Emergency Department Contribution to the Prescription Opioid Epidemic

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Study objective: We characterize the relative contribution of emergency departments (EDs) to national opioid prescribing, estimate trends in opioid prescribing by site of care (ED, office-based, and inpatient), and examine whether higher-risk opioid users receive a disproportionate quantity of their opioids from ED settings.

Methods: This was a retrospective analysis of the nationally representative Medical Expenditure Panel Survey from 1996 to 2012. Individuals younger than 18 years and with malignancy diagnoses were excluded. All prescriptions were standardized through conversion to milligrams of morphine equivalents. Reported estimates are adjusted with multivariable regression analysis.

Results: From 1996 to 2012, 47,081 patient-years (survey-weighted population of 483,654,902 patient-years) surveyed by the Medical Expenditure Panel Survey received at least 1 opioid prescription. During the same period, we observed a 471% increase in the total quantity of opioids (measured by total milligrams of morphine equivalents) prescribed in the United States. The proportion of opioids from office-based prescriptions was high and increased throughout the study period (71% of the total in 1996 to 83% in 2012). The amount of opioids originating from the ED was modest and declined throughout the study period (7.4% in 1996 versus 4.4% in 2012). For people in the top 5% of opioid consumption, ED prescriptions accounted for only 2.4% of their total milligrams of morphine equivalents compared with 87.8% from office visits.

Conclusion: Between 1996 and 2012, opioid prescribing for noncancer patients in the United States significantly increased. The majority of this growth was attributable to office visits and refills of previously prescribed opioids. The relative contribution of EDs to the prescription opioid problem was modest and declining. Thus, further efforts to reduce the quantity of opioids prescribed may have limited effect in the ED and should focus on office-based settings. EDs could instead focus on developing and disseminating tools to help providers identify high-risk individuals and refer them to treatment. [Ann Emerg Med. 2018;71:659-667.]

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INTRODUCTION

Background

In the 1990s, multiple scientific and policy reports emerged, documenting poor assessment and management of acute painful conditions. US emergency departments (EDs) were specifically cited as offenders in the "oligoanalgesia" epidemic.[1-6] Propelled by pharmaceutical marketing, what was once thought to be low-addiction potential, and regulatory pressure to "ensure all patients the right to appropriate assessment and management of their pain," prescriptions for opioid analgesics increased significantly for 15 years.[7-10] Simultaneously, misuse, abuse, ED visits, hospitalizations and fatal prescription overdoses related to opioids skyrocketed. In 2014, more than 18,000 people died of prescription drug overdose in the United States, up from 4,030 in 1999.[11-13] Death from opioid analgesics is now the most common cause-of-injury death among patients aged 35 to 54 years.[14-16] This has led to significant efforts to curb opioid prescribing.

Importance

Within the medical community, some of the most stringent prescription guidelines aimed at reducing opioid misuse have emerged, targeting ED prescribing.[17-21] ED-centered policies such as these can only successfully affect the opioid epidemic in the United States if opioid prescribing in EDs significantly contributes to the national drug problem. However, the extent to

Editor's Capsule Summary

What is already known on this topic

Opioid prescribing is one factor in the opioid epidemic, and emergency physicians treat many patients in pain.

What question this study addressed

What are the contributions of emergency physicians over time to the pool of opioids prescribed in the United States?

What this study adds to our knowledge

In analysis of noncancer patients in a nationally representative data set yearly from 1996 to 2012, a 471% increase in overall opioid prescribing existed, but the amount from the emergency department (ED) declined from 7.4% to 4.4% of the overall pool.

How this is relevant to clinical practice

Relative ED opioid prescribing has decreased over time and is not a major contributor to the overall opioid pool.

which EDs contribute to the national epidemic of prescription opioid misuse is largely unknown.[22-26]

Goals of This Investigation

The goal of this investigation is to evaluate the relative contribution of EDs to the national level of opioid prescribing compared with other sites of care. Specifically, we used national survey data to estimate the temporal trend in total quantity of opioids prescribed by site of care (eg, ED versus office visit). We also evaluated average quantities and the strength of dose of opioids prescribed and determined the likelihood of receiving a high-dose opioid prescription by site of care. Finally, we identified the source of opioid prescriptions for people in the highest consumption categories (eg, top 5% of prescription opioid consumption) compared with that of individuals with lower prescription opioid use.

MATERIALS AND METHODS

We performed a retrospective analysis of the Medical Expenditure Panel Survey from 1996 to 2012. We did not include data from later Medical Expenditure Panel Survey years because opioid prescriptions are not completely characterized and cannot be reliably converted to milligrams of morphine equivalents. The Medical Expenditure Panel Survey is a nationally representative subsurvey of the annual National Health Interview Survey administered by the Agency for Healthcare Research and Quality. It is administered to approximately 15,000 individuals annually. Health care events are reported and grouped according to the following categories: dental provider visits, visits to hospital outpatient settings, office-based medical provider visits, ED visits, inpatient visits, home health visits, miscellaneous, and prescribed medications. All visit files are mutually exclusive. Medical Expenditure Panel Survey personnel then obtain an authorization from the survey respondent to contact service providers (including pharmacies) and obtain detailed records for each event. Subjects were included in our analysis if they had at least one prescription opioid event during the study period, were older than 18 years, and had no *International Classification of Diseases, Ninth Revision (ICD-9)* codes indicating a cancer diagnosis. This investigation was certified exempt from review by the local institutional review board.

We identified opioid prescriptions with the National Drug Code contained in the prescribed medications file. The code is a unique identifier that describes the compound, formulation, dose, and quantity of a given medication. The Medical Expenditure Panel Survey then uses the Multum Lexicon to group National Drug Code codes into broad categories. We included relevant prescriptions in the narcotic analgesic and narcotic analgesic combination categories. Misclassification was a significant concern. As such, we evaluated the actual compound names for those Multum codes and eliminated observations that were not opioid analgesics or combination opioid analgesics.

To allow direct comparison across compounds, we converted prescriptions to milligrams of morphine equivalents, using conversion factors from published morphine equivalents charts (Table E1, available online at http://www.annemergmed.com). We calculated the total morphine equivalents of the prescription as the prescription's strength in milligrams multiplied by the milligrams of morphine equivalents conversion factor and the quantity of the prescription. Prescriptions lacking data on both the active ingredient and the National Drug Code were omitted from the sample. For prescriptions lacking either valid National Drug Codes or data on strength or quantity, those values were replaced by the median value recorded for the drug's active ingredient. The results were unchanged if those values were replaced by the mean recorded for the drug's active ingredient.

We linked the prescribed medications file to the files explaining medical use by site of care to determine the care setting in which each opioid was prescribed. Because the

Agency for Healthcare Research and Quality's linking procedures can ascribe a given prescription event to multiple medical events, we assigned prescriptions to the most frequent medical event (eg, if there were 2 ED events, then it was assigned to the ED, or if there were 2 ED events and 1 dental event, then it was also assigned to the ED). Events in which there was no medical event that was most commonly assigned (eg, one ED event and one inpatient event) were labeled first as ED events if they were ever associated with the ED, then as dental events, then as outpatient, then as office based, and finally as inpatient prescriptions. Prescriptions that were not associated with any medical event were labeled as "other."

To account for the prescriptions not associated with a particular medical event (approximately 30% of all prescriptions), we reported outcomes in 2 ways. For the aggregate estimates of total opioid prescribing regardless of site of care, opioids that were not associated with a medical event were included. However, when the share of total opioids originating at a given site of care were reported, opioids with no associated medical event were excluded from the total. We tested whether opioid prescriptions with missing sites originated disproportionately from the ED by comparing the rates of missing site of care for individuals receiving opioids who had an ED visit compared with those who did not.

The analysis used 4 key outcomes: the total milligrams of morphine equivalents per prescription, the quantity in total milligrams of the prescription, the rate of receipt of high-dose prescriptions, and the rate of receipt of chronic prescriptions. The total quantity came directly from data reported to the Medical Expenditure Panel Survey. The total milligrams of morphine equivalents was calculated from the strength per dose, the total number of doses, and the milligrams of morphine equivalents conversion factor explained above. A prescription was determined to be "high dose" if its strength per dose (dosage×milligrams of morphine equivalents conversion factor) was greater than or equal to 100 milligrams of morphine equivalents. Prescriptions were considered "chronic" if the prescription was refilled more than 6 times per year. For our purposes, a "refilled prescription" occurred when an individual filled an identical National Drug Code and quantity more than once in a calendar year.

Finally, the person-level analysis aggregated these per-prescription outcomes to reflect a patient's total, reported consumption within a calendar year. At the person level, we estimated the total milligrams of morphine equivalents each individual in the study sample received annually, and categorized them according to their relative use (eg, 95th percentile of opioid milligrams of morphine equivalents). We then estimated the proportion of opioids originating from each site of care for each category of opioid consumption.

Primary Data Analysis

For each of the outcomes of interest, we computed unadjusted and multivariable regression-adjusted estimates to analyze the differences in prescribing by site of care. For all outcomes reported, we used survey-specific methods to account for the use of a stratified random-sample design with purposeful oversampling of certain populations in the Medical Expenditure Panel Survey data sets. All outcomes, adjusted and unadjusted, were estimated with the survey command prefixes as specified by the Agency for Healthcare Research and Quality for Stata (version 15.0; StataCorp, College Station, TX). As a result, all findings are survey weighted to be representative of the noninstitutionalized US population from 1996 to 2012.

Using regression allowed us to identify trends and site-specific differences independent of patient characteristics. Other covariates included patient demographics (age, sex, race/ethnicity, insurance coverage, poverty status, region, marital status, and urban status), differences in the prescriptions (whether the prescription was refilled and the type of pharmacy), and controls for a variety of common conditions for opioid prescriptions (joint conditions, acute injury, back pain, headache, and major mental health diagnoses). We did not normalize the findings for the differing number of visits by site of care because the goal of the investigation was to estimate and characterize total prescribing, rather than prescribing propensity, by site of care.

After regression adjustment, we reported odds ratios or predicted values. When outcomes were binary (eg, receipt of a high-dose opioid, chronic use of opioids), we used logistic regression to control for the covariates listed above and reported odds ratios and predicted probabilities, holding other covariates at their mean values. When outcomes were counts or totals (eg, total milligrams of morphine equivalents, total quantity), we used generalized linear models with a log-link and gamma distribution to control for the covariates listed above and reported predicted values, holding other covariates at their mean values. For more details, see Appendix E1, available online at http://www.annemergmed.com.

RESULTS

From 1996 to 2012, 13% of the patient-years surveyed by the Medical Expenditure Panel Survey (483,654,902 patient-years) filled opioid prescriptions.

The mean age of respondents filling opioid prescriptions was 48.2 years (95% confidence interval [CI] 47.9 to 48.5 years), and 39.9% (95% CI 39.4% to 40.5%) were men. Compared with patients who did not fill opioid prescriptions, these patients were less well educated, less likely to live in an urban area, more likely to be from the South, more likely to be

Table 1. Characteristics of the study population, 1996 to 2012.

Characteristics	Opioid Using Patient-Years, Mean (95% CI)	Nonopioid Using Patient-Years, Mean (95% CI)
Patient-years	483,654,902	3,226,578,551
Age, y	48.2 (47.9–48.5)	45.3 (45.1–45.5)
Education, y	12.8 (12.7–12.8)	13.1 (13.0–13.1)
Men, %	39.9 (39.4–40.5)	49.4 (49.2–49.7)
Married, %	54.1 (53.4–54.9)	54.9 (54.4–55.3)
Urban, %	79.6 (77.8–81.2)	83.1 (81.7–84.3)
Region, %		
Northeast	15.0 (13.6–16.5)	19.5 (18.1–20.9)
Midwest	24.0 (22.5–25.6)	22.1 (20.8–23.5)
South	39.1 (37.3–40.8)	35.6 (34.0–37.2)
West	21.9 (20.5–23.4)	22.8 (21.6–24.2)
Race or ethnicity, %		
White	76.4 (75.4–77.3)	69.3 (68.3–70.3)
Black	11.2 (10.4–12.0)	11.4 (10.8–12.1)
Hispanic	8.5 (7.9–9.2)	13.2 (12.4–14.0)
Asian	1.7 (1.5–1.9)	4.6 (4.2–5.0)
Insurance status, %		
Private	69.0 (68.2–69.7)	71.4 (70.8–71.9)
Public	22.4 (21.7–23.1)	13.8 (13.5–14.2)
Uninsured	8.7 (8.3–9.0)	14.8 (14.4–15.2)
Diagnosis associated with opioid prescription event, %		
Joint pain	16.6 (16.12–17.11)	
Injury	17.2 (16.71–17.61)	
Back pain	12.3 (11.82–12.75)	
Headache	2.8 (2.57–2.97)	
Mental health	0.3 (0.21–0.32)	

Results are survey weighted to represent the population. Each observation is a patient-year spanning 1996 to 2012. Patients are surveyed during 2-year periods.

white, and more likely to have public health insurance, but less likely to be uninsured. More complete characteristics of the sample are given in Table 1.

Overall, from 1996 to 2012, there was a 647% increase in the total milligrams of morphine equivalents of opioids prescribed for noncancer pain in the United States, before regression adjustment. Office-based opioid prescriptions increased from 64% of the total in 1996 to 84% of the total in 2012. In contrast, the share of total milligrams of morphine equivalents prescribed originating from EDs declined from 10.0% of the total in 1996 to 3.9% of the total in 2012 (unadjusted). The Figure shows the relative unadjusted increase in milligrams of morphine equivalent opioids prescribed from 1996 to 2012 in the office-based, inpatient, and ED settings. There was a 984% increase in total milligrams of morphine equivalents prescribed in an office setting, a 368% increase in inpatient settings, and a 219% increase in the ED.

After controlling for other covariates, total opioid prescribing (measured by milligrams of morphine equivalents) in the United States increased by 471% during the study period. Regression-adjusted milligrams of morphine equivalents prescribed by office-based prescribers increased by 543%, from 9.4 to 60.2 billion milligrams of morphine equivalents from 1996 to 2012, and the share of total milligrams of morphine equivalents of opioids attributed to office-based prescribers increased from 71% to 83% of the total. Regression-adjusted milligrams of morphine equivalents of opioids prescribed by EDs increased more modestly, from 1.0 billion milligrams of morphine equivalents to 3.2 billion (224% increase). As a share of all prescribing, ED prescriptions decreased 3.0 percentage points, from 7.4% to 4.4% of the total. The share of opioid prescriptions originating from inpatient sites of care likewise decreased during the study period, from 8.9% to 6.8% of the total.

Although we observe increases in all types of opioid prescriptions (onetime, refills, and chronic prescriptions) and in all sites of care, much of the growth was concentrated in opioid refill prescriptions obtained in office settings. Table 2 shows regression-adjusted estimates of total milligrams of morphine equivalents resulting from prescriptions that were onetime compared with prescriptions that were refilled, by site of care. Overall, the amount of opioids coming from refilled prescriptions increased by 385% in the early part of the study period to the end compared with 222% for onetime prescriptions. Refilled prescriptions originating in office-based settings increased from 19 to 103 billion milligrams of morphine equivalents (446%), whereas onetime prescriptions increased by a relatively modest 277% during the study period. In contrast, the rate of growth of prescriptions with and without refills was much more similar (232% and 275%, respectively) for opioids originating in the ED.

We also investigated whether certain sites of care were associated with stronger prescriptions, larger prescriptions, or prescriptions associated with higher overdose risk. Across nearly all measures of opioid prescriptions, office-based opioid prescriptions were associated with higher total milligrams of morphine equivalents and higher quantities. In particular, we estimated that the average ED opioid prescription was smaller in quantity (95% CI –29.3% to –22.2%) and in total milligrams of morphine equivalents than the average office-based prescription (95% CI –50.3 to –42.1) (Table E2, available online at http://www.annemergmed.com).

Overall, 2.6% of office-based opioid prescriptions had a strength per dose greater than 100 milligrams of morphine equivalents. In contrast, less than 1% of inpatient and ED prescriptions was for similarly high doses (95% CI of difference –1.99% to –1.81% for inpatient and –2.57% to –2.36% for ED). Furthermore, 15.3% of office-based

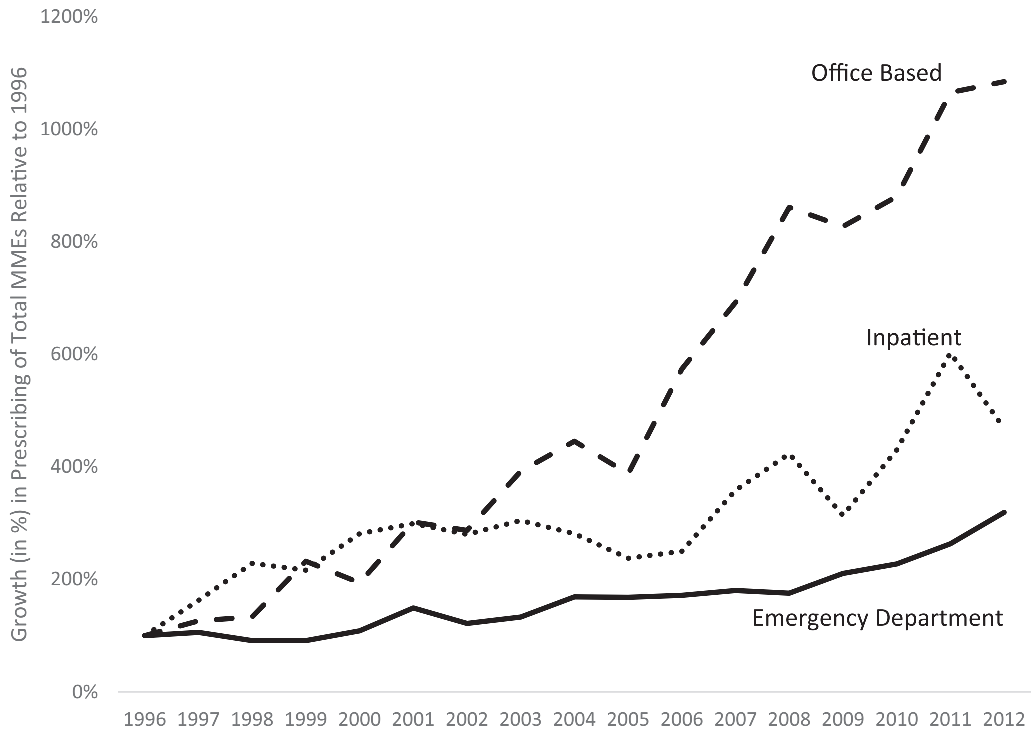

Figure. Growth in total milligrams of morphine equivalents by source of prescribing, 1996 to 2012. *MME*, Milligrams of morphine equivalents.

prescriptions had 6 or more refills, approximately twice as many as did ED or inpatient prescriptions (95% CI of difference –7.05% to –6.69%) for inpatient and –9.19% to –8.85% for ED). See Table 3 for complete details.

The average patient filling an opioid in this study obtained 44.3% of his or her opioids from office-based prescriptions, 14.0% from inpatient settings, 16.0% from EDs, and the remaining 25.7% from dental or other outpatient sources.

The share of ED prescriptions varied according to subjects' overall use of opioids, with those with higher use receiving fewer of their opioids from EDs and more from office-based prescriptions. For example, subjects in the upper half of opioid use distribution (>50th percentile and >225 milligrams of morphine equivalents annually) received 11.9% (95% CI 11.3% to 12.4%) of their opioids from the ED (compared with 54.9% from office-based practice), whereas those above the 75th percentile (>660 milligrams of morphine equivalents) received 7.8% (95% CI 7.2% to 8.4%) from the ED (69.0% from office-based practice), and subjects in the heaviest opioid use category (95% percentile, >6,000 milligrams of morphine equivalents; average annual milligrams of morphine equivalents 24,904) received only 2.4% (95% CI 1.3% to

Table 2. Average adjusted total milligrams of morphine equivalents in billions by source of care and type of prescription, 1996 to 2012.

	Office Based		Inpatient		ED	
Source, Prescription Type	**Onetime**	**Any Refills**	**Onetime**	**Any Refills**	**Onetime**	**Any Refills**
1997–1998	4.6	18.8	1.4	2.3	0.9	1.0
1999–2000	6.2	29.3	1.6	3.6	1.1	1.3
2001–2002	6.5	34.5	2.0	3.0	1.5	1.8
2003–2004	8.6	45.6	2.3	3.7	1.8	2.1
2005–2006	9.5	49.1	2.2	3.4	2.0	2.1
2007–2008	13.5	74.1	3.1	5.3	2.6	3.2
2009–2010	14.9	84.0	3.1	5.6	2.9	2.9
2011–2012	17.2	102.7	3.8	5.9	3.1	3.9
Increase, %	277	446	167	152	232	275

Regression adjustment controls for year, patient demographics, diagnoses, whether the prescription is repeated, and the type of pharmacy filling the prescription. Full regression results are available in Table E2, available online at http://www.annemergmed.com. Patients receiving opioids for cancer pain are excluded.

Table 3. Regression-adjusted opioid prescriptions by source of care, 1996 to 2012.

		Inpatient		ED	
	Office Based Predicted Value*	Difference From Office Based	95% CI†	Difference From Office Based	95% CI
Average MME	1,893.37	−1,130.05	−1,184.51 to −1,075.59	−1,453.12	−1,502.30 to −1,403.94
Average quantity	124.12	−55.65	−58.72 to −52.57	−75.66	−78.23 to −73.10
High-dose prescription‡	2.59	−1.90	−1.99 to −1.81	−2.48	−2.57 to −2.39
Chronic prescriptions with ≥6 refills§	15.33	−6.87	−7.05 to −6.69	−9.02	−9.19 to −8.85

*Predicted values control for year, patient demographics, diagnoses, whether the prescription was repeated, and the type of pharmacy filling the prescription. More complete regression results are available in Table E2, available online at http://www.annemergmed.com.
†The 95% CI reported is for the test of equivalence with office-based prescribing.
‡High-dose prescriptions are those with a strength per dose of more than 100 MME.
§Prescriptions with 6 or more refills indicate that an individual has received 6 or more iterations of the same opioid prescription in a calendar year. The same prescription is defined as the same National Drug Code (NDC) and quantity.

3.1%) of their opioids from the ED (versus 87.8% from office-based practice). Similarly, patients with chronic prescriptions or high-strength-per-dose opioid prescriptions received the majority of their opioids from office-based settings (81.8% and 81.5%, respectively) and comparatively little from EDs (4.5% and 3.5%, respectively) (Table 4).

LIMITATIONS

Our study has several limitations. The Medical Expenditure Panel Survey relies on self-reports of medical encounters to trigger a pharmacy review. Subjects wishing to conceal opioid misuse may not disclose prescriptions, resulting in an undercount of the total amount of opioids dispensed. We believe this does not significantly undermine our findings, in part because our estimates of the increase in opioid use are consistent with those of other reports using market sales data. Moreover, there is no reason to suspect that survey respondents would differentially disclose prescriptions originating from an office visit or an ED visit. Therefore, even if the total magnitude of opioid prescriptions were underestimated, the ED contribution would likely be unbiased.

Another limitation is that certain patient groups have been traditionally underrepresented in the Medical Expenditure Panel Survey, particularly patients with unstable addresses (eg, homeless) or undocumented immigration status. If these patients have higher ED use than the Medical Expenditure Panel Survey respondents in general, the ED estimates may be understated. However, these differences should not affect the temporal trends in growth by site of care. In addition, there is some systematic disagreement between the Medical Expenditure Panel Survey and other surveys such as National Hospital Ambulatory Medical Care Survey on the number of ED visits.[27]

Table 4. Total amount and distribution of annual milligrams of morphine equivalents of mean opioid user by category of user.*

Category of User	Observations	Population Size	Mean Annual MME	Share From Office Based, %	Share From Inpatient, %	Share From ED, %
Average user	37,958	391,335,756	1,902	44.3	14.0	16.0
Average by location in MME distribution						
≤25th	8,715	88,627,837	75	29.1	10.5	23.3
≥50th	20,968	215,019,375	3,369	54.9	15.3	11.9
≥75th	10,314	103,470,723	6,595	69.0	12.4	7.8
≥90th	4,223	42,465,830	14,297	82.5	8.8	4.0
≥95th	2,047	21,241,650	24,907	87.8	6.3	2.4
Average by type of prescriptions received						
High dose†	533	5,718,961	32,804	81.5	10.7	3.5
Chronic‡	2,596	24,784,514	13,164	81.8	7.4	4.5

*Results exclude patients who received opioids for cancer-related pain. Reported values represent the total amount or distribution of opioids by source of care for the average user in each category. Total MME is calculated as the sum of MMEs from all known sources (inpatient, outpatient, office based, ED, and dental visits); it excludes opioids with no known source of origin.
†High-dose prescriptions are those with a strength per dose of more than 100 MME.
‡Chronic use indicates that an individual has received 6 or more iterations of the same opioid prescription in a calendar year. The same prescription is defined as the same NDC and quantity.

Furthermore, a significant portion of opioid prescriptions reported in the Medical Expenditure Panel Survey could not be attributed to a particular source of care. We included these prescriptions in our analysis when calculating the total increase in milligrams of morphine equivalents of opioids in the sample across all sites of care, but excluded them from our site-specific and person-level analyses. To try to determine whether this lack of a source of care might affect our results, we analyzed whether the patients with ED visits were more likely to have opioid prescriptions that were not associated with a source of care. We found that patients with at least one ED visit were significantly more likely to be able to identify the site of care for their prescriptions compared with those with no ED visits. This suggests that the propensity to not report a source of care is not higher among patients with ED visits.

Finally, data from the most recent years of the Medical Expenditure Panel Survey do not include sufficient detail to convert opioid prescriptions to milligrams of morphine equivalents. As a result, our findings ended in 2012 and did not account for the observed downturn in opioid sales in the United States in more recent years.

DISCUSSION

Recent reports have highlighted rapid growth in the quantity of opioids prescribed in the United States. Some estimate that opioid prescribing has increased by 300%, from 180 milligrams of morphine equivalents per capita in 1997 to 710 in 2010.[12,23] Using data from the Medical Expenditure Panel Survey, we observed a similar 471% increase in opioid prescribing for noncancer pain in the United States between 1996 and 2012, even after adjusting for patient and prescription characteristics.

Although it is true that opioid prescribing in the ED increased significantly, from 1.0 to 3.2 billion milligrams of morphine equivalents (224% increase), this growth was dwarfed by the increase in opioid prescriptions originating in office-based settings, which increased from 9.4 to 60.2 billion milligrams of morphine equivalents (543%). Moreover, the proportion of prescription opioids originating from US EDs was a modest 7.4% of the total at the start of the study period in 1996 and actually decreased to 4.4% by the end of the study period in 2012. These results were adjusted for patient and prescription characteristics.

During the past 5 years, EDs have been at the forefront of efforts to reduce harms associated with opioid prescribing. In 2013, then New York City Mayor Michael Bloomberg announced the health authority's ED prescribing guidelines, which included a 3-day limit to the quantity of opioids that could be prescribed from New York City public hospital EDs. In 2012, Washington State Medicaid required EDs to adopt opioid diversion guidelines or face nonreimbursement for services.[28] Other states and many health plans are working on similar opioid diversion plans targeting emergency care, typically supported by state-level chapters of the American College of Emergency Physicians.[29] These organized, ED-based policy interventions were implemented after the current study period ended and therefore are unlikely to account for the slower growth in ED opioid prescribing.

It is unclear why EDs have been so central in efforts to combat this public health crisis. One consideration is that there are only 5,000 EDs in the United States—generally housed in inpatient hospitals—that are subject to higher levels of regulation and oversight than office-based practice, making intervention more feasible. Moreover, EDs account for more than 130 million annual patient visits, so successful intervention could have a large public health influence. Still, central to the policies focusing on reducing ED opioid prescriptions are the concepts that EDs are a major source of opioid prescriptions or prescribe large doses of opioids. However, our findings suggest the opposite; EDs account for a small, declining proportion of all opioid prescriptions and rarely prescribe large doses of opioids. A recent report examining deaths from opioids in Tennessee identified high-dose prescriptions (>100 milligrams of morphine equivalents per dose) as being the single greatest independent predictor of subsequent opioid death (adjusted odds ratio 11.2).[16] We found that a mere 0.1% of ED prescriptions fell into that category, whereas 2.6% of office-based prescriptions were for more than 100 milligrams of morphine equivalents per dose.

Another potential concern is that despite contributing a small amount overall, EDs might dispense disproportionate amounts of prescriptions to high-risk users. The notion is that opioid-addicted individuals move from ED to ED, taking advantage of the lack of provider continuity to acquire large quantities of opioids. However, we found that high-risk opioid users received only a fraction of their opioids from EDs. For example, individuals in the top 5% of annual opioid consumption obtained 2.4% of their total opioids from the ED compared with 87.8% from the office, whereas patients in the bottom half of opioid use distribution receive 20.5% from the ED and 31.5% from the office. Similarly, chronic opioid users received only 4.5% of their opioids from ED prescriptions (82% from office setting). Because EDs are not a major source of the total amount of opioids, high-risk opioid prescriptions, or prescriptions to high-risk opioid users, ED-based guidelines may be unlikely to prevent a significant number of opioid deaths.

An additional concern is that ED-originating prescriptions may “prime” naive patients or give them a “taste” for subsequent opioid use and lead to future abuse. Reports do confirm that persons who misuse or abuse opioids often have their first exposure through legitimate medical opioid prescriptions, often in EDs.[30] Whether these people would have ultimately misused opioids regardless of exposure from the ED is largely untested. However, a recent study demonstrated that, among Medicare beneficiaries, seemingly random exposure to opioids in the ED is associated with a higher risk of long-term opioid use.[31] It is not known whether this longer-term use results in misuse, abuse, or addiction. Still, taken together, these findings suggest that initial opioid prescriptions do have some effect on subsequent opioid use, although the magnitude and importance cannot be fully understood through the research methods used to date. Our study can only speak indirectly to this question by noting that we found only modest growth in the number of prescriptions with refills originating from the ED compared with large growth in prescriptions with refills in office settings. However, the Medical Expenditure Panel Survey data are not ideal for studying this question, and future research should focus on better understanding how important this priming phenomenon is and what strategies can be used to counteract it.

One question that emerges is, could there be harm in significantly restricting prescriptions from EDs? We offer a theoretical reason to be cautious. First, emphasizing opioid restrictions in an environment that has been generally found to undertreat pain could have a profound effect on patients with acute painful conditions without significantly curbing misuse. In fact, regulators from the Centers for Medicare & Medicaid Services recently expressed concern that posting restrictive pain medication guidelines in ED waiting rooms or treatment areas might violate hospitals’ Emergency Medical Treatment and Labor Act obligations and recommended their removal.[32] Furthermore, the ED is a safety net for multiple populations of prescription opioid users, including resource-poor patients experiencing exacerbations of chronic pain who may otherwise have limited or no access to legal prescription opioids. Such patients, regardless of whether they are in pain or dependent or addicted to opioids, are unlikely to be deterred from procuring opioids because an ED refuses to prescribe them. Rather, they could be pushed to unscrupulous medical providers or, worse, turn to the illicit drug markets.[12,33] Illicit opioid users are much more likely to experience overdose, violence, incarceration, unemployment, and other destructive social consequences.[33-38]

Of course, this is not to discount the importance of combating excessive opioid use in the ED or elsewhere. Our analysis should not be seen as advocating reckless or irresponsible prescribing from the ED. But policymakers and providers should be careful to match interventions with settings in which they are most likely to be successful. Office-based opioid prescribing, particularly for refills, is driving the increase in opioid use and should be a point of major policy. Indeed, broad prescribing guidelines from the Centers for Disease Control and Prevention that focus on chronic opioid prescribing have recently emerged and may be contributing to a reported downturn in opioid prescribing in the last 2 years.[39,40] On the other hand, EDs are not a major source of opioids overall or for individuals in the high-consumption group. As such, efforts to reduce prescribing may have limited effect. Rather, ED-based efforts to assuage this health crisis may be better served focusing on intensifying screening efforts, developing or supporting referral networks, and encouraging brief interventions for patients who have or are at high risk for developing opioid use disorder.

We found that the explosive increase in prescription opioids in the United States has been largely driven from refilled or chronic prescriptions from office-based practice and not from ED or inpatient care. The value and effect of policies directed at restricting ED prescriptions of opioids should be reevaluated in light of these findings. Policies aiming at reducing the quantity of opioids prescribed should generally focus on office-based prescriptions and specifically target reducing the amount of repeated or chronic prescriptions and focus less on hospital-based efforts.

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APPENDIX E1

Technical appendix

Data. We performed a retrospective analysis of the Medical Expenditure Panel Survey (MEPS) from 1992 to 2012. The MEPS is a nationally representative subsurvey of the annual National Health Interview Survey administered by the Agency for Healthcare Research and Quality. It is administered to approximately 15,000 individuals annually. In MEPS, noninstitutionalized individuals within a selected household give detailed description of health care events during the preceding year and then are followed with 5 in-person visits throughout the year to record current health care use. As such, any given individual may provide health care use data for a period of up to 2 years. Health care events are grouped according to the following categories: dental visits, visits to outpatient settings, office visits, ED visits, inpatient visits, home health visits, miscellaneous, and prescribed medications. MEPS personnel then obtain an authorization from the survey respondent to contact service providers (including pharmacies) and obtain detailed records for each event. Each event file contains the *ICD-9* codes, services provided, and out-of-pocket expense associated with that event. The MEPS uses a complex survey design that oversamples certain populations and requires using sampling weights to obtain national estimates. Subjects were included in our analysis if they had at least one prescription opioid event during the study period and were older than 18 years. This investigation was certified exempt from review by the local institutional review board.

Identification of Prescription Opioids

We identified opioid prescriptions with the NDC contained in the prescribed medications file. The NDC is a unique identifier that describes the compound, formulation, dose, and quantity of a given medication. The MEPS then uses the Multum Lexicon to group NDC codes into larger clinically meaningful categories. For example, the NDC for hydrocodone would be captured under the Multum code 060 or 191 for opioid analgesics. Misclassification was a significant concern. As such, we evaluated the actual compound names for Multum subclass codes 57 or 58 (analgesics) and sub-sub-class codes of 60 (narcotic analgesics) or 191 (narcotic analgesic combinations), and eliminated those observations associated with codes that were not opioid analgesics or combination opioid analgesics. We examined the compound names within Multum codes that could reasonably be expected to contain opioid analgesics. We did not review compound names in Multum codes that would not likely contain an opioid analgesic (eg, antihypertensives).

We also determined the total potency of these opioids to allow direct comparison. We converted these prescriptions to milligrams of morphine equivalents (MME), using the conversion factors in Table E1 (available online at http://www.annemergmed.com), which came from published morphine equivalents charts. We then calculated the total morphine equivalents of the prescription event that was equal to the prescription's strength in milligrams multiplied by the MME conversion factor and the quantity of the prescription. Prescriptions lacking data on both the active ingredient and the NDC were omitted from the sample. For prescriptions lacking valid NDCs or data on strength or quantity, those values were replaced by the median value recorded for the drug's active ingredient.

Linking Prescribed Medications to Site of Care

We then linked the prescribed medications file to the files explaining medical use by site of care detailed above to determine which site of care was associated with an opioid prescription event. Because the Agency for Healthcare Research and Quality's linking procedures can ascribe a given prescription event to multiple medical events, we followed the following set of rules to create our analytic data set. First, if any prescription event was associated with more than one medical event of the same type (eg, 2 outpatient visits), that single source was associated with the prescription. Second, if a prescription was associated with multiple types of medical events, the most common one was associated with the prescription (eg, if 2 ED events and 1 dental event were associated with the prescription, it was recorded as an ED prescription). Third, for the remaining prescription events, to provide conservative estimates of the difference between ED and office-based prescribing, they were labeled first as ED events if they were ever associated with the ED, then as dental events if ever associated with dental visits, then as outpatient, then as office based, and finally as inpatient prescriptions. Prescriptions that were not associated with any medical event were labeled as "other." When total opioids across all sites of care were reported, opioids that were not associated with a medical event were included; when the share of total opioids originating at a given site of care was reported, opioids with no associated medical event were excluded. The site of care was the key explanatory variable in our analysis. Subjects with cancer-related *ICD-9* codes were excluded from all estimates.

The analysis used 4 key outcomes: the total milligrams of morphine equivalents per prescription, the quantity in milligrams of the prescription, the rate of receipt of high-dose prescriptions, and the rate of receipt of chronic prescriptions. Both the strength and quantity outcomes came directly from the data reported to MEPS by individual patients. The total milligrams of morphine equivalents were calculated from that original data and the MME conversion factor explained above. A prescription was determined to be "high dose" if its strength per dose (dosage×MME conversion factor) was greater than or equal to 100 MME. It is likely a conservative estimate because patients often consume multiple doses per day. We alternatively identified high-potency prescriptions as those with an active ingredient that is more potent than morphine (eg, has an MME conversion factor >1). Prescriptions were considered "chronic" if they were refilled more than 6 times per year. For our purposes, a "refilled prescription" occurred when an individual filled an identical NDC and quantity more than once in a calendar year.

Finally, the person-level analysis aggregated these per-prescription outcomes to reflect an opioid user's total consumption within a calendar year. At the person level, we estimated the total MMEs each individual in the study sample received annually, and categorized them according to their relative use (eg, 95th percentile of opioid MMEs). We then estimated the proportion of opioids originating from each site of care for each category of opioid consumption (eg, among the individuals in the 95th percentile of opioid consumption, what proportion of the prescription opioids came from office, inpatient, or EDs).

Statistical Analyses

For each of the outcomes of interest, we computed unadjusted and multivariable regression–adjusted estimates to analyze the differences in prescribing by site of care. For all outcomes reported, we used survey-specific methods to account for the use of a stratified random-sample design with purposeful oversampling of certain populations in the MEPS data sets. All outcomes, adjusted and unadjusted, were estimated with the survey command prefixes as specified by the Agency for Healthcare Research and Quality for Stata (version 15.0). As a result, all findings are survey weighted to be representative of the noninstitutionalized US population.

Using regression allowed us to identify trends and site-specific differences independent of patient characteristics. Other covariates included patient demographics (age, sex, race/ethnicity, insurance coverage, poverty status, region, marital status, and urban status), differences in the prescriptions (whether the prescription was refilled and the type of pharmacy), and controls for a variety of common conditions for opioid prescriptions (joint conditions, acute injury, back pain, headache, and major mental health diagnoses). We did not normalize the findings for the differing number of visits by site of care because the goal of the investigation was to estimate and characterize total prescribing, rather than prescribing propensity, by site of care.

After regression adjustment, we reported odds ratios or predicted values. When outcomes were binary (eg, receipt of a high-dose opioid, chronic use of opioids), we used logistic regression to control for the covariates listed above and reported odds ratios and predicted probabilities, holding other covariates at their mean values. When outcomes were counts or totals (eg, total MME, total quantity), we used generalized linear models with a log-link and gamma distribution to control for the covariates listed above and reported predicted values, holding other covariates at their mean values.

Table E1. Milligrams of morphine equivalents conversions.

Active Ingredient	MME Conversion Factor
Butorphanol	7
Codeine	0.15
Dihydrocodeine	0.25
Fentanyl	120*
Fentanyl citrate	130
Hydrocodone	1
Hydromorphone	4
Levorphanol	11
Meperidine	0.1
Methadone	3.0
Morphine	1.0
Nalbuphine	1.0
Opium	1
Oxycodone	1.5
Oxymorphone	3
Pentazocine	0.37
Propoxyphene	0.23
Tapentadol	0.4
Tramadol	0.10

*We assumed that transdermal fentanyl patches lasted for 6 hours, so the effective conversion factor is 720, or 120×6 hours.[41]

Table E2. Full regression results.*

Outcome	Total MME† (95% CI)	Quantity (95% CI)†	Prob (High Dose) (95% CI)‡	Prob (Chronic) (95% CI)‡
Urban	0.0411	−0.00352	1.105	0.924
	(−0.0232 to 0.105)	(−0.0431 to 0.0360)	(0.808 to 1.510)	(0.824 to 1.035)
Married	−0.0437	−0.00376	0.975	1.005
	(−0.119 to 0.0313)	(−0.0394 to 0.0318)	(0.731 to 1.301)	(0.917 to 1.101)
Women	−0.0927	−0.0550	0.963	0.930
	(−0.161 to −0.0246)	(−0.0903 to −0.0197)	(0.755 to 1.229)	(0.847 to 1.022)
Race/ethnicity (reference=white)				
Black	−0.281	−0.0799	0.457	1.022
	(−0.356 to −0.205)	(−0.125 to −0.0347)	(0.321 to 0.650)	(0.900 to 1.161)
Hispanic	−0.295	−0.0993	0.614	0.823
	(−0.418 to −0.172)	(−0.149 to −0.0499)	(0.328 to 1.152)	(0.678 to 0.999)
Asian	−0.375	−0.133	0.203	0.668
	(−0.518 to −0.233)	(−0.215 to −0.0510)	(0.0466 to 0.887)	(0.428 to 1.041)
Source of care (reference=office based)				
Inpatient	−0.289	−0.111	0.415	0.557
	(−0.366 to −0.213)	(−0.157 to −0.0659)	(0.246 to 0.699)	(0.425 to 0.729)
ED	−0.624	−0.299	0.0885	0.403
	(−0.700 to −0.547)	(−0.346 to −0.251)	(0.0429 to 0.183)	(0.307 to 0.529)
Insurance type (reference=private)				
Public	0.0956	0.0689	1.057	1.18
	(0.0225 to 0.169)	(0.0260 to 0.112)	(0.794 to 1.406)	(1.059 to 1.315)
Uninsured	0.0735	0.0910	0.748	1.36
	(−0.0785 to 0.225)	(0.00426 to 0.178)	(0.465 to 1.204)	(1.143 to 1.619)
Diagnoses				
Joint pain	0.0640	0.100	0.898	1.012
	(−0.00726 to 0.135)	(0.0600 to 0.141)	(0.703 to 1.149)	(0.910 to 1.125)
Injury	−0.171	−0.114	0.728	0.844
	(−0.253 to −0.0891)	(−0.154 to −0.0742)	(0.486 to 1.090)	(0.714 to 0.998)
Back pain	0.240	0.0822	1.588	1.071
	(0.145 to 0.334)	(0.0389 to 0.126)	(1.246 to 2.024)	(0.965 to 1.188)
Headache	−0.182	−0.123	0.47	1.128
	(−0.340 to −0.0250)	(−0.195 to −0.0521)	(0.236 to 0.935)	(0.926 to 1.374)
Mental health	0.988	0.549	1.103	1.766
	(0.508 to 1.469)	(0.217 to 0.881)	(0.442 to 2.752)	(1.107 to 2.818)
Observations	81,571	81,586	81,571	30,865
Population size	836,290,552	836,447,094	836,290,552	305,793,067

*Regressions also control for age, age squared, year dummies, poverty status, pharmacy source, region, education, and whether the prescription carries refills.
†The measure is coefficient and the method is GLM, log-link.
‡The measure is odds ratio and the method is logit.