (IRRs) to express the difference in the rate of low-value opioids for acute LBP observed during the first two years of the COVID-19 pandemic (2020-2021) versus expected incidence based on the pre-pandemic timeframe (2019). IRRs were stratified by rurality.

Results: Among our cohort (n=853,775), 1,338,371 claims for opioids for acute LBP were identified, 73.9% of which were low-value. The annual prescribing of low-value opioids for acute LBP declined by 30.6% from 2019 (155.0 claims per 1000 patients) to 2021 (107.5 claims per 1000 patients) compared with the expected decline (model-predicted) of 18.6% during this period. During 2020-2021, low-value opioid prescribing for acute LBP was 79.6% of expected incidence (IRR: 0.80, $p<.001$). Low-value opioid prescribing for acute LBP was 0.74 times higher in patients residing in rural versus non-rural areas throughout 2019-2021 (IRR: 1.74, $p<.001$), and the difference in low-value prescribing between rural and non-rural patients did not change significantly during 2020-2021 (IRR: 1.02, $p=.060$).

Conclusions: Most opioids prescribed for acute LBP among this large, multi-payer Virginia cohort were low-value. The COVID-19 pandemic timeframe (2020-2021) was associated with an accelerated decline in low-value opioid prescribing for acute LBP. Persistent rural disparity in low-value opioid prescribing for acute LBP highlights the need to examine underlying drivers to reduce low-value prescribing and promote equitable, high-quality acute pain care.

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GENERAL AUDIENCE ABSTRACT

Opioids are a class of medications used to treat diverse types of pain. National guidelines recommend against the prescribing of opioids for most types of acute (short-term) pain since they are no more effective than non-opioid treatments and are associated with substantial risks. Despite these recommendations, there is some evidence that clinicians continue to prescribe opioids for acute pain.

To better understand recent patterns of opioid prescribing for acute pain, we analyzed insurance claims for over 800,000 adults living in Virginia in 2019-2021. We specifically studied claims for opioids prescribed for acute low back pain (LBP), one of the most common types of acute pain treated in outpatient healthcare settings. We used proprietary software (Milliman MedInsight Health Waste Calculator) to categorize opioid claims as low-value (inconsistent with professional guidelines) or clinically appropriate. We assessed changes in patterns of low-value opioid prescribing for acute LBP throughout 2019-2021, assessed prescribing variation among patients living in rural and non-rural areas, and evaluated prescribing patterns in the context of the COVID-19 pandemic during 2020-2021.

Our cohort received nearly one million low-value opioid prescriptions for acute LBP during the 3-year study period. The prescribing of low-value opioids for acute LBP declined throughout 2019-2021, with the rate of decline during 2020 and 2021 greater than that observed in 2019. Rural residents received significantly more low-value opioid prescriptions for acute LBP than non-rural residents throughout 2019-2021, as the pandemic timeframe did not influence the incidence rates in a significantly different manner by rurality. Declining rates of low-value opioid prescribing for acute LBP are encouraging, but rural disparity points to systematic obstacles or entrenched prescribing practices. Future research should explore why rates of low-value opioid prescribing for acute pain vary by rurality to inform future efforts to mitigate prescription opioid-related harm.

Dedication

I dedicate this work to the late Warren Bickel, PhD, who has been a steadfast role model while I worked at the Addiction Recovery Research Center at the Fralin Biomedical Research Institute and whose support allowed me this opportunity. I also dedicate this work to all those who have provided valuable support for my journey, including mentors, colleagues, family, and friends.

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List of Definitions and Terms

Acute Pain: Pain usually resolving within 30 days, whereas sub-acute pain usually resolves within 90 days, and chronic pain lasts 90 days or longer.

Cascades of Care: A sequence of additional medical tests and procedures that can follow from an initial unnecessary or incidental test result, often intended to reduce the likelihood of overlooking a potentially serious condition.[1]

De-implementation: The reduction or termination of practices that are often harmful or ineffective.

Deprescribing: The reduction or termination of prescription medications that risk adverse events or are ineffective within specific clinical scenarios.

Difference-in-Difference: A quasi-experimental method that estimates the causal effect of an event (treatment, exposure) by comparing the changes in a defined outcome over time between the control group (or a counterfactual group representing the change that would have been without the exposure) and the treatment or exposed group. Comparing the difference in the observed and the expected outcome across both time frames provides an estimate of the effect or impact of the exposure.

Incidence Rate Ratio (IRR): A measure of association that compares the incidence rate of an event (such as disease, hospitalization, or prescription) in one group to the incidence rate in another group using a ratio. IRR=1: no difference between groups; IRR>1: higher incidence rate in the exposed/intervention group; IRR <1: lower incidence rate in the exposed/intervention group.

Low-value Care: Healthcare services that offer no value in specific clinical scenarios and may be associated with waste, excess costs, and multilevel harm. May also be described as inappropriate or non-guideline concordant care.

Low-value Opioid Prescribing: When opioids are prescribed, or prescriptions are filled, in specific clinical scenarios which are not recommended (e.g. acute pain associated with migraine headaches or low back pain(LBP)), or incidences wherein an opioid is prescribed in a fashion that is contrary to recommendations (e.g. before the consideration or attempt of other options, in unnecessarily high doses or extended-release formulations for individuals with acute pain or surgery, or in quantities that are not more than pain is expected to last (i.e. 3-5 days' supply for acute pain)).

Opioid Medications: A class of drugs that bind opioid receptors in the central nervous system (brain and spinal cord), reducing pain signals.

Opioid Stewardship: A comprehensive, multidisciplinary healthcare approach that involves coordinated interventions to improve, monitor, and evaluate opioid prescribing practices. The goal of opioid stewardship is to maximize patient benefits and minimize risks such as opioid misuse, abuse, overdose, or diversion.
Examples of opioid stewardship include prescription drug monitoring programs (PDMPs), appropriate prescribing, treatment and support of people with opioid use disorder, provider and caregiver education, and consistent care pathways across healthcare systems.

Opioid Utilization: A measure of how often opioid prescriptions are filled in a population; often expressed as a rate, usually in the number of prescriptions in a population in a time period (e.g., number of low-value opioid prescriptions for acute LBP for every 1000 individuals in 2019, 2020, or 2021).

Trends Analysis: Systematic examination of data collected over time to identify, quantify, and interpret patterns or changes. In health services research, trend analyses often focus on patterns or changes in healthcare outcomes, utilization, costs, quality, or access.

List of Abbreviations

ANOVA – Analysis of Variance
APCD – All-Payer Claims Database
CDC – Centers for Disease Control and Prevention
DiD – Difference-in-difference
ED – Emergency Department
FDA – Food and Drug Administration
HWC - Health Waste Calculator
IRR – Incidence Rate Ratio
LVC – Low-Value Care
LBP - Low Back Pain
MA – Medicare Advantage
NSAIDs – Nonsteroidal Anti-Inflammatory Drugs
RUCA – Rural-Urban Commuting Area

Chapter 1

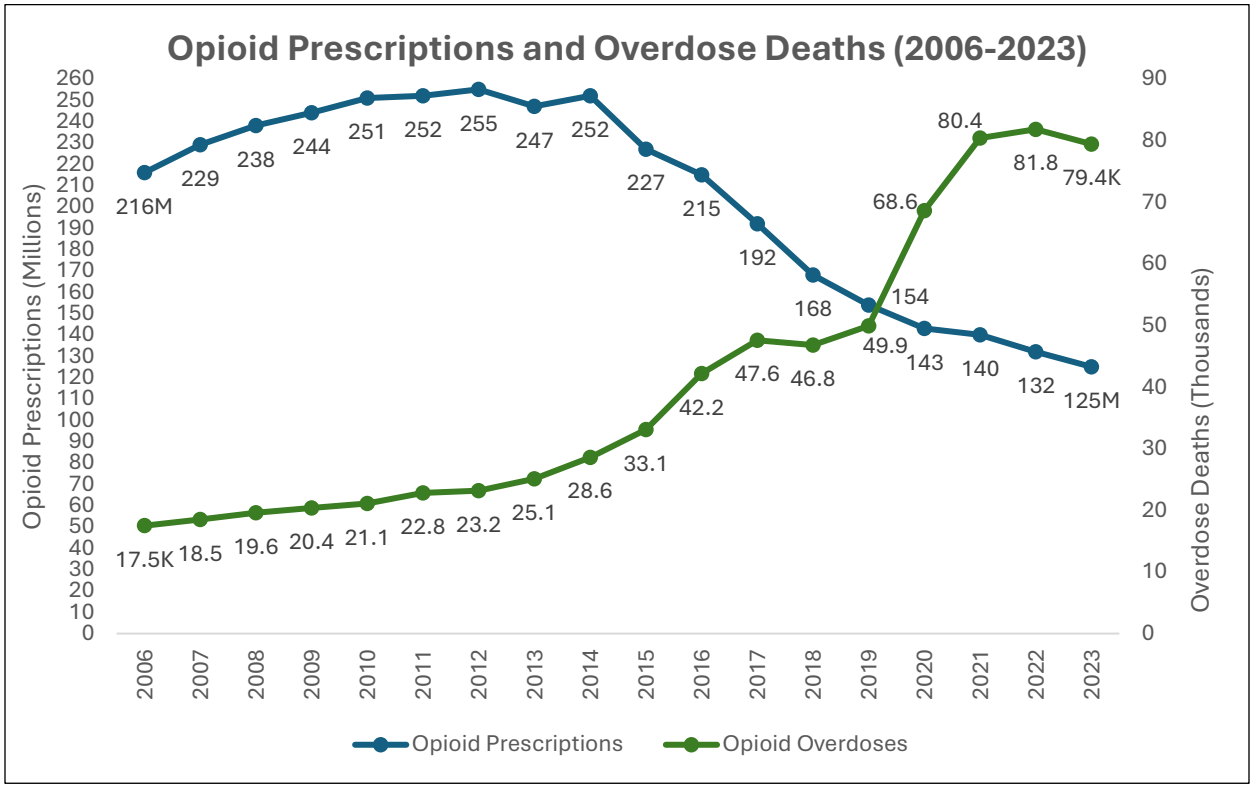
Opioid medications are commonly prescribed for the treatment of many types of pain and have played a central role in pain management for decades.[2] Despite their therapeutic benefits, opioids carry a risk of adverse effects such as dizziness, loss of consciousness, overdose, misuse, and dependence, among others.[3,4] The United States is currently experiencing a prolonged opioid overdose and addiction crisis, referred to in this chapter as the opioid epidemic. The economic burden of the opioid epidemic has been substantial, estimated at $786.8 billion in 2017, rising to nearly $4 trillion by 2024.[5,6] The opioid crisis, first described as an epidemic in 2011, has evolved and is driven by multiple factors, including pharmaceutical marketing, prescribing practices, illicit drug availability, and barriers to safe pain management.[7–11] To address the opioid epidemic, multi-sector responses have aimed to mitigate opioid related harms and improve opioid prescribing practices. At the same time, pain must be adequately managed. Balancing risk mitigation with safe and adequate pain management is a challenge. Understanding the epidemiology of opioid prescribing and its contributing factors is crucial to guiding national and state-level public health interventions.

1.0 Opioid Epidemic in the United States

To better understand the scale and evolution of this crisis, it is important to consider how the epidemic has evolved. The opioid epidemic has unfolded in three major waves, each characterized by distinct substance use patterns and population-level harm.[9] In the early 1990s, a perfect storm of clinical inertia, culture, policy, pharmaceutical marketing, and misconceptions about addiction risk contributed to prescribing increases until their peak in 2011.[7,8,12] During this timeframe, the incidence of opioid use disorder (OUD), overdose, and emergency department

(ED) visits also increased.[7,9,10] In the first wave, overdose deaths from prescription opioids sharply increased through 2007.[9] The second wave began around 2010, driven largely by heroin overdose, while the third wave emerged around 2012 with the increase in overdose deaths from synthetic opioids.[9] The opioid epidemic was declared a public health emergency by the Department of Health and Human Services in 2017.[13] Since 2011-2012, the volume and incidence of opioids prescribed in the United States returned to levels last seen in the 1990s (Figure 1).[9,14,15] Reduction in opioid prescribing coincided with less contribution of prescription opioids to overdose deaths, but the emergence of potent forms of street drugs such as fentanyl have complicated efforts to reduce overdose deaths and mitigate incidence of opioid use disorder.[10,15–17] Despite these challenges, the United States saw its first decline in opioid-overdose death incidence in 2022 (Figure 1).[9,14,18–20] The development of the opioid epidemic over the past decades provides essential context for understanding current prescribing trends and the need for public health responses.

Figure 1. Opioid Prescriptions and Overdose Deaths Between 2006 and 2023 in the United States



[From: National Center for Data Abuse Statistics. Opioid Prescriptions & Opioid Overdose Deaths. 2025. Accessed December 15, 2025. https://drugabusestatistics.org/opioid-epidemic/
Source: National Institute and Drug Abuse & CDC]

In response to the escalating harm of the opioid epidemic, national and state authorities implemented policies and programs to reduce opioid overprescribing and to improve patient safety. In addition, state-by-state legislation established prescription monitoring programs and strict laws supporting guidelines.[21] The Centers for Disease Control and Prevention (CDC) issued recommendations for appropriate opioid prescribing for acute and chronic pain in 2016.[22] There have been both successes and unintended consequences stemming from guidelines implementation and other efforts to mitigate the risks of opioid prescribing.[23,24] These recommendations focused on reducing the overprescribing of opioids, particularly for chronic pain, as well as reducing the ongoing risk involved with the prescription of opioids. However,

because confusion and misapplications impacted pain management and increased risks for patients with pain after 2016, the CDC guidelines were updated in 2022. The updated guidelines acknowledge the unintended consequences, clarify that they are not intended to be inflexible standards, promote patient-centered language, provide guidance that balances the risks of opioids with risks of untreated pain, and expand their scope to acute and sub-acute pain.[2,22,25] Additionally, opioid-related adverse events, including the risk of prescription opioid overdose, will remain an important clinical issue.[4,26] Given ongoing risks, optimizing how opioids are prescribed, especially in short-term, acute pain, has become a central focus of system quality improvement efforts.

1.0.1 Rural Disparity in Opioid Epidemic Impact and Opioid Prescribing

The opioid epidemic disproportionately impacts rural areas, where opioid overdose and substance use disorder rates are among the first and the highest observed.[7,8,27] Although national efforts have been associated with a reduction in overall opioid prescribing in the United States, opioid prescribing remains a problem in many rural regions, particularly Appalachia.[7,8,27–29] In part, opioid prescribing incidence is higher because the incidence of chronic pain is higher in rural than non-rural areas.[30,31] Rural patients face barriers to non-pharmacological pain management as well as treatment for substance use disorders compared to non-rural patients (e.g., longer distances to care and fewer providers).[7,8,27–29] These challenges are exemplified in rural Virginia, where the opioid epidemic had a particular impact and where opioid overprescribing remains a concern, as five of the nation's top ten counties for opioid prescribing are in Virginia.[14,32,33] Also, improving access to OUD treatments and addressing opioid related-harm in rural areas is a major public health priority in Virginia.[34] These disparities illustrate that,

despite progress, opioid prescribing optimizations, such as for acute pain, may be of particular importance in rural areas.

1.1 Opioids for Acute Pain

Approximately 80 million Americans received a prescription medication for acute pain in 2023, 40 million of which were opioids.[35,36] Acute pain typically resolves within 30 days. The acute pain timeframe represents a critical window in which treatment decisions can have long-term consequences for patient outcomes.[3,37] Non-opioid and non-pharmacological acute pain treatment options, including ice/heat, rest, exercise, nonsteroidal anti-inflammatory drugs (NSAIDS), weight loss, acupuncture, spinal manipulation, and psychological therapies (e.g., cognitive behavioral therapy), can be as effective as opioids in many acute pain scenarios, and carry less risk.[2,3] Opioids are associated with greater likelihood of short-term adverse events and side effects (e.g., overdose, dizziness, risk of falls, hospitalizations, gastrointestinal disruptions, exacerbations of current medical conditions, diversion, and misuse).[3,38] Yet, opioids are still commonly prescribed for acute pain. Within the acute timeframe (30 days from pain onset), exposure to opioids in specific scenarios (e.g., low back pain (LBP)) is associated with adverse patient outcomes (e.g., increased chronic pain, delayed healing), short- and long-term risks (e.g., side-effects, overdose, OUD, hyperalgesia, depression), and cascades of care thereafter (e.g., surgeries, long-term opioid-therapy).[4,39–46] Opioids act on receptors in the central nervous system, but tolerance can be developed quickly, which may result in increased dosages required to get the same relief.[4] Dependence can also develop quickly, meaning individuals are vulnerable to withdrawal syndrome without continuing or tapering off opioids. The mechanisms of action and consequences make it more likely for patients to continue using prescription opioids long-

term.[4,43,45] Tolerance, dependence, and time contribute to the risk of misuse and development of OUD.[4,42]

The use of opioids can also hinder the use of safer alternatives while increasing pain sensitivity and delaying the healing process, which increases the likelihood of the development of chronic pain.[4,41] One study found that approximately 24% of those reporting acute pain while visiting the ED developed chronic pain after 90 days.[47] The progressions described above are cascades of risk and care that can influence healthcare utilization.[40,46] For example, chronic pain management is costly in terms of healthcare utilization and burden, and the functional and quality of life outcomes for patients are not always achieved.[38,48,49] Further, long-term opioid therapy increases patient risks and the level of monitoring needed to mitigate them, and the cost to treat OUD is immense.[2,5] Therefore, opioid prescribing during acute pain can initiate cascades of multi-level harms, impacting both patient health and healthcare utilization.

Since opioids are associated with multi-level harms, the CDC guidelines emphasize the use of non-opioid options for acute pain over opioids whenever possible.[2] In 2019, the FDA and other agency reports identified opioid prescribing for acute pain as a key target to serve as a preventive strategy to avoid prescription opioid-related adverse events, improve patient outcomes, and reduce healthcare burden.[26,50] The harm of opioid prescribing for acute pain has been increasingly recognized, but the recommendations that outline the acute pain scenarios in which opioids should be specifically avoided have only recently been emphasized on a large scale, compared to how long the opioid epidemic has been occurring.[2,22,51] Therefore, the examination of the trends in opioids prescribed for acute pain according to or inconsistent with the guidelines

is expedient. Given the high prevalence of certain acute pain conditions, examining opioid prescribing practices in specific contexts can inform more targeted strategies to reduce their utilization.

1.1 Acute Low Back Pain

LBP is a leading cause of disability and is associated with high clinical and economic burden both nationally and globally.[52,53] Among acute pain conditions, LBP is one of the most common pathologies treated in primary care worldwide.[52,54,55] The incidence of acute LBP has increased in the United States, at least in the ED, between 2016 and 2023.[56] As the incidence of LBP continues to rise and drive healthcare utilization, understanding treatment patterns has become increasingly important.

One of the most notable treatment patterns is the continued reliance on opioids for acute LBP, despite limited benefits and well-established risks. While the frequency of opioid prescriptions among visits has decreased in the ED, opioids remained the most commonly administered medication (40.7%), and the second most common prescription at discharge (23.2 %) between 2016-2023.[56] This widespread use highlights an ongoing dependence on opioid therapy even when safer, evidence-based alternatives exist. Because of its prevalence and frequent exposure to opioids, acute LBP provides a proxy for studying the incidence of prescribing for acute pain. Section 1.2 discusses the specific risks of, and the recommendations related to the prescription of opioids for acute LBP.

1.2 Guidelines for Opioid Prescribing for Acute Pain

Recommendations for the prescribing of opioids aim to reduce overprescribing and mitigate risks to patients.[2,51,57–59] Prescribing recommendations address several factors:

- Strength of dose (i.e., it is recommended to use the lowest effective dose for acute pain)
- Prescription quantity (e.g., do not use longer than the expected duration of pain)
- Indication for which the prescription is given (e.g., opioids for migraine headaches, LBP)
- Patient (e.g., adults, opioid-naïve; their history of risk factors - mental health, history of substance use)
- Setting (e.g., Emergency department, surgery, primary care)
- Mechanism of drug delivery (e.g., do not use extended-release opioids for acute pain)
- Discussion of risks with patients (e.g., patient education on risks, storage)

See examples of CDC recommendations in Table 1.

Table 1. CDC Clinical Practice Guideline for Prescribing Opioids for Pain - United States, 2022[2]

Nonopioid therapies are at least as effective as opioids for many common types of acute pain. Clinicians should maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider opioid therapy for acute pain if benefits are anticipated to outweigh risks to the patient. Before prescribing opioid therapy for acute pain, clinicians should discuss with patients the realistic benefits and known risks of opioid therapy. Common types of acute pain: Low back pain, neck pain, pain related to other musculoskeletal injuries (e.g., sprains, strains, tendonitis, and bursitis), pain related to minor surgeries typically associated with minimal tissue injury and mild postoperative pain (e.g., simple dental extraction), dental pain, kidney stone pain, and headaches, including episodic migraine.
When opioids are initiated for opioid-naïve patients with acute, subacute, or chronic pain, clinicians should prescribe the lowest effective dosage.
When diagnosis and severity of acute pain warrant the use of opioids, clinicians should prescribe immediate-release opioids at the lowest effective dose and for no longer than the expected duration of pain severe enough to require opioids.
Clinicians should work with patients to prevent prolonged opioid use, prescribe and advise opioid use only as needed (e.g., hydrocodone 5 mg/acetaminophen 325 mg, one tablet not more frequently than every 4 hours as needed for moderate to severe pain) rather than on a scheduled basis (e.g., one tablet

every 4 hours), and encourage and include an opioid taper if opioids will be taken around the clock for more than a few days.
Advise patients that short-term opioid use can lead to unintended long-term opioid use and of the importance of working toward planned discontinuation of opioid use as soon as feasible, including a plan to appropriately taper opioids as pain resolves if opioids have been used around the clock for more than a few days.
Review increased risks for respiratory depression when opioids are taken with benzodiazepines, other sedatives, alcohol, nonprescribed or illicit drugs (e.g., heroin), or other opioids. Discuss risks for household members and other persons if opioids are intentionally or unintentionally shared with others for whom they are not prescribed, including the possibility that others might experience overdose at the same or at a lower dosage than prescribed for the patient and that young children are susceptible to unintentional ingestion. Discuss storage of opioids in a secure, preferably locked location and options for safe disposal of unused opioids, and the value of having naloxone available.

[Source CDC, 2022[2]]

1.2.1 Low-Value Opioid Prescribing for Acute Pain

A subset of prescribing patterns that are inconsistent with recommendations described in Table 1 is considered low-value care (LVC).[2,51,57,58,60] LVC refers to healthcare services that offer no clinical benefit in specific clinical scenarios and may be associated with waste, excess costs, and multilevel harm.[61,62] In 2012, the American Board of Internal Medicine launched Choosing Wisely, a de-implementation campaign, in collaboration with professional organizations and medical societies, to discourage the utilization of LVC.[51,63] Among LVC, utilization rates of low-value pharmaceutical services contribute the most to wasteful spending.[64] Reducing low-value opioid prescribing is an important optimization. Opioid prescribing for acute LBP is a specific example of low-value opioid prescribing.[2,57,58,60]

Opioid prescriptions for acute LBP are considered low-value because most cases resolve within six weeks and can be managed with conservative measures such as ice and heat, rest, and avoiding strenuous activity or lifting.[2,3] Moreover, non-opioid and non-pharmacological

treatments, such as physical therapy, reduce long-term opioid use and improve functional outcomes for patients with acute LBP, whereas opioids can hinder recovery.[65] Since LBP is a common complaint for acute pain, opioid prescribing for acute LBP can serve as a useful proxy for low-value opioid prescribing for acute pain more broadly when evaluating trends.[52] Other examples of specific guidelines that would reduce low-value opioid prescribing include the following:

Table 2. Examples of Guidelines that Discourage Low-Value Opioid Prescribing

Recommendation	**Professional Organization**	**The Rationale**
Do not prescribe opioid analgesics as first-line therapy to treat *chronic non-cancer pain.* If drug therapy appears indicated, non-opioid medication (e.g., NSAIDs, anticonvulsants, etc.) should be trialed prior to commencing opioids.	American Society of Anesthesiologists-Pain Medicine	Physicians should consider multimodal therapy, including non-drug treatments such as behavioral and physical therapies prior to pharmacological intervention.
Do not prescribe opioid or butalbital-containing medications as first-line treatment for recurrent *headache disorders.* Use may be appropriate when other treatments fail or are contraindicated. Such patients should be monitored for the development of *chronic headaches.*	American Society of Anesthesiologists-Pain Medicine	These medications impair alertness and may produce dependence or addiction syndromes, an undesirable risk for the young, otherwise healthy people most likely to have recurrent headaches. They increase the risk that episodic headache disorders such as migraine will become chronic and may produce heightened sensitivity to pain.
Do not use opioids or butalbital for *migraine* except as a last resort.	American Academy of Neurology	Opioid and butalbital treatment for migraine should be avoided because more effective, migraine-specific treatments are available. Frequent use of opioids and butalbital can worsen headaches. Opioids should be reserved for those with medical conditions precluding use of migraine-specific treatments or for those who fail these treatments.

Do not prescribe opiates in acute disabling *low back pain* before evaluation and a trial of other alternatives is considered.	American Academy of Physical Medicine and Rehabilitation	Early opiate prescriptions in acute disabling low back pain are associated with longer disability, increased surgical rates, and a greater risk of later opioid use. Opiates should be prescribed only after a physician evaluation by a licensed health care provider and other alternatives are trialed.

[Source: Choosing Wisely, 2023;[51] Shaw et al. 2018[57]]

1.3 Measuring and Analyzing Prescribing Trends

Evaluating the low-value opioid prescribing for acute pain is crucial for identifying where, by whom, and to whom the greatest risk of cascades of harm is possible. However, there are several challenges faced in measuring low-value opioid prescribing for acute pain, such as the identification of specific incidents of non-recommended services through health data (e.g., electronic health records (EHR) or insurance claims). Identifying LVC requires clear and reliable definitions and methods to distinguish these services from appropriate care. Data from claims and EHR data are prone to data quality and completeness issues related to factors such as fragmentation between health systems, patient coverage gaps, or inconsistent use of medical billing codes.[66,67] While leveraging claims or EHR data offers opportunities to measure low-value opioid prescribing for acute pain at scale, doing so requires precise definitions and tools to differentiate low-value from appropriate care.

To address measurement challenges, several tools and algorithms have been developed to identify low-value healthcare services within claims data.[66,68] For example, the Milliman MedInsight Health Waste Calculator (HWC) uses proprietary algorithms to generate estimates of low-value versus clinically appropriate opioid prescribing for acute LBP.[66,68–71] HWCs have been used to report on LVC.[70–76] HWCs, or similar tools, allow for the analysis of patterns of low-

value care, enabling health services researchers to estimate the utilization low-value health care services, track trends over time,[66,68,77] identify disproportionately affected populations,[78] and identify targets for interventions. The availability of tools such as the HWC facilitates trend analysis, especially when paired with comprehensive data sources like All-Payer Claims Databases (APCDs).[76]

Although this study does not evaluate the effectiveness of opioid stewardship or other de-implementation efforts, it aligns with emerging calls to incorporate contextual factors, such as the COVID-19 pandemic, into research on low-value opioid prescribing. A recent review suggested that future research on the de-implementation of low-value opioid prescribing should include factors outside of the healthcare system (e.g., health system strain from a worldwide pandemic, insurance), and explore how opioid stewardship interventions and others impact disparities in pain management with an emphasis on their appropriateness.[79,80] A retrospective cohort study of longitudinal observational claims data is an appropriate method to examine low-value opioid prescribing for acute LBP and identify existing rural disparities in low-value acute pain treatments. A difference-in-difference (DiD) analysis allows for the examination of trends over time, the isolation of the impact of events and outside factors that affect the healthcare system, and how these factors affect rural disparity.[81] Several studies have demonstrated the use of DiD or similar analyses to measure LVC while accounting for the impact of the COVID-19 pandemic timframe.[77,82–84] Starting in March 2020, healthcare services were universally interrupted due to the impending threat of COVID-19 and subsequent public health policies.[85] Many services had to be postponed, appointments were limited, and fear of contracting COVID-19 affected individuals' willingness to venture out after stay-at-home orders subsided.[85,86] These

considerations underscore the importance of using longitudinal observational methods, such as retrospective cohort and DiD analyses, to assess trends in low-value opioid prescribing over time and across populations.

1.5 Trends in the Utilization of Low-Value Opioid Prescribing

Opioid Prescribing Before the COVID-19 Pandemic

Before the COVID-19 pandemic, opioid prescribing incidence declined annually since 2011.[14,87] However, reductions in low-value opioid prescribing for acute pain were less clear.[68,77,88] Existing examinations of opioid prescribing trends do not always distinguish opioid prescriptions by appropriateness (i.e., low-value versus clinically appropriate), but instead focus on total opioids prescribed for chronic LBP, acute LBP treated only in EDs, opioids for non-cancer pain, or opioids for non-cancer LBP.[56,89–92] In Virginia, the incidence of opioid prescribing has decreased over time, but less is known about low-value opioid prescribing for acute LBP.[14] This gap in the evidence underscores the need for more focused evaluation of low-value opioid prescribing specifically for acute LBP.

1.5.2 Opioid Prescribing During the Pandemic

The COVID-19 pandemic disrupted healthcare services, creating a natural experiment for reexamining entrenched prescribing practices, including those deemed low-value.[93] Early evidence suggests that overall opioid prescribing for acute pain temporarily decreased between April and May 2020 before rebounding to pre-pandemic levels by December 2020.[14,94–97] However, one study showed that incidence of low-value opioid prescribing for acute LBP and headache increased between March and June 2020.[98] Despite this emerging evidence, little is

known about how low-value opioid prescribing for acute LBP specifically evolved from pre-pandemic through 2021 among a multi-payer cohort.

Current evidence has largely focused on national trends or individual payers. For example, low-value opioid prescribing for acute LBP and other non-recommended conditions decreased among Medicare beneficiaries between 2016 and 2019, but this trend was not observed across other payer types, wherein the incidence of prescribing may differ.[99] Similarly, while ED visits have increased for LBP, the percentage of ED visits for LBP where opioids were prescribed or administered declined from 2016 to 2022.[56,89] Yet, opioids are still the most commonly prescribed medication.[56,89] These studies focus primarily on ED settings and Medicare populations, limiting our understanding of broader prescribing trends across ambulatory care.

The Commonwealth of Virginia has diverse payer representation and known rural-urban disparities in opioid prescribing,[100] yet limited studies have examined the trend in low-value opioid prescribing for acute LBP. Examining trends in low-value opioid prescribing for acute LBP in Virginia during the pandemic can facilitate understanding whether national declines translated across settings and populations—and to identify potential targets for further research and future efforts to reduce low-value opioid prescribing for acute pain in Virginia, or beyond.

1.5.3 Rural Disparity in Low-Value Opioid Prescribing for Acute LBP During the COVID-19 Pandemic

The utilization of LVC, including low-value opioid prescribing for chronic pain, differs by rural residency and race/ethnicity.[27,31,78,82] Since low-value opioid prescribing for acute LBP can lead

to cascades of harms that could contribute to other rural health disparities, examining rural variation in low-value prescribing patterns for acute pain may reveal an actionable target for reducing both chronic pain burden and opioid-related harm in rural patients.[27,29] Although the COVID-19 pandemic timeframe is associated with an abrupt disruption in healthcare delivery, it is yet to be understood how low-value opioid prescribing for acute LBP was impacted in rural versus non-rural areas between 2019-2021. Collectively, these gaps underscore the need to understand rural variation in low-value opioid prescribing for acute LBP in the context of the COVID-19 pandemic timeframe.

Research Gap

Several critical knowledge gaps remain.

- Total opioid prescribing incidence has declined across Virginia and the United States since 2011. It is less clear if the prescribing of opioids for acute pain has declined proportionately during the same timeframe. No peer-reviewed studies report on the incidence of low-value opioid prescribing for acute pain in Virginia.
- The COVID-19 pandemic impacted the delivery of low-value health services; utilization rates declined briefly after the pandemic declaration, but most returned to pre-pandemic levels by the end of 2020. However, the impact of the pandemic on low-value opioid prescribing for acute pain is not well understood.
- Opioid prescribing incidence is known to be higher in rural areas. The extent to which the prescribing of low-value opioid prescribing for acute pain contributes to disproportionate opioid prescribing in rural areas is not well documented.

- Variation in the impact of the COVID-19 pandemic on the prescribing of low-value opioid prescribing for acute pain in rural versus non-rural areas has not been well-described in peer-reviewed literature.

Problem Statement

Given the clinical risks associated with using opioids for acute pain, it is crucial to understand trends. However, gaps remain in our knowledge regarding the magnitude of low-value opioid prescribing for acute LBP over time, whether these trends differ from overall opioid prescribing for acute LBP, and which subpopulations are disproportionately affected. Addressing these questions is essential to inform the development of equitable, evidence-based strategies to reduce opioid-related harm across Virginia, and potentially beyond.

Thesis Purpose & Structure

The purpose of this thesis was to improve understanding of low-value opioid prescribing trends and rural variation in low-value opioid prescribing for acute LBP during 2019-2021 using a large multi-payer cohort. We used the Virginia APCD, which is comprised of medical and pharmaceutical claims for multiple payers from more than 5 million patients in Virginia. This retrospective cohort study employed a DiD analysis to both describe trends and assess the impact of the COVID-19 pandemic on the incidence of low-value opioid prescribing for acute pain. Additionally, it explored variation in incidence and variation in pandemic impact between rural and non-rural patients. Chapter 2 is a full manuscript describing the study background, methods, results, and discussion presented in scholarly journal format. Chapter 3 includes a summary of

the study results and a discussion of their implications, along with recommendations for future research.

Specific Aims and Hypotheses

This study will achieve the following specific aims:

Aim 1. Describe trends in low-value opioid prescribing for acute LBP among a large multi-payer Virginia cohort during 2019-2021.

Hypothesis: Low-value opioid prescribing for acute LBP declined between 2019 and 2021.

Aim 2. Evaluate the impact of the COVID-19 pandemic timeframe on low-value prescribing for acute LBP among a large multi-payer Virginia cohort.

Hypothesis: Low-value opioid prescribing for acute LBP declined to a lesser extent during 2020-2021 (during the first 2 years of the COVID-19 pandemic) compared with what would be expected based on the trend in 2019 (before the COVID-19 pandemic).

Aim 3. Assess rural variation in low-value opioid prescribing for acute LBP among a large multi-payer Virginia cohort during 2019-2021.

Hypothesis: Low-value opioid prescribing for acute LBP was higher in rural areas than in non-rural areas throughout 2019-2021.

Aim 4. Assess rural variation in the impact of the COVID-19 pandemic timeframe on low-value opioid prescribing for acute LBP among a large multi-payer Virginia cohort.

Hypothesis: During 2020-2021 (the first 2 years of the COVID-19 pandemic), the rate of low-value opioid prescribing for LBP declined to a lesser extent in rural areas compared with non-rural areas.

Chapter 2

INTRODUCTION

In the United States, 80 million adults receive prescriptions for acute pain each year, half of which are opioids.[35,36] Opioids generally pose a greater risk than non-opioid or non-pharmacological alternatives for acute pain, including an increased likelihood of having chronic pain, receiving long-term opioid therapy, and increased healthcare utilization.[3,41,48,101] Consequently, clinical and professional guidelines recommend against opioids for most acute pain scenarios.[6-9,16,17] While overall opioid prescribing has declined annually in the United States since 2011,[14,87] there is evidence that the prescribing of low-value opioid prescribing for acute pain has not, despite guidelines.[68,77] Understanding the trends and population variation (e.g., rurality, payer type, and biological sex) in low-value opioid prescribing for acute pain is essential to identifying potential targets for efforts to reduce low-value opioid prescribing for acute pain.

The COVID-19 pandemic (2020-2021) disrupted healthcare delivery in varied ways.[102] For most services, particularly low-value services, utilization decreased early in the pandemic but returned to pre-pandemic levels by the end of 2020 or early 2021.[83,95,98,103] For opioid prescribing, Lee et al. reported an increase in opioid prescribing for acute and chronic pain. For opioids prescribed for acute pain and for specific low-value indications (acute LBP and headaches), two studies reported increases early in the pandemic.[94,98] However, Gottlieb and Bernard showed that opioid prescribing for acute LBP at discharge from the emergency department declined between 2016 and 2023, but that decline was blunted from 2019 to 2023.[56] Therefore, there is some ambiguity

about whether low-value opioid prescribing for acute LBP declined across settings and payer types during 2019–2021, or how the pandemic timeframe influenced these trends.

Individuals living in rural areas have historically experienced higher overall opioid prescribing rates.[7,27] They additionally experience greater barriers to non-opioid pain management and more harm from prescription opioid misuse than those in non-rural regions.[7,27,28] Other types of low-value care have been documented as more prevalent in rural areas and among other demographic groups.[31,78,82] It's important to identify rural variation in low-value opioid prescribing for acute pain, since this service can contribute to a greater likelihood of chronic pain, and the burden of chronic pain is higher in rural areas.[30] However, among peer-reviewed literature on opioid prescribing trends, there is no examination of rural variation in low-value opioid prescribing for acute LBP.

To address these gaps, we used insurance claims to evaluate trends in the incidence of low-value opioid prescribing for acute LBP in rural and non-rural ambulatory care during 2019-2021. We also evaluated the impact of the COVID-19 pandemic on the low-value opioid prescribing for acute pain in rural and non-rural ambulatory care. We hypothesized that incidence of low-value opioid prescribing for acute LBP: a) declined between 2019 and 2021, b) declined more during the first two years of the COVID-19 pandemic than the annual declines observed pre-pandemic, c) were higher in rural areas than non-rural areas between 2019 and 2021, and d) in rural areas declined to a lesser extent than in non-rural areas during the first two years of the COVID-19 pandemic. As an additional exploratory analysis, we assessed payer-level variation in the

incidence of low-value opioid prescribing for acute LBP and the impact of the pandemic on these rates.

METHODS

Study Design & Participants

In this retrospective cohort study, we used insurance claims from the Virginia All-Payer Claims Database (APCD) to evaluate the incidence of opioids prescribed for acute LBP from January 1, 2019 to December 31, 2021. The Virginia APCD collects medical and pharmaceutical claims for >5 million individuals insured by public and private payers.[104] Our cohort included adults (≥18 years of age) continuously enrolled for ≥12 months with commercial, Medicaid, or Medicare Advantage (MA) payers. Due to the use of deidentified data, the Institutional Review Board (IRB) of Carilion Clinic determined that this project did not meet the definition of human subjects research, per 45-CFR-46.102(d).

Data

We extracted population-level claims from the APCD, aggregated by demographics (age range, biological sex, payer, rurality). APCD contributors (payers) for whom both medical and pharmaceutical claims were unavailable were excluded from the analysis (e.g., Medicare Fee-For-Service (FFS)). Individual patients with missing demographic data (<2% of total claims) were also excluded. Monthly trends in individual parent payers from Medicaid, Medicare Advantage, and commercial were visually inspected to exclude those that had two or more consecutive months of missing data, extremely low claims volume, or erratic patterns were also

excluded. Rurality was classified using USDA Rural-Urban Commuting Area codes (i.e., RUCA 1-3 = non-rural; 4-10 = rural),[105] consistent with the Health Resources & Services Administration classifications.[106]

For this study, we defined low-value opioid prescriptions for acute LBP as non-cancer, non-sickle-cell-related acute LBP treated with opioids, similar to the definition used in previous studies.[66,83] We identified claims for opioid prescriptions occurring within 28 days of an evaluative visit with diagnosis codes for LBP and used the Milliman MedInsight Health Waste Calculator (HWC) (v. 7.2)[69] to categorize each prescription as low-value or clinically appropriate based on recommendations from medical and professional organizations (Tables S1-4).[2,51,57,68,77]

We calculated monthly and annual incidence rates of total, low-value, and clinically appropriate opioid prescriptions for acute LBP per 1000 patients in the overall cohort (2019-2021). Trends were visualized using monthly rates; however, the difference-in-differences (DiD) model and interaction plots used bi-monthly incidence, similar to methods used in other studies.[82,84]

Statistical Analysis

Descriptive statistics were calculated for the cohort. To examine trends in incidence of low-value opioid prescribing for acute LBP and the potential influence of the co-occurring COVID-19 pandemic between 2019-2021, we applied a heterogeneous DiD model to compare bi-monthly incidence of total and low-value opioid prescribing for acute LBP during the pandemic timeframe (March 1, 2020-December 31, 2021) with expected bi-monthly incidence based on the trend during the pre-pandemic timeframe (January 1, 2019–February 28, 2020). We used a

heterogeneous DiD model to account for variation in the influence of the pandemic timeframe. Bi-monthly incidence rates were modeled using adjusted-rate Poisson regression, stratified by rurality (primary) and payer (exploratory). We used a Poisson model because we were interested in the average change in incidence (count) of low-value opioid prescribing for acute LBP per 1000 patients in the population across 2019-2020, and between 2019 and 2020-2021. If we had examined the incidence of opioid prescriptions among only those who had a visit for acute LBP over this timeframe, then a binomial model may have been more appropriate since it would count incidence in a fixed number of opportunities to get an opioid prescription for acute LBP.[107] Incidence rate ratios (IRRs) were calculated from log-prescribing rates, adjusting for temporal trends (year, month-pair) and the demographic variables (age, biological sex, rurality, payer), which would reduce the influence of non-parallel trends between demographic groups or the timeframes compared. Since this work examines trends in healthcare delivery (e.g., opioid prescribing) during the timeframe that the COVID-19 pandemic started, we account for its potential influence with the DiD analysis by considering incidence in groups exposed to the timeframe (2020-2021) compared to a timeframe that did not contend with any pandemic policy or factor that could have impacted healthcare delivery (2019). For hypothesis a, we report the relative change in the annual observed and expected (model-predicted) opioid prescribing for acute LBP between 2019 and 2021. For hypothesis b, we report the difference between the expected trend (based on 2019) and the observed trend during the pandemic timeframe (2020-2021).

To explore demographic variation, the DiD effect (the influence of the pandemic timeframe) was allowed to vary by month-pair (e.g., March-April), rurality, and payer in the model, thereby

reducing the influence of non-parallel trends in each variable on results. Type III ANOVAs were used to assess the importance of each variable and interaction to the model, and the correlation information criterion was used to evaluate the model's fit.[108] Variation in pandemic influence on different populations was expected; thus, we included interactions for Rural x DiD, Payer x DiD, and Month-Pair x DiD. We also included Rural x Payer in alignment with our variables of interest and Rural x Sex because it improved model fit. The observed monthly trends for the 12-, 24-, and 36-month continuous enrollment cohorts across 2019-2021 were remarkably similar, so we did not conduct a formal sensitivity analysis.

We compared the incidence of total and low-value opioid prescribing for acute LBP, and the pandemic impact on low-value opioid prescribing for acute LBP between rural and non-rural areas. The IRR for the interaction between the DiD effect and rurality indicates if low-value opioid prescribing for acute LBP changed in a significantly different manner between rural patients and non-rural patients during the COVID-19 pandemic timeframe, compared to what we expected it to (i.e., how much low-value opioid prescribing for acute LBP changed in the pre-pandemic timeframe between rural and non-rural patients). For hypothesis c, we report on the difference between rural and non-rural incidence of low-value opioid prescribing for acute LBP throughout 2019 and 2021. For hypothesis d, we report whether the change in prescribing trend was greater in rural than in non-rural areas during the first two years of the pandemic, compared to 2019. For the exploratory analysis, we report payer-level incidence rate variations and difference in effect of the pandemic timeframe on incidence based on payer (Medicaid and MA to commercial). All statistical analyses were performed in R v.4.3.1, with a significance level of .05.

RESULTS

Our final cohort included 853,776 patients during 2019-2021 (mean age 59.0 years; 56.3% female; 11.6% rural; 13.6% Medicaid) (Table 1). Demographic characteristics remained stable throughout the study period, though the proportion of Medicaid patients increased from 9.4% in 2019 to 18.2% in 2021, reflecting, in part, Virginia's 2019 Medicaid expansion.[109] See flow diagram in Appendix (Figure S1).

Table 1. Demographic Composition of Cohort

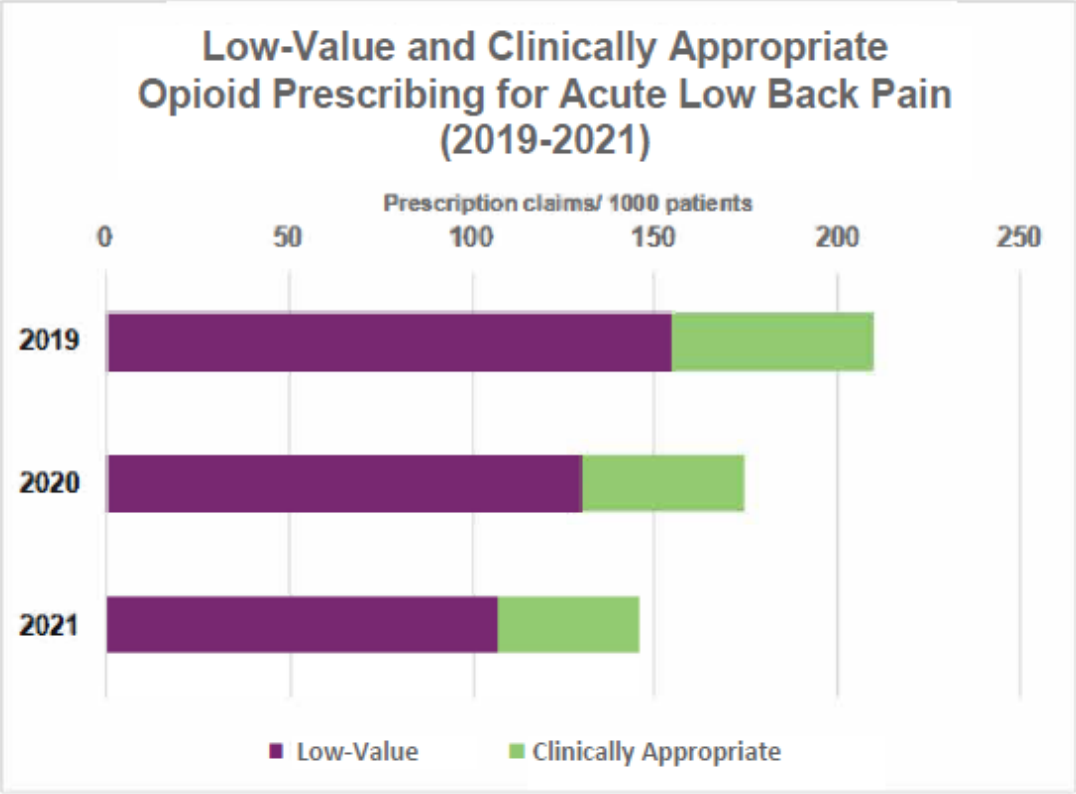
	Number of Patients (%)		
	2019	**2020**	**2021**
Characteristic	N = 832,084	N = 818,474	N = 910,769
Rurality			
Rural	96,359 (11.6)	98,690 (12.1)	102,414 (11.2)
Non-rural	735,725 (88.4)	719,784 (87.9)	808,355 (88.8)
Payer			
Commercial	311,741 (37.5)	274,036 (33.5)	302,991 (33.3)
Medicaid	78,280 (9.4)	109,184 (13.3)	165,662 (18.2)
Medicare Advantage	442,064 (53.1)	435,254 (53.2)	442,116 (49.5)
Age (Years)			
18-39	162,114 (19.5)	164,712 (20.1)	207,257 (22.8)
40-64	253,915 (30.5)	247,322 (30.2)	284,440 (31.2)
65-79	316,364 (38.0)	306,892 (37.5)	317,757 (34.9)
80+	99,691 (12.0)	99,548 (12.2)	101,315 (11.1)
Sex			
Female	470,304 (56.5)	461,076 (56.3)	512,326 (56.2)
Male	361,780 (43.5)	357,398 (43.7)	398,443 (43.8)

Trends in Total and Low-Value Opioid Prescribing for Acute LBP

Among 1,338,371 claims for opioids prescribed for acute LBP during 2019-2021, 989,056 (73.9%) were categorized as low-value (Table S5). At the onset of the COVID-19 pandemic (March-April 2020), total opioid prescribing (low-value plus clinically appropriate) for acute

LBP decreased from 189.1 prescriptions/1000 patients in January-February 2020 to 148.7 prescriptions/1000 patients in April-May 2020. Total and low-value opioid prescribing incidence rates returned to near pre-pandemic levels by October 2020 before declining throughout the rest of 2020 and 2021 (Figure 1 and S2).

Figure 1. Low-Value and Clinically Appropriate Opioids for Acute Low Back Pain (2019-2021)



While the total volume of opioid prescriptions for acute LBP decreased from 2019 to 2021, the proportion of prescriptions categorized as low-value remained at 73.3%-74.3% (Table S5). The relative change from the annual rate of low-value opioid prescribing for acute LBP in 2019 to the annual rate in 2021 was 30.6%. The relative change from the annual rate of low-value opioid prescribing for acute LBP in 2019 to the expected annual rate in 2021 was 18.6%. Moreover, our DiD analysis showed that the rate of low-value prescribing for acute LBP was 79.6% of expected

incidence during 2020-2021 (IRR: 0.80 [95% CI: 0.69-0.92], p<.001) (Table 2). See Table S6-S8 for complete model results for total, low-value, and clinically appropriate opioid prescribing for acute LBP. See Figures S3 and S4 for interactions between rurality and sex, and rurality and payer.

Table 2. Summary Table of Rate Regression Effects for Utilization of Opioids for Acute Low Back Pain in Virginia (2019-2021)

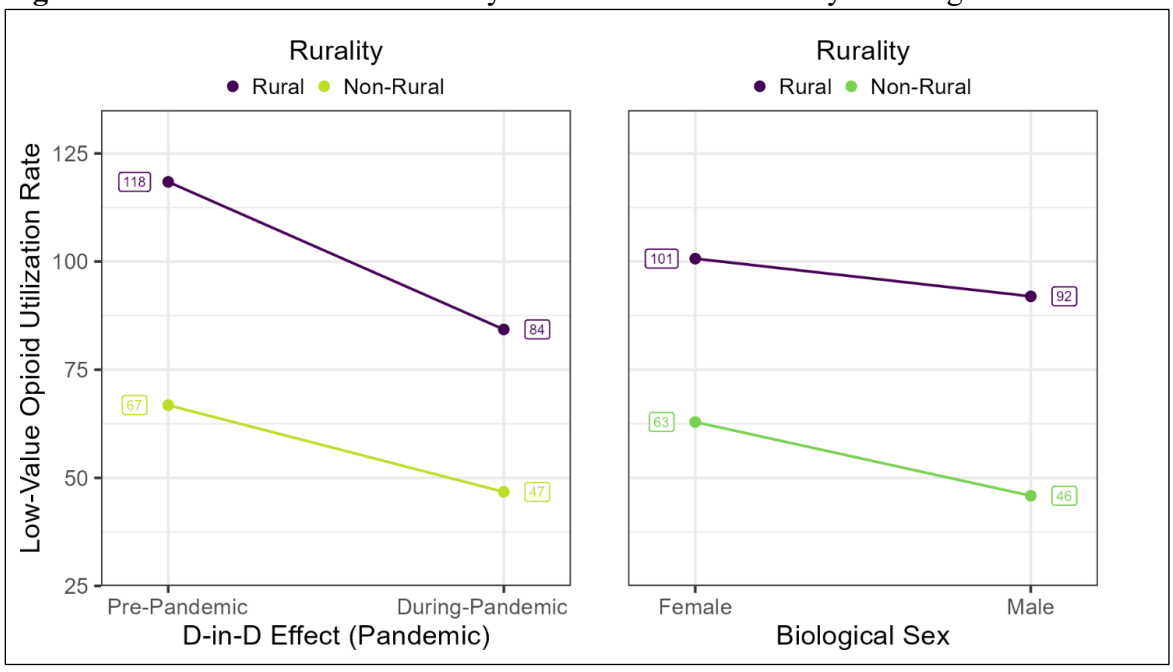
Term	***Total*** [a]	***Inappropriate*** [a]	***Clin. Appropriate*** [a]
DiD (False) vs.	1.0	1.0	1.0
DiD (True)	0.775 (0.672, 0.895)	0.796 (0.687, 0.921)	0.721 (0.619, 0.839)
Rurality (Non-Rural) vs. [b]	1.0	1.0	1.0
Rurality (Rural)	1.696 (1.247, 2.307)	1.738 (1.297, 2.329)	1.576 (1.167, 2.329)
DiD x Rurality (Non-Rural) vs. [c]	1.0	1.0	1.0
DiD x Rurality (Rural)	1.022 (0.961, 1.086)	1.017 (0.954, 1.085)	1.035 (0.962, 1.115)
Payer (Commercial) vs. [b]	1.0	1.0	1.0
Payer (Medicaid)	2.069 (1.581, 2.708)	1.992 (1.504, 2.639)	2.255 (1.727, 2.944)
Payer (Medicare Advantage)	4.951 (3.847, 6.370)	5.268 (4.104, 6.762)	4.085 (3.100, 5.384)
DiD x Payer (Commercial) vs. [c]	1.0	1.0	1.0
DiD x Payer (Medicaid)	0.554 (0.484, 0.635)	0.552 (0.477, 0.639)	0.562 (0.470, 0.671)
DiD x Payer (Medicare Advantage)	1.201 (1.075, 1.342)	1.195 (1.068, 1.337)	1.218 (1.059, 1.401)
Rurality x Payer (Commercial) vs. [d]	1.0	1.0	1.0
Rurality x Payer (Medicaid)	0.985 (0.671, 1.444)	1.012 (0.693, 1.478)	0.928 (0.595, 1.446)
Rurality x Payer (MA	0.754 (0.557, 1.021)	0.747 (0.561, 0.994)	0.774 (0.523, 1.1440
Rurality x Sex (F) vs. [d]	1.0	1.0	1.0
Rurality x Sex (M)	1.216 (1.073, 1.379)	1.253 (1.097, 1.431)	1.253 (1.097, 1.431)

[a] Incidence rate ratios for total, inappropriate, and clinically appropriate opioid prescriptions per 1000 patients per variable represent the cumulative difference in observed rates from expected rates.
[b] Rurality and payer represent the pre-pandemic (unexposed) timeframe (January 2019 - February 2020) to December 31, 2021, because interactions with DiD are present.
[c] DiD x Payer and DiD x Rurality; DiD represents the rate difference between model-predicted, pre-pandemic-based expected rates (representing what rates would have been had the pandemic not happened) and the during-pandemic timeframe (March 2020-December 2021)(representing rates during the exposure), or the interaction (effect of pandemic timeframe) on rates in each variable compared to in a reference variable.
[d] Rurality x Payer represents the difference in rural/non-rural rates between commercial and other payers. Rurality x Sex represents the difference in rural/non-rural rates in males compared to females.

Rural Variation

During 2019-2021, total prescribing of opioids for acute LBP was higher in rural versus non-rural areas (IRR: 1.70 [95% CI: 1.25, 2.31], p<.001) (Table 2). Throughout 2019 and 2021, 76.0% of opioids prescribed for acute LBP in rural areas were categorized as low-value versus 73.3% in non-rural areas (Table S9). Low-value prescribing incidence was 0.74 times higher (or 73.8% greater) in rural versus non-rural areas (IRR: 1.74 [95% CI: 1.30-2.64], p<.001). The rural to non-rural difference in low-value opioid prescribing incidence for acute LBP was unaffected by the pandemic (IRR: 1.02 [95% CI: 0.95-1.09], p=.060) (Table 2 and Figure 2). Similarly, clinically appropriate opioid prescribing incidence for acute LBP was 0.58 times higher in rural areas compared to non-rural areas (IRR: 1.58 [95% CI: 1.17-2.33], p=.022); the rural to non-rural difference in clinically appropriate opioid prescribing for acute LBP was not significantly influenced by the pandemic (IRR: 1.04 [95% CI: 0.96-1.12], p=.354).

Figure 2. Interaction Plots for Rurality x DiD Effect and Rurality x Biological Sex

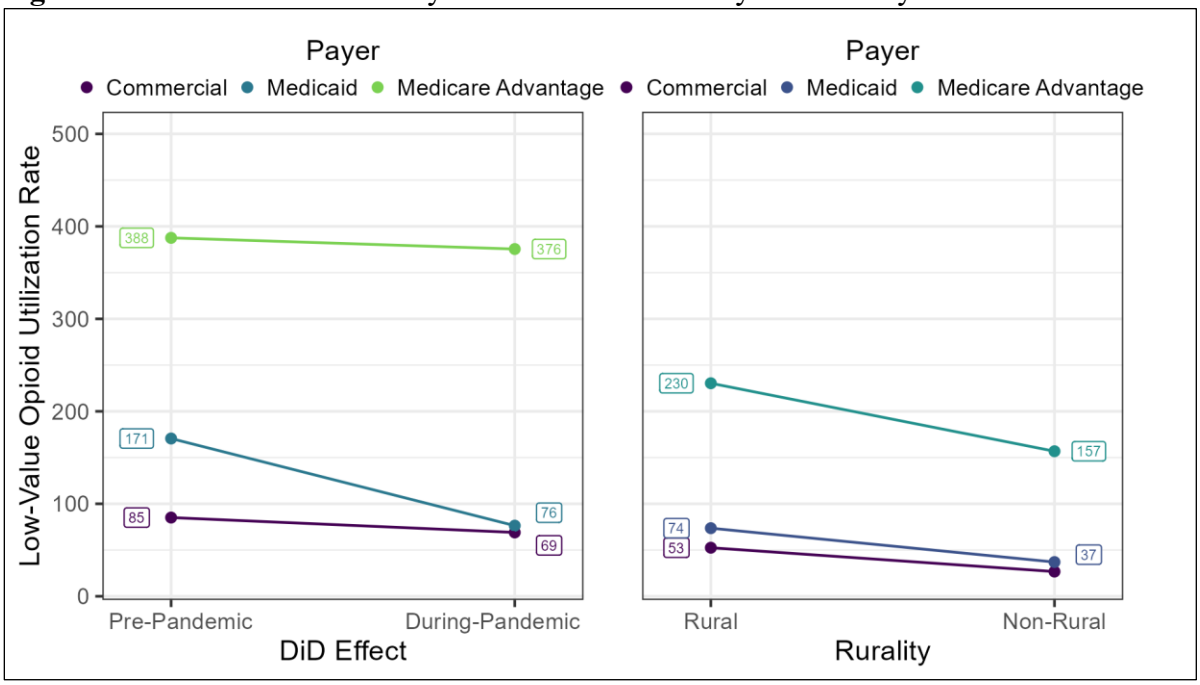


Note. The rate refers to prescriptions per 1000 patients.

Payer Variation

During 2019-2021, 70.6% of Medicaid, 74.3% of MA, and 73.3% of commercial claims for acute LBP were categorized as low-value (Table S9). The rate of low-value opioid prescribing for acute LBP was significantly higher for both Medicaid and MA patients compared to commercial throughout 2019–2021 (IRR: 1.99 [95% CI: 1.50-2.64], p<.001; IRR: 5.27 [95% CI 4.10, 6.76], p<.001, respectively) (Table 2). Prescribing low-value opioids for acute LBP declined across all payers relative to expected incidence during the pandemic. The observed versus expected low-value opioid prescribing for acute LBP in Medicaid was 0.45 times lower than in commercially insured patients (IRR: 0.55 [95% CI: 0.48-0.64], p<.001), while observed versus expected low-value opioid prescribing for acute LBP among patients covered by MA was 0.20 times higher than in commercially insured patients (IRR: 1.20 [95% CI: 1.07-1.34], p=.002) (Table 2 and Figure 3).

Figure 3. Interaction Plots for Payer x DiD Effect and Payer x Rurality



Note. The rate refers to prescriptions per 1000 patients.

Clinically appropriate opioid prescribing for acute LBP was significantly higher in both Medicaid and MA patients compared to commercial throughout 2019–2021 (IRR: 2.26 [95% CI: 1.73-2.94], p<.001; IRR: 4.09 [95% CI: 3.10-5.38], p<.001, respectively) (Table 2). The observed versus expected incidence of clinically appropriate opioids for acute LBP in Medicaid was 0.44 times lower than in commercially insured patients (IRR: 0.56 [95% CI: 0.47-0.67], p<.001), while observed versus expected clinically appropriate prescribing among patients covered by MA was 0.22 times higher than in commercially insured patients (IRR: 1.22 [95% CI: 1.06-1.40], p=.006) (Table 2).

DISCUSSION

This retrospective study of more than 850,000 Virginia patients identified a steady pre-pandemic decline in low-value opioid prescribing for acute LBP, an overall 30.8% decline between 2019 and 2020, and an accelerated decline during the pandemic period compared with pre-pandemic rates. There was a rural disparity in low-value opioid prescribing for acute LBP (73.8% higher incidence than non-rural) across 2019-2021. The decline in low-value opioid prescribing for acute LBP is encouraging, yet the results of this study also indicate persistent inequities that warrant targeted attention in future efforts to improve acute pain care. This work highlights future research opportunities and important considerations that may inform tailored interventions, such as improving access to buprenorphine prescribers, enhancing pain management education for clinicians, and expanding telehealth services to ensure equitable care and mitigate opioid-related risks, particularly in rural areas.

We hypothesized that the incidence of low-value opioid prescribing for acute LBP would decline, and to a lesser extent than expected incidence, as certain low-value opioid prescribing for acute pain incidence rates have not declined proportionally to overall incidences up to 2018.[68,77] Our analysis found that total opioid prescribing for acute LBP declined in 2019. While the utilization of other low-value services during the pandemic generally rebounded to pre-pandemic levels or above,[83,103] our analysis revealed that low-value opioid prescribing for acute LBP rebounded to near pre-pandemic levels but then continued to decline. Differences between low-value service trends may be due to the influence of pandemic-related contextual factors on clinical decision making. This further contrasts with increases seen in opioid prescribing for acute pain in Lee et al., and low-value opioid prescribing for back pain and headaches in Levine et al.[94,98] The decline in low-value opioid prescribing for acute LBP was greater throughout the first two years of the pandemic than in 2019. The observed decline in low-value opioid prescribing for acute LBP during the pandemic timeframe could be due to changes in patient care-seeking behaviors (e.g., not seeking care), changes in how healthcare of delivered (e.g., telemedicine, in-person visit limitation for certain services), or changes in clinician prescribing behavior, as was suggested for other health services.[2,38] The decline in low-value opioid prescribing for acute LBP from 2019 to 2021 is promising, but it remains essential to understand whether these patterns reflect real and sustained improvements in the value of care for acute pain. One unexpected finding was that the rate of clinically appropriate opioid prescribing for acute LBP also declined during the pandemic, which warrants a closer look into the potential implications.

Rural Variation

This is the first study to identify disparate incidence of low-value opioid prescribing for acute LBP across healthcare settings in a large multi-payer cohort. We hypothesized that the low-value opioid prescribing for acute LBP would be higher in rural areas, as it is known that overall opioid prescribing is greater in rural areas, wherein distance to care, poverty, and social isolation contribute to underutilization of safer pain treatment.[27,28,31,110] Rockwell et al. reported similar rural disparity in incidence of high-risk non-steroidal anti-inflammatory drugs for pain in Virginia during the pandemic, and highlighted that ensuring safer options for treating pain go beyond just non-opioid treatments for those with certain chronic health conditions.[82] However, a greater incidence of inappropriate prescribing of NSAIDS for those with chronic kidney disease, hypertension, or heart failure in rural areas highlights that there can be unintended consequences of reducing opioid prescribing without efforts to ensure that the alternatives don't also cause harm. Rural-specific drivers may include limited access to alternative pain treatments, broadband, and provider shortages.[27,28,97] The lack of the hypothesized differential pandemic impact on rural versus non-rural incidence of low-value opioid prescribing for acute LBP is encouraging in that there was a similar decline regardless of rurality and that the pandemic did not exacerbate the disparity. However, significantly greater low-value opioid prescribing for acute LBP in rural than non-rural areas is concerning because of the risks associated. The rural disparity in low-value opioid prescribing for acute LBP may indicate an opportunity to focus on reducing the reliance on prescription opioids and increasing the use of safer treatments for acute pain in rural areas.

Payer Variation

Our additional analysis of payer variation showed that opioid prescribing for acute LBP was higher in Medicaid and MA than in commercial payers during 2019-2021. These results are not surprising since a higher incidence of low-value opioid prescribing for acute LBP has been documented in Medicare programs.[77,111] Mafi et al. showed that low-value opioid prescribing for acute LBP was 182.1 per 1000 in Medicare FFS in 2018, whereas the rate was 287 per 1000 in MA in our cohort in 2019.[112] The incidence of low-value opioid prescribing for acute LBP declined across all payers, but the impact of the pandemic differed between them. The payer-level variation in pandemic impact on low-value opioid prescribing for acute LBP could be due to differences in limiting factors, such as access to safer options or care-seeking behaviors of the patients covered.[86] Payer-level variations related to low-value opioid prescribing for acute LBP may also be influenced by differences in the covered population's characteristics or the payer programs that encourage use of higher-value services.[113,114] Patient utilization, payer policies, and limiting factors should be considered when exploring how to further reduce low-value opioid prescribing for acute LBP and facilitate greater utilization of safer acute pain treatment options, particularly in rural areas. Medicaid expansion in Virginia started in 2019.[109] In our cohort, the number of Medicaid beneficiaries increased as low-value opioid prescribing for acute LBP decreased. The increase in the volume of patients covered by Medicaid may have influenced access to or utilization of care during the study timeframe.

Other factors may contribute to the difference in pandemic impact on low-value and clinically appropriate opioid prescribing. For example, telemedicine expanded exponentially during the pandemic, and the amount of opioid prescribing via telemedicine fluctuated with policy changes.[115,116] Temporary allowances via telemedicine caused some confusion in relation

to clinical guidelines for in-person evaluation; however, it appeared to allow for continuity in care for those with chronic pain.[95] Further work is needed to understand the effect of allowances for opioid prescribing for acute pain via telemedicine, media attention on the opioid overdose during the pandemic, or discussions on the changes in prescribing policy during the pandemic impacted rates.

Limitations

One strength of using a heterogeneous DiD design for observational data is the ability to estimate the impact of a policy or intervention when an experimental approach is not possible. This approach allowed comparison of what low-value opioid prescribing for acute LBP would have looked like in the absence of the pandemic, while accounting for differences across cohorts (e.g., demographics) and covarying pandemic impact across multiple variables to isolate differential effects on subgroups of the population. We acknowledge limitations to our study. First, APCD claims do not represent all patients in Virginia (e.g., uninsured, and some commercial patients), and Medicare Fee-for-Service and dual-eligible patients were excluded due to the inaccessibility of Part D medication claims. Our cohort included approximately 15% of insured adults across Virginia from three major payer classes. Given Virginia's population and geographic diversity, we expect the results to be generalizable within and beyond Virginia. Second, the HWC algorithms may not capture all clinical nuances that could affect the categorization of a particular claim, such as the use of non-pharmacological therapies. Therefore, future work could consider additional ICD codes and alternative algorithms to better capture the clinical strategies that may be appropriate. Third, we analyzed the number of filled opioid prescriptions, which may not have detected significant variations in clinician prescribing patterns (e.g., changes in dose or days'

supply). For example, Lee et al. reported that the days' supply of opioid prescriptions for chronic or acute pain may have increased during this timeframe. Lastly, there are limitations to the DiD analysis.

The increase in volume of Medicaid beneficiaries during our study period and the declining incidence of opioids prescribed for acute LBP observed pre-pandemic limited our ability to isolate the impact of the pandemic. To mitigate this limitation, our DiD model accounted for the population shift and pre-pandemic prescribing rates. While the greatest proportion of our sample is from MA, our model isolated the effect of individual payers. The overrepresentation of MA claims among our cohort may have inflated the overall incidence of low-value opioid prescribing for acute LBP. The average incidence among the cohort may have been different if there had been more representation from other payers or younger populations. We did not formally assess for non-parallel trends, but we accounted for differences by including time (e.g., year and month-pair) and demographics (e.g., rural) in the model. While trends in each outcome across 2019-2021 in the 12-, 24-, and 36-month continuous enrollment cohorts were visually similar, we did not conduct a sensitivity analysis. Also, large sample sizes can lead to being overpowered, making slight differences statistically significant but not necessarily clinically significant. Given the cascading harms for patients and the healthcare system associated with this low-value service, any avoided utilization is meaningful. These DiD related limitations may have influenced the results and should be considered and discussed in future research.

Future Directions

The reasons for the accelerated pandemic-era decline, the higher rural rates, and the lack of change in the rural–non-rural gap are unknown. Expanding the timeframe of study beyond 2021 is needed to determine whether the pandemic-related declines in low-value opioid prescribing for acute LBP are sustained beyond our study timeframe, as well as whether the declines reflect improved prescribing practices or other systemic factors. In the future, qualitative or mixed-methods research could identify specific social, economic, and healthcare system factors for low-value opioid prescribing for acute pain (e.g., physician bias, lack of alternative pain management resources). Also, examining if reductions in low-value opioid prescribing for acute LBP occur simultaneously with the increase in the use of higher-value treatments of acute pain LBP could reveal further target gaps in care and inform what interventions are needed to address them.

Although we did assess the incidence of clinically appropriate prescribing in line with professional guidelines during the pandemic, our analysis was not set up to directly compare low-value to clinically appropriate prescribing incidence. The first criterion for categorizing a prescription as clinically appropriate was whether the patient had cancer and sickle-cell disease. Since the incidence of these two conditions is unlikely to shift significantly during this timeframe, changes in their identification could be explored as a reason for a decline in clinically appropriate prescriptions.[117] If clinically appropriate opioid prescribing for acute LBP had instead increased compared to low-value rates, it may have suggested a shift towards increasing attempts to trial non-opioid medications first before the use of opioids. However, we did not measure the alternative or concurrent use of non-pharmacological options. Future research exploring how often these various treatment combinations occur will be important for understanding how the quality of acute pain treatment has changed over time.

In the future, more work is needed to understand rural drivers of low-value opioid prescribing. The inclusion of more payers and estimation of low-value opioid prescribing for acute pain among the uninsured in rural areas versus non-rural areas may yield important insights concerning rural variation in low-value opioid prescribing for acute pain. Additional work is needed to explore factors that would influence rural variation in the utilization of the higher-value treatments for acute pain to inform future efforts to de-implement low-value opioid prescribing for acute LBP. Future interventions focused on addressing rural disparity in incidence of low-value opioid prescribing for acute pain and the associated harm could include expanded reimbursement for physical therapy, integrated behavioral health, or rural telehealth services (e.g., physical therapy, behavioral health).

Future work could extend the examination of the trend in low-value opioid prescribing in Medicaid to determine if the decrease in incidence observed in Medicaid during the pandemic eased through 2025 or remained. If there is a loss in funding for Medicaid programs in Virginia, it would be expedient to examine whether the rate of low-value opioid prescribing for acute LBP increases, as this may point to a greater impact of Medicaid expansion on rate change during the pandemic timeframe than the pandemic itself. It may also highlight the value of such coverage. A decline in low-value opioid prescribing for acute LBP in all payers suggests an essential trend in the desired direction for reducing low-value care, but it remains critical to link this change to patient outcomes and healthcare cost savings.

Conclusion

Opioid prescribing for acute pain is associated with multi-level risks of harm and is not recommended in most acute pain scenarios. The decline in low-value opioid prescribing for acute LBP is encouraging, but further work is needed to determine if this decline coincides with increases in higher-value care. Pandemic-related factors contributed to declines in low-value opioid prescribing for acute LBP, but continued monitoring would determine their long-term impact. Persistent rural disparity in low-value opioid prescribing for acute LBP warrants further studies to explore its drivers to inform efforts to reduce the incidence of low-value opioid prescribing and ensure equitable, high-quality acute pain treatment because of the risks of opioid prescribing.

Chapter 3

This thesis examined low-value opioid prescribing for acute LBP in a large Virginia cohort from 2019 through 2021 using claims data from the Virginia ACPD and the Milliman MedInsight HWC. The primary goal was to describe trends in the incidence of low-value opioid prescribing for acute LBP, evaluate how the COVID-19 pandemic influenced these trends, and examine variation in the low-value opioid prescribing for acute LBP and pandemic impact in rural versus non-rural patients. The results of this study may inform further work to improve patient safety, mitigate opioid-related harms, reduce health disparities, and improve health equity in the delivery of high-quality care.

Aim 1 was to describe trends in the incidence of low-value opioid prescribing for acute LBP among a large multi-payer Virginia cohort during 2019-2021. Total opioid prescribing for acute LBP declined during the study period; low-value prescribing declined proportionally. However, approximately three-quarters of the opioids that were prescribed for acute LBP were inconsistent with evidence-based guidelines for acute LBP management (i.e., low-value). The results of this study align with national evidence showing ongoing declines in opioid prescribing.[14,15] The pattern in low-value opioid prescribing for acute LBP may signal a disconnect between guideline dissemination and clinical practice, among other factors. Among the cohort, 1,338,371 claims for opioids for acute LBP were identified, of which approximately 989,056 (74%) were low-value. While there appears to be improvements in low-value prescribing patterns, any excess opioid prescribing inconsistent with guidelines is concerning, given avoidable harms and lack of use of

safer alternatives. Therefore, greater efforts are needed to improve patient safety in the treatment of acute pain.

Aim 2 was to evaluate the impact of the COVID-19 pandemic timeframe on low-value opioid prescribing for acute LBP among a large multi-payer Virginia cohort. The heterogeneous difference-in-differences analysis revealed that the COVID-19 pandemic timeframe was associated with accelerated declines in low-value opioid prescribing for acute LBP compared with pre-pandemic trends. The pandemic accelerated a downward trajectory in low-value opioid prescribing for acute LBP. The decline in low-value opioid prescribing for acute LBP may be due to the limited access to non-opioid and non-pharmacological treatments for acute pain during the pandemic; however, it remains to be explored as to what specific factors influenced a greater decline during the pandemic. The observed decline in opioid prescribing for acute LBP may point to the success of efforts to reduce the low-value opioid prescribing for acute pain; in addition, contextual factors during the COVID-19 pandemic timeframe served to enhance the reduction in low-value opioid prescribing for acute LBP pain.

Aim 3 was to assess rural variation in low-value opioid prescribing for acute LBP among a large multi-payer Virginia cohort during 2019-2021. Rural patients had a higher incidence of low-value opioid prescribing for acute LBP than patients in non-rural areas. This rural disparity in low-value opioid prescribing for acute pain in our cohort likely reflects many contributing factors, including provider uncertainty or limited visit time, particularly in rural or under-resourced communities.[7,118,119] A higher burden of chronic disease, limited access to non-opioid pain management options, and longer travel distances to specialty care also likely contribute to

rural differences.[7,31,120,121] This warrants further work to identify how to address the rural disparity in low-value opioid prescribing for acute LBP. Greater low-value opioid prescribing for acute pain in rural areas is concerning given the associated cascades of harm, including exacerbation of health disparities and the additional vulnerabilities related to mitigating opioid-related harms, such as less access to opioid use disorder and provision of mental health services in these areas.

Aim 4 was to assess rural variation in the impact of the COVID-19 pandemic timeframe on low-value opioid prescribing for acute LBP among a large multi-payer Virginia cohort. The finding that the pandemic timeframe did not shift rural variation in low-value opioid prescribing for acute LBP may highlight certain structural and contextual influences that shape opioid use patterns within the cohort. The lack of a differential pandemic timeframe influence indicates that targeted rural strategies, not general healthcare disruptions, are necessary to address persistent disparities in low-value opioid prescribing.

Future Directions

This study identified that low-value opioid prescribing for acute LBP improved in a large Virginia cohort. Extending this analysis beyond 2021 will help determine whether observed pandemic-era reductions in total and low-value opioid prescribing for acute LBP represent sustained progress or short-term effects. Continued monitoring using APCD data will also allow for the assessment of evidence on the long-term effectiveness of opioid stewardship policies and effectiveness of other de-implementation efforts.

Further research should examine the impact of policy changes, clinical education programs, or telemedicine expansion of non-opioid options for acute pain treatment on low-value opioid prescribing for acute LBP at the state level. Further work should establish if the decline in low-value opioid prescribing for acute LBP coincides with increases in higher-value acute pain treatments because this is essential to maximize patient benefit. Also, further examination of the decline in low-value opioid prescribing patterns for acute LBP should explore if they translate to improved patient outcomes, such as less long-term prescription opioid therapy, OUD, or hospital utilization, to quantify the broader public health implications of low-value care.

Examination of the incidence of low-value opioid prescribing for acute LBP at the population-level revealed rural variation, pointing to demographic and systematic factors. Future research should aim to examine individual-level differences to isolate the specific drivers of differences and risks related to rural variations in the incidence of low-value opioid prescribing for acute LBP to inform interventions to optimize prescribing. Future interventions focused on addressing rural disparity in low-value opioid prescribing for acute pain could include expanded reimbursement for physical therapy or other non-pharmacological alternative interventions, integrated behavioral health, or relevant rural telehealth services.

Conclusion

This thesis demonstrates that low-value opioid prescribing for acute LBP in a large Virginia cohort has declined overall during 2019-2021. The COVID-19 pandemic accelerated the decline in low-value opioid prescribing for acute LBP but did not change the underlying rural disparity. Ensuring that efforts such as opioid stewardship programs and de-implementation initiatives are

equitably implemented across populations and geographic areas is essential. In this context, continued reductions in low-value opioid prescribing for acute LBP may indicate progress toward safer pain management, but achieving population-level benefit will likely require targeted strategies to ensure that rural patients have comparable access to high-value, guideline-concordant care.

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Appendix

Table S1. Oral Opioids Included in the Analysis

Opioid Name	Example Brand Name
buprenorphine	Subutex, Suboxone
codeine	Tylenol/Codeine, Fiorinal/Codeine
dihydrocodeine	Panlor SS, Synalgos-DC
fentanyl	Duragesic, Actiq
hydrocodone	Vicodin, Norco, Lortab
hydromorphone	Dilaudid, Exalgo
levorphanol	Levo-Dromoran
meperidine	Demoral
methadone	Methadose
morphine	MS Contin, Kadian, Embeda
oxycodone	OxyContin, Percocet, Roxicodone
oxymorphone	Opana, Numorphan
propoxyphene	Darvon, Darvocet
sufentanil	Sufenta
tapentadol	Nucynta
tramadol	Ultram, ConZip, Ryzolt

All forms and combinations of the named medications were identified with claims data.

Table S2. Diagnosis Codes for Cancers and History of Cancers

Cancers	ICD-10
Malignant neoplasms	C00.0, C00.1, C00.2, C00.3, C00.4, C00.5, C00.6, C00.8, C00.9, C01, C02.0, C02.1, C02.2, C02.3, C02.4, C02.8, C02.9, C03.0, C03.1, C03.9, C04.0, C04.1, C04.8, C04.8.8C049, C05.0, C05.1, C05.2, C05.8, C05.9, C06.0, C06.1, C06.2, C06.80, C06.89, C06.9, C07, C07.8, C07.80, C08.0, C08.0.0, C08.1, C08.9, C09.0, C09.1, C09.8, C09.9 C10.0, C10.1, C10.2, C10.3, C10.4, C10.8, C10.9, C11.0, C11.1, C11.2, C11.3, C11.8, C11.9, C12, C13.0, C13.1, C13.2, C13.8, C13.9, C14.0, C14.2, C15.3, C15.4, C15.5, C15.8, C15.9, C16.0, C16.1, C16.2, C16.3, C16.4, C16.5, C16.6, C16.8, C16.9, C17.0, C17.1, C17.2, C17.8, C17.9, C18.0, C18.1, C18.2, C18.3, C18.4, C18.5, C18.6, C18.7, C18.8, C18.9, C19, C20, C21.0, C21.1, C21.2, C21.8, C22.8, C22.9, C23, C23.1, C24.0, C24.1, C24.8, C24.9, C25.0, C25.1, C25.2, C25.3, C25.4, C25.7, C25.8, C25.9, C26.0, C26.1, C26.9, C27.0, C27.1, C27.2, C27.3, C27.8, C27.9, C28.0, C28.1, C28.2, C28.3, C28.4, C28.5, C28.6, C28.7, C28.8, C28.9, C29.0, C29.1, C29.2 C41.0, C41.1, C41.2, C41.3, C41.4, C41.9, C44.00, C44.09, C44.100, C44.101, C44.102, C44.109, C44.191, C44.192, C44.199, C44.201, C44.202, C44.209, C44.291, C44.292, C44.299, C44.300, C44.301, C44.309, C44.390, C44.391, C44.399, C44.40, C44.49, C44.500, C44.501, C44.509, C44.590, C44.591, C44.599, C44.601, C44.602, C44.609, C44.691, C44.692, C44.699, C44.701, C44.702, C44.709, C44.791, C44.792, C44.799, C44.80, C44.89, C44.90, C44.99, C47.0, C47.20, C47.21, C47.22, C47.3, C47.4, C47.5, C47.6, C47.9, C48.0, C48.1, C48.2, C48.8, C49.3, C49.4, C49.5, C49.6, C49.8, C49.9 C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.212, C50.219, C50.221, C50.222, C50.229, C50.312, C50.319, C50.321, C50.322, C50.329, C50.412, C50.419, C50.421, C50.422, C50.429, C50.512, C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929, C51.0, C51.1, C51.2, C51.8, C51.9, C52, C53.0, C53.1, C53.8, C53.9, C54.0, C54.1, C54.2, C54.3, C54.8, C54.9, C55, C56.1, C56.2, C56.9, C57.00, C57.01, C57.02, C57.10, C57.11, C57.12, C57.20, C57.21, C57.22, C57.30, C57.31, C57.32, C57.40, C57.41, C57.42, C57.50, C57.51, C57.52, C57.60, C57.61, C57.62, C57.80, C57.81, C57.82, C57.90, C57.91, C57.92, C61, C62.00, C62.01, C62.02, C62.10, C62.11, C62.12, C62.90, C62.92, C63.00, C63.01, C63.02, C63.10, C63.11, C63.12, C63.20, C63.7, C63.8, C63.9, C64.1, C64.2, C64.9, C65.1, C65.2, C65.9, C66.1, C66.2, C66.9, C67.0, C67.1, C67.2, C67.3, C67.4, C67.5, C67.6, C67.7, C67.8, C67.9, C68.0, C68.1, C68.8, C68.9, C69.00, C69.01, C69.02, C69.10, C69.11, C69.12, C69.20, C69.21, C69.22, C69.30, C69.31, C69.32, C69.40, C69.41, C69.42, C69.50, C69.51, C69.52, C69.60, C69.61, C69.62, C69.80, C69.81, C69.82, C69.90, C69.91, C69.92, C7B, C70.0, C70.1, C70.9, C71.0, C71.1, C7.12, C7.13, C71.4,

	C71.5, C71.6, C71.7, C71.8, C71.9, C72.0, C72.1, C72.20, C72.21, C72.22, C72.30, C72.31, C72.32, C72.40, C72.41, C72.42, C72.50, C72.59, C72.9, C73, C74.00, C74.01, C74.02, C74.10, C74.11, C74.12, C74.90, C74.91, C74.92, C75.0, C75.1, C75.2, C75.3, C75.4, C75.5, C75.8, C75.9, C76.0, C76.1, C76.2, C76.3, C76.40, C76.41, C76.42, C76.50, C76.51, C76.52, C76.8, C77.0, C77.1, C77.2, C77.3, C77.4, C77.5, C77.8, C77.9, C78.00, C78.01, C78.02, C78.1, C78.2, C78.30, C78.39, C78.4, C78.5, C78.6, C78.7, C78.80, C78.89, C79.00, C79.01, C79.02, C79.10, C79.11, C79.19, C79.2, C79.31, C79.32, C79.40, C79.49, C79.51, C79.52, C79.60, C79.61, C79.62, C79.70, C79.71, C79.72, C79.81, C79.82, C79.89, C79.9, C80.0, C80.1, C80.2, C96.20, C9.629, Z85.00, Z85.01, Z85.028, Z85.038, Z85.05, Z85.068, Z85.07, Z85.09, Z85.118, Z85.12, Z85.20, Z85.21, Z85.238, Z85.3, Z85.41, Z85.42, Z85.43, Z85.44, Z85.46, Z85.47, Z85.48, Z85.49, Z85.51, Z85.528, Z85.53, Z85.54, Z85.59, Z85.810, Z85.828, Z85.830, Z85.831, Z85.840, Z85.841, Z85.848, Z85.850, Z85.858, Z85.89, Z85.9, Z86.000, Z86.001, Z86.008, Z86.003.
Melanomas	C43.0, C43.10, C43.11, C43.12, C43.20, C43.21, C43.22, C43.30, C43.31, C43.39, C43.4, C43.51, C43.52, C43.59, C43.60, C43.61, C43.62, C43.70, C43.71, C43.72, C43.8, C43.9, D03.0, D03.10, D03.11, D03.12, D03.20, D03.21, D03.22, D03.30, D03.39, D03.4, D03.51, D03.52, D03.59, D03.60, D03.61, D03.62, D03.70, D03.71, D03.72, D03.8, D03.9, Z85.820
Sarcomas	C22.3, C22.4, C46.0, C46.1, C46.2, C46.3, C46.4, C46.50, C46.51, C46.52, C46.7, C46.9, C92.30, C92.31, C92.32, C96.22, C96.4, C96.A
Lymphomas	C84.Z, C85.9, C81.00, C81.02, C81.03, C81.06, C81.07, C81.08, C81.10, C81.12, C81.13, C81.16, C81.17, C81.18, C81.20, C81.22, C81.23, C81.26, C81.27, C81.28, C81.30, C81.32, C81.33, C81.36, C81.37, C81.38, C81.40, C81.41, C81.42, C81.43, C81.44, C81.46, C81.47, C81.48, C81.49, C81.70, C81.71, C81.72, C81.73, C81.74, C81.75, C81.76, C81.77, C81.78, C81.79, C81.90, C81.91, C81.92, C81.93, C81.94, C81.95, C81.96, C81.97, C81.98, C81.99, C82.00, C82.01, C82.02, C82.03, C82.04, C82.06, C82.07, C82.08, C82.09, C82.10, C82.11, C82.12, C82.13, C82.14, C82.16, C82.17, C82.18, C82.19, C82.20, C82.22, C82.23, C82.26, C82.27, C82.28, C82.30, C82.31, C82.32, C82.33, C82.34, C82.36, C82.37, C82.38, C82.39, C82.40, C82.41, C82.42, C82.43, C82.44, C82.46, C82.47, C82.48, C82.49, C82.50, C82.52, C82.53, C82.56, C82.57, C82.58, C82.60, C82.61, C82.62, C82.63, C82.64, C82.66, C82.67, C82.68, C82.69, C82.80, C82.82, C82.83, C82.86, C82.87, C82.88, C82.90, C82.91, C82.92, C82.93, C82.94, C82.95, C82.96, C82.97, C82.98, C82.99, C83.00, C83.01, C83.02, C83.03, C83.04, C83.06, C83.07, C83.08, C83.09, C83.10, C83.11, C83.12, C83.13, C83.14, C83.15, C83.16, C83.17, C83.18, C83.19, C83.30, C83.31, C83.32, C83.33, C83.36, C83.37, C83.38, C83.39, C83.50, C83.51, C83.52, C83.53, C83.54, C83.55, C83.56, C83.57, C83.58, C83.59, C83.70, C83.71, C83.72, C83.73,

	C83.74, C83.75, C83.76, C83.77, C83.78, C83.79, C83.80, C83.81, C83.82, C83.83, C83.84, C83.85, C83.86, C83.87, C83.88, C83.89, C83.90, C83.91, C83.92, C83.93, C83.94, C83.96, C83.97, C83.98, C83.99, C84.40, C84.42, C84.43, C84.46, C84.47, C84.48, C84.60, C84.62, C84.63, C84.66, C84.67, C84.68, C84.70, C84.72, C84.73, C84.76, C84.77, C84.78, C84.90, C84.92, C84.93, C84.96, C84.97, C84.98, C84.A0, C84.A1, C84.A2, C84.A3, C84.A4, C84.A6, C84.A7, C84.A8, C84.A9, C84.Z0, C84.Z2, C84.Z3, C84.Z6, C84.Z7, C84.Z8, C85.10, C85.11, C85.12, C85.13, C85.14, C85.15, C85.16, C85.17, C85.18, C85.19, C85.20, C85.22, C85.23, C85.26, C85.27, C85.28, C85.80, C85.82, C85.83, C85.86, C85.87, C85.88, C85.90, C85.91, C85.92, C85.93, C85.94, C85.95, C85.96, C85.97, C85.98, C85.99, C86.0, C86.1, C86.2, C86.3, C86.4, C86.5, C91.51, C91.52, Z8571, Z8572,
Leukemias	C90.10, C90.11, C90.12, C91.00, C91.01, C91.02, C91.11, C91.12, C91.30, C91.31, C91.32, C91.40, C91.41, C91.42, C91.60, C91.61, C91.62, C91.90, C91.91, C91.92, C91.A0, C91.A1, C91.A2, C91.Z0, C91.Z1, C91.Z2, C92.00, C92.01, C92.02, C92.11, C92.12, C92.21, C92.22, C92.40, C92.41, C92.42, C92.50, C92.51, C92.52, C92.60, C92.61, C92.62, C92.90, C92.91, C92.92, C92.A1, C92.A2, C92.Z0, C92.Z1, C92.Z2, C93.00, C93.01, C93.02, C93.10, C93.11, C93.12, C93.30, C93.31, C93.32, C93.90, C93.91, C93.92, C93.Z0, C93.Z1, C93.Z2, C94.00, C94.01, C94.02, C94.20, C94.21, C94.22, C94.30, C94.31, C94.32, C94.80, C94.81, C94.82, C95.00, C95.01, C95.02, C95.10, C95.11, C95.12, C95.90, C95.91, C95.92, C96.2
Carcinoid tumors and Carcinomas	C44.01, C44.02, C44.111, C44.112, C44.119, C44.121, C44.122, C44.129, C44.202, C44.209, C44.211, C44.212, C44.219, C44.221, C44.222, C44.229, C44.310, C44.311, C44.319, C44.320, C44.321, C44.329, C44.41, C44.42, C44.49
Other	C94.40, C94.41, C94.42, C88, C96.0, C96.5, C96.6, C96.21, C17.3, C22.2, C84.00, C84.01, C84.02, C84.03, C84.04, C84.05, C84.06, C84.07, C84.08, C84.09, C84.10, C84.11, C84.12, C84.13, C84.14, C84.15, C84.16, C84.17, C84.18, C84.19

Table S3. Diagnosis Codes for Sickle-Cell Anemia

Sickle-Cell	ICD-10
Hb-SS disease with crisis, unspecified	D57.00
Hb-SS disease with acute chest syndrome	D57.01
Hb-SS disease with splenic sequestration	D57.02
Sickle-cell disease without crisis	D57.1
Sickle-cell/Hb-C disease without crisis	D57.20
Sickle-cell/Hb-C disease with acute chest syndrome	D57.211
Sickle-cell/Hb-C disease with splenic sequestration	D57.212
Sickle-cell/Hb-C disease with crisis, unspecified	D57.219
Sickle-cell trait	D57.3
Sickle-cell thalassemia without crisis	D57.40
Sickle-cell thalassemia with acute chest syndrome	D57.411
Sickle-cell thalassemia with splenic sequestration	D57.412
Sickle-cell thalassemia with crisis, unspecified	D57.419
Other sickle-cell disorders without crisis	D57.80
Other sickle-cell disorders with acute chest syndrome	D57.811
Other sickle-cell disorders with splenic sequestration	D57.812
Other sickle-cell disorders with crisis, unspecified	D57.819

Table S4. Milliman's MedInsight Health Waste Calculator Specifications for Low-Value Opioids for Acute Low Back Pain

Starting Population	All claims for those aged ≥18 years who received an opioid prescription during the acute timeframe (<28 days) for low back pain between 2019-2021
Classified as Clinically Appropriate	Claims for patients with a diagnosis of cancer or sickle cell anemia. Claims for patients with an indication of a trial of other options before the prescription (e.g., getting non-steroidal anti-inflammatories within a specified timeframe before the opioid prescription)
Classified as Low-Value	All remaining

Other studies have applied this methodology to evaluate low-value opioid prescribing.[1–3]

Table S5. Unadjusted Rate of Annual Opioids for Acute Low Back Pain and Percentage of Total Opioids Attributed to Low-Value in a Virginia Cohort (2019-2021)

	Prescription Claims per 1000 Patients [a]			
	2019	**2020**	**2021**	**2019 to 2021** [c]
Total	210.1	174.7	146.5	**177.1**
Low-Value	155.0	130.0	107.5	**130.8**
Clinically Appropriate	55.1	44.7	39.0	**46.3**
	Percentage of Low-Value [b]			
	73.8%	74.3%	73.3%	**73.9%**

[a] Annual opioid utilization rate (number of prescription claims divided by total number of patients multiplied by 1000)

[b] Percentage (or proportion) of the annual opioid prescriptions that were low-value.

[c] The three-year mean (2019-2021)

Table S6. Summary Table of Rate Regression Effects on Total Opioids for Acute Low Back Pain in a Virginia Cohort (2019-2021)

Term	*IRR [a] (95% CI)*	*Estimate*	*Std. Err.*	*Z (Wald)*	*P-Value*
Year (Since 2019)	0.918 (0.871, 0.967)	-0.086	0.027	10.27	**0.0014****
DiD (False) vs.	1.0	0.0			
DiD (True)	0.775 (0.672, 0.895)	-0.254	0.073	12.11	**<.001*****
Rurality (Non-Rural) vs. [b]	1.0	0.0			
Rurality (Rural)	1.696 (1.247, 2.307)	0.528	0.157	11.33	**<.001*****
DiD x Rurality (Non-Rural) vs. [c]	1.0				
DiD x Rurality (Rural)	1.022 (0.961, 1.086)	0.022	0.031	0.48	0.490
Payer (Commercial) vs. [b]	1.0	0.0			
Payer (Medicaid)	2.069 (1.581, 2.708)	0.727	0.137	28.01	**<.001*****
Payer (MA)	4.951 (3.847, 6.370)	1.599	0.129	154.62	**<.001*****
DiD x Payer (Commercial) vs. [c]	1.0				
DiD x Payer (Medicaid)	0.554 (0.484, 0.635)	-0.590	0.070	71.93	**<.001*****
DiD x Payer (MA)	1.201 (1.075, 1.342)	0.183	0.057	10.48	**0.0012****
Rurality x Payer (Commercial) vs. [d]	1.0				
Rurality x Payer (Medicaid)	0.985 (0.671, 1.444)	-0.016	0.196	0.01	0.937
Rurality x Payer (MA)	0.754 (0.557, 1.021)	-0.282	0.154	3.34	0.068
Months (Jan-Feb) vs. [b]	1.0	0.0			
Months (Mar-April)	1.064 (1.041, 1.088)	0.062	0.011	30.72	**<.001*****
Months (May-Jun)	1.071 (1.051, 1.091)	0.069	0.010	52.44	**<.001*****
Months (Jul-Aug)	1.045 (1.009, 1.082)	0.044	0.018	6.09	**0.014***
Months (Sep-Oct)	1.030 (0.992, 1.069)	0.029	0.019	2.31	0.128
Months (Nov-Dec)	0.975 (0.942, 1.009)	-0.025	0.017	2.15	0.143
DiD x Months (Jan-Feb) vs. [c]	1.0				
DiD x Months (Mar-April)	1.001 (0.980, 1.023)	0.002	0.011	0.02	0.893
DiD x Months (May-Jun)	0.983 (0.956, 1.012)	-0.017	0.015	1.29	0.256
DiD x Months (Jul-Aug)	1.055 (1.023, 1.087)	0.054	0.015	12.02	**<.001*****
DiD x Months (Sep-Oct)	1.024 (0.992, 1.057)	0.024	0.016	2.01	0.147
DiD x Months (Nov-Dec)	0.969 (0.936, 1.002)	-0.032	0.017	3.34	0.067
Age (18-39 years) vs.	1.0	0.0			
Age (40-64 years)	4.335 (3.821, 4.918)	1.466	0.064	518.87	**<.001*****
Age (65-79 years)	1.142 (0.945, 1.381)	0.13	0.097	1.89	0.170
Age (80+ years)	0.750 (0.628, 0.896)	-0.288	0.091	10.07	**0.002****
Sex (F) vs.	1.0	0.0			
Sex (M)	0.750 (0.677, 0.830)	-0.288	0.052	30.74	**<.001*****
Rurality x Sex (F) vs. [d]	1.0				
Rurality x Sex (M)	1.216 (1.073, 1.379)	0.196	0.064	9.39	**0.002****

[a] Incidence rate ratios for low-value opioid prescriptions per 1000 patients per year, sex, age, month pair, payer, and rurality represent the cumulative difference in observed rates from expected rates.

[b] Months (Month-Pairs), Payer (commercial, Medicaid, or Medicare Advantage (MA)), and Rurality represent the pre-pandemic (unexposed) timeframe (January 2019 - February 2020) to December 31, 2021.

[c] DiD x Month, DiD x Payer, and DiD x Rurality; DiD represents the rate difference between model-predicted, pre-pandemic-based expected rates (representing what rates would have been had the pandemic not happened) and the during-pandemic timeframe (March 2020-December 2021)(representing rates during the exposure), or the interaction (impact of pandemic timeframe) on rates in each variable compared to in a reference variable.

[d] Rurality x Payer represents the difference in rural/non-rural rates between commercial and other payers. Rurality x Sex represents the difference in rural/non-rural rates in males compared to females.

* denotes a p-value of <.05, ** denotes a p-value <.01, and *** denotes a p-value <.001; CI = Confidence Interval

Table S7. Summary Table of Rate Regression Effects on Low-Value Opioids for Acute Low Back Pain in a Virginia Cohort (2019-2021)

Term	*IRR [a] (95% CI)*	*Estimate*	*Std. Err.*	*Z (Wald)*	*P-Value*
Year (Since 2019)	0.906 (0.860, 0.955)	-0.098	0.027	13.32	**<.001*****
DiD (False) vs.	1.0	0.0			
DiD (True)	0.796 (0.687, 0.921)	-0.228	0.075	9.33	**0.002***
Rurality (Non-Rural) vs. [b]	1.0	0.0			
Rurality (Rural)	1.738 (1.297, 2.329)	0.055	0.149	13.69	**<.001*****
DiD x Rurality (Non-Rural) vs. [c]	1.0				
DiD x Rurality (Rural)	1.017 (0.954, 1.085)	0.017	0.033	0.27	0.060
Payer (Commercial) vs. [b]	1.0	0.0			
Payer (Medicaid)	1.992 (1.504, 2.639)	0.689	0.144	23.06	**<.001*****
Payer (MA)	5.268 (4.104, 6.762)	1.662	0.127	170.25	**<.001*****
DiD x Payer (Commercial) vs. [c]	1.0				
DiD x Payer (Medicaid)	0.552 (0.477, 0.639)	-0.594	0.075	63.54	**<.001*****
DiD x Payer (MA)	1.195 (1.068, 1.337)	0.178	0.057	9.62	**0.002****
Rurality x Payer (Commercial) vs. [d]	1.0				
Rurality x Payer (Medicaid)	1.012 (0.693, 1.478)	0.012	0.193	0.00	0.950
Rurality x Payer (MA)	0.747 (0.561, 0.994)	-0.291	0.146	4.00	**0.046***
Months (Jan-Feb) vs. [b]	1.0	0.0			
Months (Mar-April)	1.063 (1.039, 1.088)	0.062	0.012	26.34	**<.001*****
Months (May-Jun)	1.059 (1.032, 1.086)	0.057	0.013	19.45	**<.001*****
Months (Jul-Aug)	1.036 (1.002, 1.071)	0.035	0.017	4.31	**0.038***
Months (Sep-Oct)	1.020 (0.985, 1.057)	0.020	0.018	1.23	0.267
Months (Nov-Dec)	0.969 (0.937, 1.002)	-0.031	0.017	3.37	0.066
DiD x Months (Jan-Feb) vs. [c]	1.0				
DiD x Months (Mar-April)	0.995 (0.973, 1.017)	-0.005	0.011	0.21	0.650
DiD x Months (May-Jun)	0.987 (0.961, 1.014)	-0.013	0.014	0.87	0.351
DiD x Months (Jul-Aug)	1.058 (1.024, 1.093)	0.056	0.017	11.46	**<.001*****
DiD x Months (Sep-Oct)	1.030 (0.992, 1.070)	0.029	0.019	2.33	0.127
DiD x Months (Nov-Dec)	0.959 (0.929, 0.990)	-0.042	0.016	6.50	**0.011***
Age (18-39 years) vs.	1.0	0.0			
Age (40-64 years)	4.437 (3.893, 5.058)	1.490	0.067	497.59	**<.001*****
Age (65-79 years)	1.073 (0.890, 1.295)	0.071	0.096	0.55	0.459
Age (80+ years)	0.661 (0.538, 0.810)	-0.415	0.104	15.81	**<.001*****
Sex (F) vs.	1.0	0.0			
Sex (M)	0.729 (0.653, 0.813)	-0.316	0.056	31.95	**<.001*****
Rurality x Sex (F) vs. [d]	1.0				
Rurality x Sex (M)	1.253 (1.097, 1.431)	0.226	0.068	11.03	**<.001*****

[a] Incidence rate ratios for low-value opioid prescriptions per 1000 patients per year, sex, age, month pair, payer, and rurality represent the cumulative difference in observed rates from expected rates.

[b] Months (Month Pairs), Payer (commercial, Medicaid, or Medicare Advantage (MA)), and Rurality represent the pre-pandemic (unexposed) timeframe (January 2019 - February 2020), because interactions with DiD are present.

[c] DiD x Month, DiD x Payer, and DiD x Rurality; DiD represents the rate difference between model-predicted, pre-pandemic-based expected rates (representing what rates would have been had the pandemic not happened) and the during-pandemic timeframe (March 2020-December 2021)(representing rates during the exposure), or the interaction (impact of pandemic timeframe) on rates in each variable compared to in a reference variable.

[d] Rurality x Payer represents the difference in rural/non-rural rates between commercial and other payers. Rurality x Sex represents the difference in rural/non-rural rates in males compared to females.

* denotes a p-value of <.05, ** denotes a p-value <.01, and *** denotes a p-value <.001; CI = Confidence Interval

Table S8. Summary Table of Rate Regression Effects on Clinically Appropriate Opioids for Acute Low Back Pain in a Virginia Cohort (2019-2021)

Term	*IRR [a] (95% CI)*	*Estimate*	*Std. Err.*	*Z (Wald)*	*P-Value*
Year (Since 2019)	0.952 (0.900, 1.008)	-0.049	0.029	2.84	0.092
DiD (False) vs.	1.0	0.0			
DiD (True)	0.721 (0.619, 0.839)	-0.328	0.078	17.69	**<0.001*****
Rurality (Non-Rural) vs. b	1.0	0.0			
Rurality (Rural)	1.576 (1.167, 2.329)	0.455	0.199	5.22	0.022**
DiD x Rurality (Non-Rural) vs. c	1.0				
DiD x Rurality (Rural)	1.035 (0.962, 1.115)	0.035	0.038	0.86	0.354
Payer (Commercial) vs. b	1.0	0.0			
Payer (Medicaid)	2.255 (1.727, 2.944)	0.455	0.136	35.70	<0.001***
Payer (MA)	4.085 (3.100, 5.384)	0.813	0.141	99.89	<0.001***
DiD x Payer (Commercial) vs. c	1.0	0.0			
DiD x Payer (Medicaid)	0.562 (0.470, 0.671)	-0.577	0.091	40.63	**<0.001*****
DiD x Payer (MA)	1.218 (1.059, 1.401)	0.197	0.713	7.67	**0.006****
Rurality x Payer (Commercial) vs. [d]	1.0				
Rurality x Payer (Medicaid)	0.928 (0.595, 1.446)	-0.075	0.226	0.11	0.173
Rurality x Payer (MA)	0.774 (0.523, 1.1440	-0.257	0.200	1.65	0.120
Months (Jan-Feb) vs. [b]	1.0	0.0			
Months (Mar-April)	1.067 (1.023, 1.113)	0.065	0.021	9.27	**0.002****
Months (May-Jun)	1.106 (1.071, 1.141)	0.100	0.016	38.05	**<0.001*****
Months (Jul-Aug)	1.071 (1.019, 1.126)	0.068	0.026	7.19	**0.007****
Months (Sep-Oct)	1.057 (0.994, 1.125)	0.056	0.032	3.09	0.079
Months (Nov-Dec)	0.992 (0.945, 1.041)	-0.008	0.025	0.10	0.747
DiD x Months (Jan-Feb) vs. [c]	1.0	0.0			
DiD x Months (Mar-April)	1.020 (0.977, 1.064)	0.020	0.022	0.81	0.357
DiD x Months (May-Jun)	0.973 (0.921, 1.028)	-0.028	0.028	0.98	0.322
DiD x Months (Jul-Aug)	1.046 (0.992, 1.103)	0.045	0.027	2.74	0.098
DiD x Months (Sep-Oct)	1.006 (0.960, 1.055)	0.006	0.024	0.06	0.799
DiD x Months (Nov-Dec)	0.995 (0.942, 1.051)	-0.005	0.028	0.03	0.867
Age (18-39 years) vs.	1.0	0.0			
Age (40-64 years)	4.049 (3.562, 4.602)	1.40	0.065	457.89	**<0.001*****
Age (65-79 years)	1.379 (1.110, 1.713)	0.321	0.111	8.44	**0.004****
Age (80+ years)	1.053 (0.854, 1.299)	0.052	0.107	0.23	0.628
Sex (F) vs.	1.0	0.0			
Sex (M)	0.810 (0.717, 0.915)	-0.211	0.062	11.52	**<0.001*****
Rurality x Sex (F) vs. [d]	1.0				
Rurality x Sex (M)	1.119 (0.952, 1.316)	0.113	0.083	1.86	0.173

[a] Incidence rate ratios for clinically appropriate opioid prescriptions per 1000 patients per year, sex, age, month pair, payer, and rurality represent the cumulative difference in observed rates from expected rates.

[b] Months (Month Pairs), Payer (commercial, Medicaid, or Medicare Advantage (MA)), and Rurality represent the pre-pandemic (unexposed) timeframe (January 2019 - February 2020), because interactions are present.

[c] DiD x Month, DiD x Payer, and DiD x Rurality; DiD represents the rate difference between model-predicted, pre-pandemic-based expected rates (representing what rates would have been had the pandemic not happened) and the during-pandemic timeframe (March 2020-December 2021)(representing rates during the exposure), or the interaction (impact of pandemic timeframe) on rates in each variable compared to in a reference variable.

[d] Rurality x Payer represents the difference in rural/non-rural rates between commercial and other payers. Rurality x Sex represents the difference in rural/non-rural rates in males compared to females.

* denotes a p-value of <.05, ** denotes a p-value <.01, and *** denotes a p-value <.001; CI = Confidence Interval

Table S9. Unadjusted Rate of Total Annual Opioids for Acute Low Back Pain and Percentage of Total Opioids Attributed to Low-Value in a Virginia Cohort by Demographic Characteristic (2019-2021)

	Prescription Claims per 1000 Patients [a] **(*Low-Value Percentage*)** [b]			
Year	**2019**	**2020**	**2021**	**2019 to 2021** [c]
Age (Years)				
18-39	56.2 (72.4)	40.1 (72.9)	27.0 (71.2)	**41.1 (72.2)**
40-64	342.2 (76.5)	293.7 (77.2)	228.8 (75.7)	**288.2 (76.5)**
65-79	203.1 (71.9)	171.6 (72.0)	164.0 (72.0)	**179.6 (71.9)**
80+	146.2 (66.7)	111.6 (68.8)	104.9 (67.1)	**120.9 (67.5)**
Biological Sex				
Female	229.5 (74.3)	190.4 (74.9)	161.9 (73.7)	**193.9 (74.2)**
Male	184.8 (73.0)	154.5 (73.8)	126.5 (72.9)	**155.3 (73.2)**
Rurality				
Rural	373.6 (76.2)	310.0 (76.1)	274.6 (75.7)	**319.4 (76.0)**
Non-Rural	188.7 (73.1)	156.2 (74.0)	130.3 (72.8)	**158.4 (73.3)**
Payer				
Commercial	103.6 (73.1)	79.4 (74.0)	65.1 (72.7)	**82.7 (73.3)**
Medicaid	196.7 (71.0)	104.4 (70.9)	57.4 (70.0)	**119.5 (70.6)**
Medicare Advantage	287.6 (74.3)	252.3 (74.9)	235.6 (73.8)	**258.5 (74.3)**

[a] Annual opioid utilization rate (number of prescription claims in each demographic characteristic group divided by the number of patients in each demographic characteristic group, multiplied by 1000).
[b] The percentage (or proportion) of the annual opioid prescriptions that were low-value.
[c] The three-year mean (2019-2021). Percentages may not total 100 due to rounding.

Figure S1. Flow Diagram

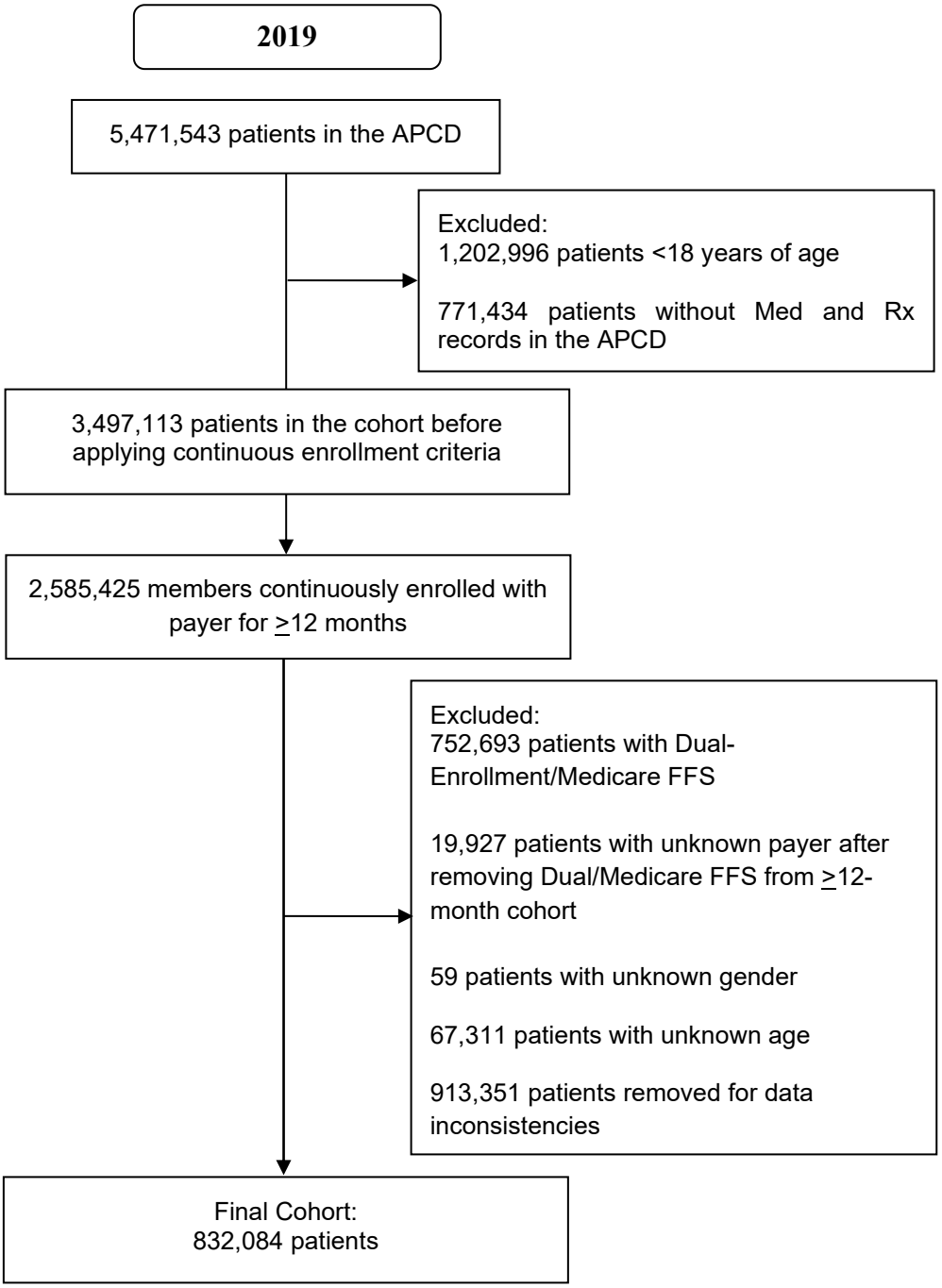
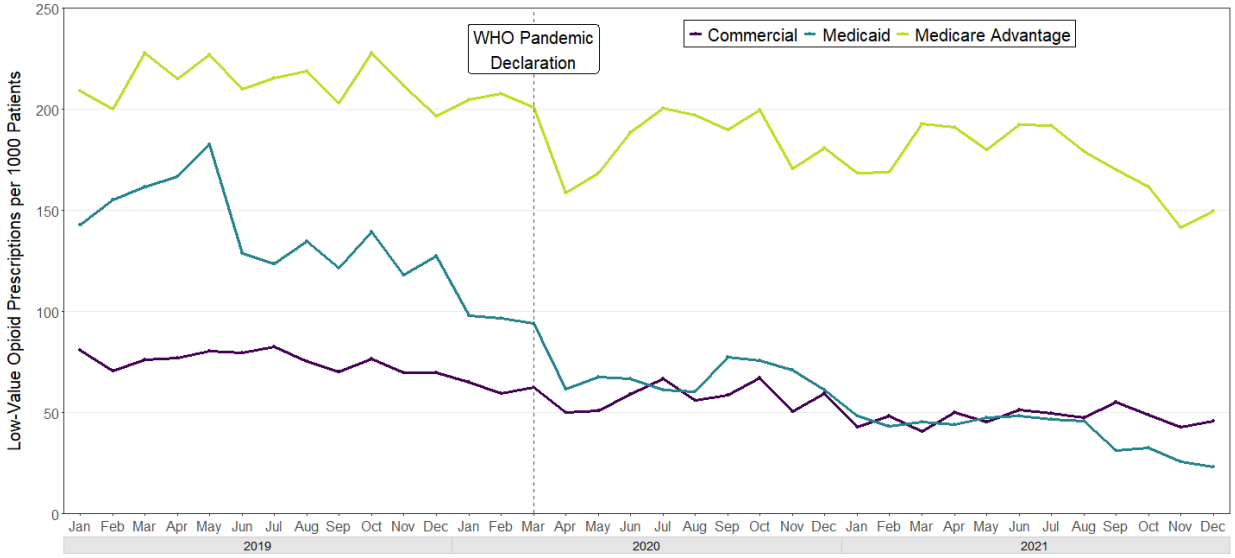


Figure S2. Trends in Incidence of Opioids for Acute Low Back Pain in a Virginia Cohort (2019-2021)



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