The Opioid Epidemic and Dermatology: Prescribing Patterns and Complications in the Medicare Population

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Abstract

Importance: The ongoing United States opioid epidemic has been fueled by prescription opioids. Increases in opioid-related deaths and complications mandates clinicians in all fields to scrutinize their prescribing patterns.

Objective: To characterize the current status and potential complications of opioid prescribing practices among dermatologists for Medicare beneficiaries.

Design: Cross-sectional study using Medicare Part D prescriber data to evaluate opioid prescriptions by dermatologists in 2014. The number of prescribers, opioid claims, beneficiaries, and days supplied as well as the type of opioid and geographic location of prescribers were extracted and analyzed. The top 1% of dermatologists prescribing opioids were identified and evaluated for geographic location, type of practice, and time in practice. A systematic literature review was conducted to estimate the impact of opioid prescribing practices on the exposed population.
Setting: United States

Participants: Dermatologists included in the Medicare Part D prescriber database.

Interventions/Exposures: N/A

Main Outcome: Practice characteristics, epidemiology, and consequences of dermatology-prescribed opioids.

Results: Of 12,537 dermatologists, 5,305 (42.3%) prescribed 0 opioids claims, 5,408 (43.1%) prescribed 1-10 opioid claims, and 1,824 (14.5%) prescribed more than 10 opioid claims. Among dermatologists prescribing at least 10 opioid claims, a mean of 1.0 opioid claims was given to each beneficiary with a mean supply of 4.4 days. 111 (96.5%) of the dermatologists in the top 1% of opioid prescribers work in a surgical practice. Estimates suggest that dermatology-prescribed opioids will annually lead to 3,877-7,602 beneficiaries continuing to use opioids at 1 year and 1,825-4,209 at 3 years. 9,882-22,806 will experience gastrointestinal or CNS side effects and 588-999 will experience fractures.

Conclusions and Relevance: Opioid prescribing among dermatologists is limited and concentrated in the surgical setting, but may be associated with a substantial number of adverse events that serve as a reminder to emphasize non-opioid pain medications in the post-operative setting.

Contribution

As a co-first author, my role included fine-tuning what questions to ask and how to ask them with a broad data set, analyzing the data, and assisting in writing portions of the final manuscript. My primary role lay in delving into the data, analyzing it, and helping present the results in a coherent manner. Calculations
included analyzing how many dermatologists prescribed 0, 1-10, or >10 opioid claims. For prescribers of >10 opioid claims and for the top 1% of prescribers we analyzed practices including the average number of opioid claims, the number of beneficiaries, the mean day supply per opioid claim, the mean opioid claims per beneficiary, and the type of opioid prescribed. Further characteristics of high prescribers we examined included geographic distribution, gender, type of practice, and time in practice. Lastly, I analyzed the data to project risk associated with opioid prescriptions from dermatologists including risk of CNS side effects, left-over pills, fracture, GI side effects, and continued opioid use at 1 and 3 years. I also contributed to writing the results section of the manuscript and created the figures/tables.

Severine, also a co-first author, did much of the background research included in the introduction and discussion of our paper. She wrote the entire initial draft of the manuscript and made updated edits both from Dr. Mostaghimi and from the reviewers as needed throughout the process.

Ryan and David helped collect some of the required data on individual dermatologists practice type and helped call offices to verify if they were medical or surgical.

Dr. Mostaghimi, the project’s founder, guided the narrative in what pieces are relevant, worked closely on reviewing the data and the updates, and provided countless edits/suggestions.
Appendix: Accepted into JAMA Dermatology; not yet published. Full manuscript begins on next page.

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**Conflicts of interest:** The authors have no conflicts of interest.
Key Points

1. Question: What is the nature and impact of opioid prescriptions by dermatologists among Medicare patients?

2. Findings: In this cross-sectional study using 2014 Medicare Part D prescriber data, opioid prescriptions by dermatologists were few and concentrated among dermatologists in surgical practices. We project that this use places more than 7,000 Medicare beneficiaries at risk for addiction, close to 1,000 at risk of fractures, and more than 22,000 at risk for gastrointestinal or central nervous system side effects.

3. Meaning: Opioid prescribing among dermatologists is limited but associated with potential adverse effects for elderly patients. Non-opioid alternatives should be emphasized.
Abstract

Importance: The ongoing United States opioid epidemic has been fueled by prescription opioids. Increases in opioid-related deaths and complications mandates clinicians in all fields to scrutinize their prescribing patterns.

Objective: To characterize the current status and potential complications of opioid prescribing practices among dermatologists for Medicare beneficiaries.

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Conclusions and Relevance: Opioid prescribing among dermatologists is limited and concentrated in the surgical setting, but may be associated with a substantial number of adverse events that serve as a reminder to emphasize non-opioid pain medications in the post-operative setting.
Introduction

The United States opioid epidemic is a national emergency. From 2000 to 2014, nearly half a million persons died from drug overdoses, with 61% of overdose-related deaths in 2014 attributable to opioids. In 2015 alone, an estimated 1.9 million people in the United States met criteria for opioid abuse or dependence. The rise in opioid misuse, overdoses, deaths, and hospital admissions has increased in parallel with opioid sales, which quadrupled between 1999 and 2010.

Little is known about opioid prescribing patterns in dermatology. Evaluations of opioid prescription in other fields have encouraged changes in practice, as even a short course of opioids can place patients at risk for addiction. Current dermatology guidelines recommend oral opioids as a second-line agent after a trial of non-steroidal anti-inflammatory drugs (NSAIDs) and/or acetaminophen following surgical excisions and Mohs Microsurgery (MMS). Prior studies on opioid prescribing practices in dermatology suggest limited use of opioids following MMS but derive from observational studies with limited cohorts of dermatologists and patients.

In this study, we sought to broaden this evaluation by examining the use and potential complications associated with opioid prescriptions within the United States Medicare population.

Methodology

Data Collection

The Part D Prescriber Public Use File (PUF) is a public Centers for Medicare & Medicaid Services (CMS) dataset that contains information on prescription drug events incurred by Medicare beneficiaries with a Part D prescription drug plan. The Part D prescription drug plan covers approximately 72% of the roughly 57 million people on Medicare, a federal insurance plan for Americans who are 65 years and older or have certain disabilities. Part D Prescriber PUFs are currently available for 2013-2015 and contain information organized by specific drug events on physician information (National Provider Identifier (NPI), name, geographic location, specialty), drug name, drug utilization (beneficiary count, claim count, and day supply), and total drug costs. In order to protect the privacy of Medicare beneficiaries, drug events derived from 10 or fewer claims are excluded from the Part D
Prescriber PUFs\textsuperscript{19}. Additionally, any beneficiary counts, claim counts, 30-day fill counts, drug costs, and days’ supply with values in between 0 and 10 are suppressed.

CMS offers additional opioid-specific data via the Medicare Part D Opioid Prescribing Mapping Tool\textsuperscript{19}. Among these are the Medicare Part D Opioid Prescriber Summary Files available for 2013-2014, which combine all individual opioid drug events to calculate the opioid prescribing rates of physicians in the Medicare Part D program. These files contain physician information on those prescribing 0 opioid claims, 1-10 opioid claims, and greater than 10 opioid claims. Compared to the Part D Prescriber PUFs, opioid drug events are approached as a class rather than as individual drugs in this dataset.

The top 1\% of opioid prescribers and a random sample of the same size from the remaining dermatologists prescribing >10 opioid claims were identified using the Part D Opioid Prescriber Summary File for 2014. Information on gender and geographic location were collected using the Part D Prescriber Look-Up Tool offered by CMS\textsuperscript{20}. Graduation year from medical school and sub-specialization were obtained from the prescriber’s state medical board website. The type of each prescriber’s practice was assessed by searching for descriptions of their practice on Google. Practices were designated as surgical if the prescriber practiced Mohs or cosmetic surgery. Phone calls were made to individual offices when clarification about the type of practice was needed. This study was granted institutional review board exemption by the Partners Healthcare IRB.

\textit{Data Analysis}

The number of dermatologists prescribing 0 opioid claims, 1-10 opioid claims, and greater than 10 opioid claims was calculated using the Part D Opioid Prescriber Summary File from 2014.

All subsequent calculations for prescribing characteristics of dermatologists prescribing greater than 10 opioid claims and dermatologists in the top 1\% of opioid prescribers were performed using the Part D Prescriber PUF for 2014. The average number of day supply per opioid claim was obtained by dividing the total day supply by the total claim count for each opioid drug event. The average number of opioid claims per beneficiary was determined by dividing total opioid claim count by beneficiary count for each opioid drug event. The gender breakdown, geographic distribution, and type of practice among the top 1\% of opioid prescribers and a random
sample of remaining dermatologists prescribing >10 opioid claims were compared using a chi square test. The average number of years since medical school graduation between these two groups was compared using a student’s t test.

Mapping Geographic Variation

The opioid claim count was summed for each state and divided by the number of Medicare beneficiaries for the same state\textsuperscript{21} to yield the number of opioid claims per 1,000 Medicare beneficiaries per state. The same calculation was repeated for states grouped by geographic regions. State-based data were translated into a map with different colors corresponding to different amounts of opioid claims per 1,000 Medicare beneficiaries.

Modeling of Risks

We performed a comprehensive literature search for observational studies and systematic reviews reporting the risks associated with opioid use in the setting of acute pain control, particularly in the elderly (eTable 1 in Supplement). Search terms included, “opioids”, “risks”, “elderly”, “acute”, “post-operative”, “outpatient”. References of articles were also manually searched for additional relevant studies. The rate of each adverse event was summarized as a range and then multiplied by the total number of beneficiaries receiving opioids in the 2014 Part D Prescriber PUF to obtain a projected number of affected Medicare beneficiaries. The predicted incidence of fracture for our population was calculated by taking the total day supply derived from opioid claims in 2014 and dividing by 365 to obtain the number of person-years, which was then multiplied by the incidence of fracture reported per 1000 person-years in the literature. The number of left-over pills was determined using data from Harris et al\textsuperscript{22} reporting a mean of 8.9 pills prescribed and 3.7 pills consumed following MMS, resulting in a mean of 5.2 left-over pills which was then multiplied by the total number of opioid claims for 2014.

Results
A total of 12,537 dermatologists were identified using the Part D Opioid Prescriber Summary File (Table 1). 5,305 (42.3%) prescribed 0 opioids claims, 5,408 (43.1%) prescribed 1-10 opioid claims, and 1,824 (14.5%) prescribed more than 10 opioid claims.

Among dermatologists prescribing at least 10 opioid claims in the Part D Prescriber PUF, a total of 91,334 opioid claims were prescribed to 76,019 beneficiaries (Table 2). Each dermatologist prescribed a mean (SD) of 63 (109) opioid claims to 61 (89) beneficiaries. Each beneficiary received an average of 1.0 opioid claims with a supply of 4.4 days. Hydrocodone/acetaminophen accounted for 60.4% of opioid claims, followed by codeine/acetaminophen (19.1%), oxycodone HCl/acetaminophen (9.9%), and tramadol (8.3%).

We next identified 115 dermatologists in the top 1% of dermatologists prescribing opioids. These dermatologists accounted for 42.2% of opioid claims and prescribed a total of 38,520 opioid claims to 32,205 beneficiaries. Each dermatologist prescribed a mean (SD) of 335 (234) opioid claims to 280 (148) beneficiaries, and each beneficiary received an average of 1.2 opioid claims with a supply of 4.2 days.

Among the top 1% of dermatologists prescribing opioids, 99 (86.1%) were male physicians, compared to 84 (78.1%) in a random sample of the same size from the remaining dermatologists prescribing >10 opioid claims (p=0.081) (Table 3). 108 (93.9%) dermatologists in the top 1% of prescribers worked in a surgical practice, versus 74.6% in the comparison group (p=0.00058). 83 (72.2%) of dermatologists in the top 1% had practices located in Southern states, with less of a geographic predominance among the remaining dermatologists (p=0.0029). The average number of years since medical school graduation was 24 for both groups (p=1.00).

Dermatologists in Southern states prescribed higher numbers of opioid claims per 1,000 Medicare beneficiaries compared to the rest of the United States (Figure 1). Aggregated by region, dermatologists in the South prescribed 2.77 opioid claims per 1,000 Medicare beneficiaries, compared to 1.60 in the West, 0.89 in the Midwest, and 0.83 in the Northeast (eTable 2 in Supplement).

The frequencies of several risks associated with opioid use in the elderly, including addiction, gastrointestinal side effects (including constipation, nausea, and vomiting), central nervous system (CNS) side effects (including dizziness, somnolence, and unsteadiness), and fracture, were identified from the literature (Table 4). We estimate that 3,877-7,602 beneficiaries will continue to use opioids 1 year after their prescription and 1,825-
Discussion

In this study, we investigate current opioid prescribing practices among dermatologists in Medicare and explore their implications for the Medicare population. This data suggests that opioid prescribing within dermatology is limited. Among dermatologists listed in the 2014 Part D Prescriber PUF, approximately one in eight prescribe more than 10 opioid claims, typically providing one four-day course per beneficiary. A closer evaluation of the top 1% of opioid prescribers reveals their concentration in surgical practices, suggesting that opioid use in dermatology stems primarily from the need for acute pain control following surgical procedures. Our findings confirm the results of prior observational studies demonstrating limited use of opioids following MMS\textsuperscript{14,15}, but extend these conclusions on a larger scale by looking at prescribing practices among all dermatologists practicing within Medicare Part D.

Dermatologists in southern states exhibit heavier use of opioids than other regions. Most dermatologists among the top 1% of opioid prescribers have practices located in southern states, exceeding the proportion practicing in the South among a random sample of dermatologists prescribing $\geq$10 opioid claims. While we were not able to control for the volume of patients seen by these dermatologists, we concurrently found that dermatologists in southern states exhibit a higher opioid prescribing rate per 1,000 Medicare beneficiaries, more than tripling the number prescribed in the Northeast. These observations are in line with previously reported increased prescribing rates among physicians in southern states\textsuperscript{28}, pointing to regional influences on dermatologist attitudes towards opioids that may benefit from region-specific interventions.

Although overall use may be low, short courses of opioids are associated with adverse effects, including addiction. The risk is likely potentiated in older adults given age-related changes in drug pharmacokinetics and the tendency towards polypharmacy\textsuperscript{29}. Our calculations estimate that over 7,000 Medicare patients may be at risk for...
long-term opioid use from prescriptions they receive from dermatologists. Many more will be harmed from other adverse effects, including fractures, gastrointestinal side effects, and CNS side effects.

The substantial number of potentially affected Medicare beneficiaries serves as a reminder to carefully weigh the risks of opioids when selecting agents for acute pain management. As suggested by current guidelines, NSAIDs and acetaminophen should be used as first-line pain control agents, followed by opioids for additional control in certain high-risk patients. Following MMS, acetaminophen plus ibuprofen achieves lower pain scores with fewer side effects when compared to acetaminophen plus codeine. Furthermore, 25% of patients undergoing MMS do not use any of their prescribed opioids and those who use their prescription only consume 41% of their course, suggesting that patients may not require these drugs. Based on these consumption habits we calculated that a total of 474,937 pills would be left unused by Medicare patients receiving prescriptions from their dermatologist, creating a large opioid reservoir that poses a substantial risk for future misuse.

Overall, the combination of patient and societal risks combined with the superior efficacy of non-opioid pain medications strongly suggests that dermatologists revisit habitual opioid-prescribing practices and consider the use of non-opioid pain medications alone in the management of acute pain.

**Limitations**

Our data must be interpreted in the context of the study design. The use of Medicare Part D data files limits our results to opioid prescribing practices among dermatologists participating in Medicare Part D and thus does not reflect practices applying to the general population. Given the higher rates of skin cancer and the greater need for Mohs among older adults, our findings may overestimate opioid prescribing by dermatologists to the general population. Additionally, in our creation of Figure 1, we utilized the number of Medicare beneficiaries enrolled in Part A and B to calculate the number of opioid claims per 1,000 Medicare beneficiaries per state. The use of data from different Medicare plans for this calculation may misestimate the rate of opioids per 1,000 Medicare beneficiaries.

There are specific limitations associated with the use of Medicare Part D data files. The exclusion of data for claim counts or beneficiary counts with values below 10 in the 2014 Part D Prescriber PUFs prevents more
accurate descriptions of opioid prescribing practices within Medicare. The data files also lack information on pill count per claim, limiting the accuracy of our calculations for number of leftover pills. While the studies we used to model the risks of opioid use focused only on opioid-naïve patients, we lack patient-level information to know the opioid status of our patients. Our extrapolations using data in opioid-naïve patients may therefore misrepresent the number affected by adverse events. Finally, although our analysis of the top 1% of opioid prescribers in dermatology suggests the use of prescription opioids in the setting of acute pain control, Medicare Part D data files do not provide information on the specific indications for opioid prescriptions to confirm our findings. Additional studies are needed to evaluate the full spectrum of indications for prescription opioids and to understand the decision-making behind opioid-prescribing practices within dermatology. Research in these areas will help to identify more specific recommendations to limit opioid prescribing by dermatologists.

Conclusions

Our study, in conjunction with current literature, suggests that the prescription of opioids by dermatologists is limited and concentrated among dermatologists in surgical practices primarily in Southern states. Despite modest opioid prescribing practices, efforts must be made to reduce opioid prescriptions and minimize the risks associated with opioid use in the elderly Medicare population. When clinically appropriate, dermatologists should follow current guidelines recommending an initial approach using non-opioid agents alone in the post-surgical setting.
Acknowledgement Section

Author Contributions: Cao and Karmouta had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Mostaghimi. Acquisition, analysis, and interpretation of data: Cao, Karmouta, Li, Din. Drafting of the manuscript: Cao. Critical revision of the manuscript for important intellectual content: Mostaghimi, Cao, Karmouta, Li, Din. Statistical analysis: Karmouta. Obtained funding: Not applicable. Administrative, technical, or material support: Not applicable. Study supervision: Mostaghimi.

Funding/Support: This project was supported by the National Center for Advancing Translational Sciences, National Institutes of Health, Award Number TL1TR001062.

Funding/Sponsor was involved?

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<tr>
<td>Collection, management, analysis and interpretation of data</td>
<td>Yes</td>
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<tr>
<td>Preparation, review, or approval of the manuscript</td>
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Decision to submit the manuscript: No
for publication

Financial Disclosure: None reported

Acknowledgements: None

References


5. Liebschutz JM, Xuan Z, Shanahan CW, et al. Improving Adherence to Long-term Opioid Therapy Guidelines to Reduce Opioid Misuse in Primary Care: A Cluster-Randomized Clinical Trial. *JAMA Intern*


Firoz BF, Goldberg LH, Arnon O, Mamelak AJ. An analysis of pain and analgesia after Mohs


Table 1 Number and percent of dermatologists by number of opioid claims using the 2014 Part D Opioid Prescriber Summary File

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<tr>
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<th>No. (%) of dermatologists</th>
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<tr>
<td>0 opioid claims</td>
<td>5305 (42.3%)</td>
</tr>
<tr>
<td>1-10 opioid claims</td>
<td>5408 (43.1%)</td>
</tr>
<tr>
<td>&gt;10 opioid claims</td>
<td>1,824 (14.5%)</td>
</tr>
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*Total number of dermatologists= 12,537
Table 2 Current opioid prescribing practices among dermatologists prescribing >10 opioid claims and the top 1% of opioid prescribers using the 2014 Part D Prescriber PUF

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<th>&gt;10 opioid claims</th>
<th>Top 1%</th>
</tr>
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<tr>
<td>No. (%)(^a) of dermatologists</td>
<td>1,449 (12.6(^b))</td>
<td>115 (1%)</td>
</tr>
<tr>
<td>No. of opioid claims</td>
<td>91,334</td>
<td>38,520</td>
</tr>
<tr>
<td>No. of beneficiaries(^c)</td>
<td>76,019</td>
<td>32,205</td>
</tr>
<tr>
<td>Mean ± SD (Median) opioid claims per dermatologist</td>
<td>63 ± 109 (27)</td>
<td>335 ± 234 (285)</td>
</tr>
<tr>
<td>Mean ± SD (Median) beneficiaries per dermatologist</td>
<td>61 ± 89 (28)</td>
<td>280 ± 148 (246)</td>
</tr>
<tr>
<td>Mean day supply per opioid claim</td>
<td>4.4</td>
<td>4.2</td>
</tr>
<tr>
<td>Mean opioid claims per beneficiary(^c)</td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td>Type of opioid by % of total opioid claims</td>
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<td></td>
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<tr>
<td>Hydrocodone/acetaminophen</td>
<td>60.4</td>
<td>59.4</td>
</tr>
<tr>
<td>Codeine/acetaminophen</td>
<td>19.1</td>
<td>18.0</td>
</tr>
<tr>
<td>Oxycodone HCl/acetaminophen</td>
<td>9.9</td>
<td>10.4</td>
</tr>
<tr>
<td>Tramadol HCl</td>
<td>8.3</td>
<td>8.6</td>
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<tr>
<td>Other(^d)</td>
<td>2.3</td>
<td>1.7</td>
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\(^a\) Total number of dermatologists=11,526

\(^b\) Number (%) of dermatologists prescribing >10 opioid claims in Table 1 differs from Table 2 due to use of different datasets to complete each Table. The Part D Opioid Prescriber Summary File (Table 1) includes dermatologists prescribing >10 of any opioid as a class, while the Part D Prescriber PUF (Table 2) includes dermatologists prescribing >10 of any individual opioid drug

\(^c\) Value may be underestimated due to suppression of beneficiary counts with values below 10.
Other opioids include: oxycodone HCl, tramadol HCl/acetaminophen, fentanyl, morphine sulfate, butorphanol tartrate, hydrocodone/ibuprofen, methadone HCl, hydromorphone HCl, codeine/butalbital/ASA/caffeine.
Table 3 Characteristics of dermatologists prescribing >10 opioid claims and the top 1% of prescribers using the 2014 Part D Prescriber PUF

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<thead>
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<th>Characteristic</th>
<th>&gt;10 opioid claims</th>
<th>Top 1%</th>
<th>p value</th>
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<tr>
<td>Gender</td>
<td>No. (%)</td>
<td>No. (%)</td>
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<tr>
<td>Female</td>
<td>25 (21.9%)</td>
<td>16 (13.9%)</td>
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</tr>
<tr>
<td>Male</td>
<td>84 (78.1%)</td>
<td>99 (86.1%)</td>
<td></td>
</tr>
<tr>
<td>Geographic distribution*</td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
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<tr>
<td>Northeast</td>
<td>9 (7.9%)</td>
<td>7 (6.1%)</td>
<td>0.0029</td>
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<tr>
<td>Midwest</td>
<td>13 (11.4%)</td>
<td>9 (7.8%)</td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>55 (48.2%)</td>
<td>83 (72.2%)</td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>37 (32.5%)</td>
<td>17 (14.8%)</td>
<td></td>
</tr>
<tr>
<td>Type of practice</td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Surgical</td>
<td>85 (74.6%)</td>
<td>108 (93.9%)</td>
<td>0.00058</td>
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<tr>
<td>General Dermatology</td>
<td>29 (25.4%)</td>
<td>7 (6.1%)</td>
<td></td>
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<tr>
<td>Time in practice</td>
<td>Mean ± SD (Median)</td>
<td>Mean ± SD (Median)</td>
<td></td>
</tr>
<tr>
<td>Years since medical school graduation</td>
<td>24 ± 11.5 (23)</td>
<td>24 ± 8.6 (24)</td>
<td>1.00</td>
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South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia

Midwest: Indiana, Illinois, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin

Table 4 Projections of risks associated with opioid prescriptions from dermatologists

<table>
<thead>
<tr>
<th>Risks</th>
<th>Frequency of risk</th>
<th>Number affected</th>
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<tr>
<td>Opioid use at 1 year</td>
<td>5.1-10%\textsuperscript{12, 23}</td>
<td>3,877-7,602</td>
</tr>
<tr>
<td>Opioid use at 3 years</td>
<td>2.4-5.3%\textsuperscript{12}</td>
<td>1,825-4,029</td>
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<tr>
<td>Gastrointestinal side effects: constipation, nausea, vomiting</td>
<td>13-30%\textsuperscript{24-5}</td>
<td>9,882-22,806</td>
</tr>
<tr>
<td>CNS side effects: dizziness, unsteadiness, tiredness, somnolence</td>
<td>13-30%\textsuperscript{24-5}</td>
<td>9,882-22,806</td>
</tr>
<tr>
<td>Fracture</td>
<td>531-902 per 1,000 person-years\textsuperscript{26-7}</td>
<td>588-999</td>
</tr>
<tr>
<td>Left-over pills</td>
<td>Mean of 5.2 left-over pills per prescription\textsuperscript{22}</td>
<td>474,937</td>
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