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Coprescribing of opioids and high-risk medications in the USA: a cross-sectional study with data from national ambulatory and emergency department settings

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ABSTRACT

Objective Describe trends in opioid plus high-risk medication coprescribing in the USA.

Design Analyses of serial, cross-sectional, nationally representative data of the National Ambulatory Medical Care Survey (NAMCS) over 2007–2016 and the National Hospital Ambulatory Medical Care Survey (NHAMCS) over 2007–2018.

Setting US ambulatory (NAMCS) and emergency department (ED, NHAMCS) settings.

Participants Patient visits in which the patient was 18 years and older with an opioid prescription in the NAMCS or NHAMCS databases.

Primary and secondary outcome measures Frequency of opioid plus high-risk medication coprescribing.

Results From a combined sample of 700 499 visits over 2007–2018, there were 105 720 visits (15.1%) where opioids were prescribed. n=31 825 were from NAMCS and n=73 895 were from NHAMCS. The mean prevalence of coprescription of opioids and high-risk medications for the combined NAMCS and NHAMCS sample was 18.4% in 2007, peaked at 33.2% in 2014 and declined to 23.8% in 2016. Compared with adults receiving opioid prescriptions alone, those coprescribed opioids and high-risk medications were older, more likely female, white and using private or Medicare insurance (p<0.0001).

Conclusions Coprescribing is more common in ambulatory than ED settings and has been declining, yet one in four patient visits where opioids were prescribed resulted in coprescribed, high-risk medications in 2016. Efforts and research to help lower the rates of high-risk prescribing are needed.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Large sample size (n=105 720 in the analytical sample).
⇒ Rigorous sampling methods for National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) create a sample that is representative of US population and, therefore, results can be generalised to generate recommendations.
⇒ NAMCS and NHAMCS count patient visits, not individual patients; therefore, this study is unable to comment on how doses for opioids and/or high-risk drugs have changed over time for individuals.

INTRODUCTION

Opioids are widely prescribed to treat many types of acute and chronic pain, among other diagnoses.[1] In the USA in 2017, there were 58 opioid prescriptions for every 100 persons[2] and one-third (30.7%) of individuals who went to an emergency department (ED) for pain were given or prescribed an opioid.[3]

The benefits of opioids, however, are accompanied by significant risks of complications, including overdose: more than 70% of the approximately 71 000 drug overdose deaths in the USA in 2019 involved opioids.[4] In 2019, 40.2% of all suspected drug overdose deaths in the ED were from opioids.[5] Salzman *et al*[6] used National Hospital Ambulatory Medical Care Survey (NHAMCS) data to show that between 1999 and 2013, the number of opioid-related ED visits increased from 125 000 in 1999 to over 300 000 in 2013. Encouragingly, within the last 5 years (ie, since 2014), opioid prescribing has decreased.[7 8] Efforts to address the opioid epidemic such as use of prescription drug monitoring programmes[9] and the 2016 Centers for Disease Control and Prevention (CDC) opioid guidelines[10] have contributed to this decline in opioid prescribing.[11 12]

Although rates of opioid prescribing are declining, rates of overdose and other serious complications remain at epidemic levels. Importantly, rates of synthetic opioid-related (excluding methadone) deaths between 2013 and 2019 increased 1040%

(prescriptions and illicit sources),[13] non-fatal drug overdoses in EDs increased almost 10.0% between 2016 and 2017[14] and between 2018 and 2019,[5] and there is emerging evidence that overdoses have increased during the COVID-19 pandemic.[15] This suggests that reducing opioid prescribing alone may not suffice to stem the tide of opioid harms, and thus other targets of intervention should be sought. One major concern with opioid prescribing is coprescription with other medications that put an individual at higher risk for complications (eg, respiratory depression).[16] The coprescription of benzodiazepines with opioids is of particular concern given the up to 10-fold increase in mortality risk when these drugs are taken together.[17–19]

It is unknown how frequently opioids are coprescribed with benzodiazepines, muscle relaxants, cannabinoids, hypnotics, tricyclic antidepressants and gabapentinoids, all of which are high-risk medications (ie, have an increased, associated risk of respiratory depression) when taken with opioids.[20–25] Our objective was to evaluate the annual frequencies and trends of these coprescriptions using nationally representative samples of patient visits in the USA over the preceding decade.

METHODS

Data

We used data from the National Ambulatory Medical Care Survey (NAMCS) and NHAMCS, both of which collect cross-sectional data annually regarding the provision and use of medical services in the USA. The NAMCS collects data from office-based healthcare provider visits, and the NHAMCS collects data from hospital EDs and outpatient departments throughout the USA. These data are collected, maintained and distributed annually by the National Center for Health Statistics of the CDC. Both surveys rely on multistage probability sampling to capture a representative sample of provision and access to care among the US population. Physicians and other clinicians are randomly assigned a 1-week (NAMCS) or 4-week (NHAMCS) reporting period in which to capture and convey data. Detailed descriptions of these data sets are well documented and publicly available.[26]

We analysed data from 2007 to the most recently available year of data for NAMCS (2016) and NHAMCS (2018). We included only ED visits from NHAMCS as outpatient visits were categorised as having poor data quality over 2012–2017 and no further data collection over 2018–2020.[27] We examined data from NAMCS and NHAMCS (ie, not just one or the other) in order to provide a more complete description of high-risk coprescribing. Additionally, NAMCS and NHAMCS data structures are compatible to merge and examine in aggregate (hereafter referred to as 'the combined sample'). We followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines to report the results from this study.[28]

Data collection, measurement and analyses

Study sample

The analysis for this study was conducted from October 2020 to March 2021. The unit of analysis was the patient visit. Visits in which the patient was 18 years of age or older and had an existing opioid prescription or was newly prescribed an opioid at the point of care were included in the analytical sample. Data that were missing for prescription information or age were excluded from these analyses. We derived opioid prescriptions from the 'DRUG ID' variables in the data sets. We compiled and derived a list of opioids using the Ambulatory Care Drug Database System,[29] and high-risk coprescriptions were identified using subject matter expertise accompanied by literature review (online supplemental appendix table A).

Outcome

The main outcomes for this analysis were the annual frequencies of opioid plus high-risk medication coprescribing.

Effect modifiers

We examined demographic and clinical variables, such as natal sex, race, ethnicity, age, new versus continuing prescription, region and urbanicity (ie, residency in a metropolitan statistical area (MSA) vs residency not in an MSA). We examined these data separately and in the combined sample.

Other strata

In addition to examining the frequencies of high-risk medications with concurrent opioid prescription, we also examined trends by year and by type of medication. We also compared the demographic characteristics of the sample of visits where an opioid only was prescribed versus visits where an opioid and one or more high-risk medications were prescribed. Lastly, we compared the top five reasons for visits among patient visits with an opioid prescription and high-risk medication, stratified between NAMCS and NHAMCS.

Statistical analysis

We used SAS V.9.4 (SAS Institute) for all analyses and visualisations; for the descriptive statistics, we reported number and percentage (n (%)) or mean and SD (n (SD)), along with 95% CIs for all estimates. We also described demographic differences between adults prescribed an opioid only versus adults prescribed an opioid plus a high-risk medication with frequencies (n (%)), means and SDs (n (SD)) and 95% CIs, in addition to Rao-Scott χ^2 tests for categorical variables and a t-test for age (the only continuous variable). Using frequentist methodology, we set alpha=0.05 as our statistical threshold for type 1 error.

Patient and public involvement

It was not possible for the authors of this study to involve the public in the design of this research study, as the data sets (ie, NAMCS and NHAMCS) are publicly available

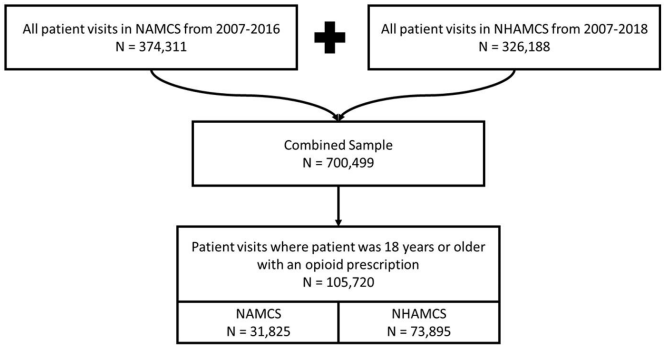

Figure 1 Flow diagram of participants in the study. NAMCS, National Ambulatory Medical Care Survey; NHAMCS, National Hospital Ambulatory Medical Care Survey.

data sets that the CDC collects, creates, cleans and then publishes. Prior to their publishing, these data sets are confidential to the CDC. Additionally, the information of individuals who were included in these data sets is deidentified prior to publishing, so subject involvement would not be possible.

With regard to dissemination, we plan to share results and recommendations with public health officials and clinicians at governmental, non-profit, healthcare and academic organisations so that they can use the results to inform actions to increase prescribing safety for the general public.

RESULTS

From a combined sample of 700 499 visits between 2007 and 2018, there were n=105 720 visits (n=31 825 from NAMCS and n=73 895 from NHAMCS) where opioids were prescribed (figure 1). On average, the mean ages (SD) in the combined sample, NAMCS and NHAMCS, respectively, were 47.6 (18.1), 55.1 (16.7) and 44.4 (17.7) years. There were more females represented by patient visits for combined, NAMCS and NHAMCS (57.6%, 57.7% and 57.5%, respectively); most patient visits were characterised by patients who were identified as non-Hispanic White (56.5%, 69.4% and 50.9%, respectively) or non-Hispanic Black (14.0%, 9.3% and 16.0%, respectively). Additionally, most patient visits were attended by patients who were living in the South (30.1%, 11.6% and 38.1%, respectively), living in an MSA (81.2%, 86.3% and 79.0%, respectively) and using private (30.0%, 34.5% and 27.8%, respectively) and/or Medicare (21.1%, 30.0% and 17.4%, respectively) insurance mechanisms. There were statistically significant differences in the age, race/ethnicity and health insurance status of patients between patient visits in NAMCS versus NHAMCS (alpha=0.05) (table 1).

Mean prevalence of coprescription of opioids and high-risk medications for the combined sample was 18.4% in 2007, peaked at 33.2% in 2014 and declined to 23.8% in 2016 (figure 2). A similar time trend was seen in the ambulatory setting. In ambulatory clinics, coprescription of opioids and high-risk medications was 38.2% in 2007, peaking at 50.0% in 2014 and declining to 45.9% in 2016. The ED setting followed a different time pattern; in 2007, the mean prevalence was 13.5%, peaking at 18.6% in 2017 and decreasing to 16.9% as of 2018. Neither the combined sample, the ambulatory setting, nor the ED setting has decreased to levels observed in the mid-2000s.

Coprescription of high-risk medications with concurrent opioid prescription in the combined sample was with benzodiazepines (11.2%), muscle relaxants (10.1%), gabapentinoids (4.4%), hypnotics (2.4%), tricyclic antidepressants (1.2%) and cannabinoids (<0.1%). This ranking is approximately the same by setting—for ambulatory and ED settings, respectively, benzodiazepines (20.2%; 7.3%) had the highest coprevalence, followed by muscle relaxants (15.4%; 7.7%), gabapentinoids (12.6%; 0.9%), hypnotics (6.8%; 0.5%), tricyclic antidepressants (3.7%; 0.2%) and cannabinoids (0.1%; <0.1%) (table 2). In ambulatory settings, there was a higher frequency of continuing prescriptions versus new prescriptions for all extracted high-risk medications (new vs continuing prescriptions are not distinguished in the ED setting). Ambulatory settings also had the highest frequencies of coprescriptions for all high-risk medications when compared with the combined sample and ED. Notably, NAMCS had more than twice the coprevalence of benzodiazepines, more than 12 times the coprevalence of gabapentinoids and hypnotics and approximately 18 times the coprevalence of tricyclic antidepressants compared with NHAMCS.

Compared with patient visits with an opioid prescription only (n=80 699), patient visits characterised by an opioid prescription and high-risk medication (n=25 021) were more likely to be older, female, white and using private and/or Medicare insurance mechanisms (table 3). All results were p<0.0001.

Pain was the most frequent reason documented at patient visits with a coprescription of opioid and high-risk medications in NAMCS and NHAMCS. For NAMCS, the top reason for visits where opioids were prescribed was documented as 'general visit/medication refill' (21.9%), followed by musculoskeletal pain (16.3%), postoperative visit (3.4%), unspecified/other pain (2.5%) and headache/pain in head (1.7%); for NHAMCS, the top reason for visits where opioids were prescribed was musculoskeletal pain (37.4%), followed by chest pain (5.8%), abdominal pain (4.1%), headache/pain in head (4.0%) and motor vehicle accident injury (2.8%) (online supplemental appendix table B).

DISCUSSION

In a nationally representative US sample of 105 720 combined ambulatory and ED adult patient visits over 2007–2018, on average, 18.4%–33.2% of patient visits resulting in an opioid prescription also had another high-risk medication prescribed. This mean prevalence was highest in 2014 (33.2%) and while it has declined steadily since, it nonetheless remained high at around 20.0% in 2016. Furthermore, while prevalence of coprescribing

Table 1 Demographic characteristics of patients with an opioid prescription, NAMCS (2007–2016) and NHAMCS (2007–2018)

n (%)	NAMCS (n=31 825)	95% CI	NHAMCS (n=73 895)	95% CI	P value	Combined (n=105 720)	95% CI
Sex					0.420		
Female	57.7	57.2 to 58.3	57.5	57.1 to 57.8		57.6	57.3 to 57.9
Male	42.3	41.7 to 42.8	42.5	42.2 to 42.9		42.5	42.2 to 42.8
Age, mean (SD)					<0.001		
Overall	55.1 (16.7)	54.9 to 55.3	44.4 (17.7)	44.3 to 44.5		47.6 (18.1)	47.5 to 47.7
Age (groups)					<0.001		
18–29	7.4	7.1 to 7.7	24.4	24.1 to 24.7		19.3	19.0 to 19.5
30–39	11.6	11.3 to 12.0	20.4	20.1 to 20.7		17.8	17.5 to 18.0
40–49	17.7	17.3 to 18.1	19.3	19.0 to 19.5		18.8	18.5 to 19.0
50–59	23.1	22.6 to 23.5	16.3	16.1 to 16.6		18.4	18.1 to 18.6
60–69	19.4	18.9 to 19.8	9.3	9.1 to 9.5		12.4	12.2 to 12.6
70–79	12.9	12.6 to 13.3	5.7	5.5 to 5.8		7.9	7.7 to 8.0
80–89	6.8	6.6 to 7.1	3.8	3.6 to 3.9		4.7	4.6 to 4.8
90+	1.1	1.0 to 1.2	0.9	0.8 to 1.0		1.0	0.9 to 1.0
Race and ethnicity							
Non-Hispanic Black	9.3	8.9 to 9.6	16.0	15.7 to 16.3	<0.001	14.0	13.8 to 14.2
Non-Hispanic White	69.4	68.9 to 70.0	50.9	50.5 to 51.3		56.5	56.2 to 56.8
Non-Hispanic 'Other' race*	2.8	2.6 to 3.0	2.5	2.3 to 2.6		2.6	2.5 to 2.7
Hispanic	6.8	6.5 to 7.0	9.6	9.4 to 9.8		8.7	8.6 to 8.9
Missing	11.7	11.4 to 12.1	21.0	20.8 to 21.3		18.2	18.0 to 18.5
Geographical region							
Missing†	66.4	65.8 to 66.9	–	–	–	20.0	19.7 to 20.2
South	11.6	11.3 to 12.0	38.1	37.7 to 38.4		30.1	29.8 to 30.4
West	9.2	8.9 to 9.5	22.1	21.8 to 22.4		18.2	18.0 to 18.5
Midwest	7.7	7.4 to 8.0	23.5	23.2 to 23.8		18.7	18.5 to 19.0
Northeast	5.2	4.9 to 5.4	16.3	16.0 to 16.6		13.0	12.7 to 13.2
Metropolitan statistical area (MSA)							
Yes	86.3	85.9 to 86.7	79.0	78.7 to 79.3	–	81.2	81.0 to 81.4
No	13.7	13.3 to 14.1	11.9	11.6 to 12.1		12.4	12.2 to 12.6
Missing‡	–	–	9.2	8.9 to 9.4		6.4	6.3 to 6.5
Health insurance							
Private	34.5	34.0 to 35.1	27.8	27.5 to 28.2	<0.001	30.0	29.6 to 30.1
Medicare	30.0	29.2 to 30.2	17.4	17.1 to 17.7		21.1	20.8 to 21.3
Missing	17.5	17.0 to 17.9	16.8	16.5 to 17.0		17.0	16.7 to 17.2
Medicaid	9.2	8.9 to 9.5	19.2	19.0 to 19.5		16.2	16.0 to 16.4
Self-pay	4.9	4.7 to 5.2	14.0	13.8 to 14.3		11.3	11.1 to 11.5
Worker's compensation	2.2	2.1 to 2.4	1.2	1.1 to 1.2		1.5	1.4 to 1.6
Other	1.8	1.6 to 1.9	2.6	2.5 to 2.7		2.3	2.2 to 2.4
No charge (ie, charity care)	0.3	0.2 to 0.4	1.0	1.0 to 1.1		0.8	0.8 to 0.9
Type of care							

Continued

Table 1 Continued

n (%)	NAMCS (n=31 825)	95% CI	NHAMCS (n=73 895)	95% CI	P value	Combined (n=105 720)	95% CI
Primary care	42.1	41.5 to 42.6	–	–	–	–	–
Medical care	31.3	30.7 to 31.8	–	–		–	–
Surgical care	26.7	26.2 to 27.2	–	–		–	–
Emergency department	–	–	100.0	100.0 to 100.0		–	–

*'Other' race includes Asian, American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander and multiracial.
†Region not collected for NAMCS from 2012 to 2016.
‡MSA not collected for NHAMCS (ED) for 2012.
ED, emergency department; NAMCS, National Ambulatory Medical Care Survey; NHAMCS, National Hospital Ambulatory Medical Care Survey.

in non-ED settings (ie, NAMCS) seems to have declined since 2014, coprescribing in ED settings (ie, NHAMCS) seems to have stagnated and increased slightly since 2007.

These ED findings are corroborated by recent findings from the National Syndrome Surveillance Program; a 2019 study revealed that nearly 1 in 5 (18.7%) overdoses from benzodiazepines also involved opioids.[10] These findings must also be considered alongside the 1040% increase in illicit, synthetic opioid overdose rate from 2013 to 2019, as it highlights the urgency of understanding opioid (mis) use both inside and outside clinical settings.[13 30]

We found that in the outpatient setting, there were higher rates of coprescription of the high-risk medications when they were being refilled versus when new medications were being prescribed. This could again be because primary care providers are often responsible for managing patients' prescriptions over longer periods of time and may not be the initiator of the prescription.[31 32] Alternatively, this finding may reflect same-prescriber, temporal offset between initiation of the high-risk coprescriptions and subsequent prescriptions.

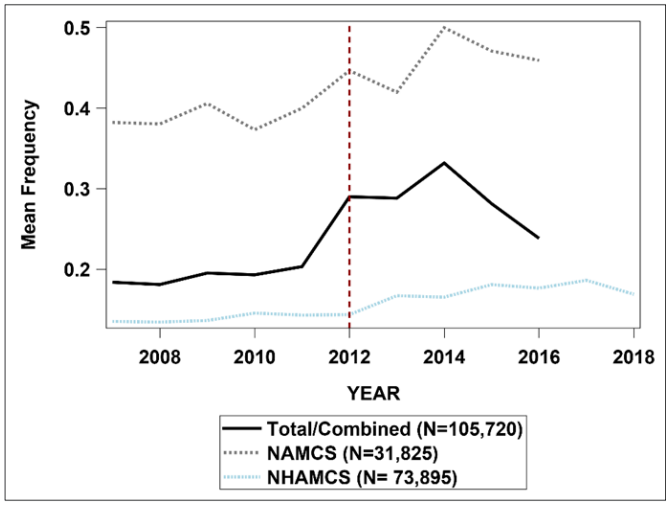

Figure 2 Mean frequency of high-risk coprescription(s) with opioids. Mean frequency of coprescription of opioids with high-risk drugs increased from 2007 to 2014 for all strata; mean frequency decreased from 2014 to 2016 overall and for National Ambulatory Medical Care Survey (NAMCS) and plateaued from 2014 to 2018 for National Hospital Ambulatory Medical Care Survey (NHAMCS). There is a red line through 2012 because data capture changed from paper to electronic collection for both surveys and could have initially inflated results.

These findings also suggest that medication reconciliation and electronic medical record (EMR) alerts to potentially risky coprescribing are two promising (and already existing) interventions.[33] In a prospective cohort study of veteran patients, Malte *et al*[33] found that a medication EMR flag for providers conferred meaningful differences in reducing risky coprescribing of opioids and benzodiazepines. The effects of EMR flags/alerts for providers may be even more potent when multiple high-risk conditions for opioid misuse are present—Malte *et al* also found that when patients were flagged for older age (ie, 65 years or older) and mental health conditions, such as post-traumatic stress disorder, both risky coprescribing and general opioid prescribing decreased.[33 34]

We found that mean coprescribing of opioids and high-risk medications is consistently higher in ambulatory care settings compared with the ED. This finding is unsurprising given that primary care providers are often responsible for high-risk prescribing, whether those providers initiated the prescriptions or were refilling them. Additionally, deprescribing medications is difficult especially for primary care providers; this could be a reason for we observed a higher prevalence of continuing versus new prescriptions in NAMCS.[31 32] Primary care physicians write approximately 45% of all opioid prescriptions in the USA, a fact that likely reflects the much higher volume of patients seen by primary care compared with subspecialties.[22] In support of this, Levy *et al*[32] found that in 2012 family practices were responsible for the highest crude number of opioid prescriptions (52.5 million) compared with other specialties. The specialties with the highest opioid prescriptions as a proportion of total prescriptions were pain medicine, surgery and physical rehabilitation.

Visits with patients who had both an opioid and high-risk coprescription were with significantly older patients (on average) than visits with patients on opioids alone. There may be increased frequency of visits for patients on opioids plus at least one high-risk medication, as practitioners may be seeing patients more frequently

Table 2 New and continuing opioid coprescriptions, NAMCS (2007–2016), NHAMCS (2007–2018) and combined sample

	NAMCS (N=31 825)						NHAMCS (N=73 895)*		Combined (N=105 720)	
Coprescriptions (%)	Combined (new and continuing)	95% CI	Continuing (n=18 631)	95% CI	New (n=13 194)	95% CI	Overall	95% CI	Overall	95% CI
Benzodiazepines	20.2	19.8 to 20.6	21.4	20.8 to 22.0	18.6	17.9 to 19.2	7.3	7.1 to 7.5	11.2	11.0 to 11.4
Muscle relaxants	15.4	15.1 to 15.8	15.6	15.1 to 16.1	15.2	14.6 to 15.8	7.7	7.5 to 7.9	10.1	9.9 to 10.2
Gabapentinoids	12.6	12.2 to 12.9	14.3	13.6 to 14.6	10.3	9.8 to 10.8	0.9	0.8 to 1.0	4.4	4.3 to 4.5
Hypnotics	6.8	6.5 to 7.1	7.5	7.1 to 7.9	5.8	5.4 to 6.2	0.5	0.4 to 0.5	2.4	2.3 to 2.5
Tricyclic antidepressants	3.7	3.5 to 3.9	3.9	3.6 to 4.2	3.3	3.0 to 3.6	0.2	0.2 to 0.2	1.2	1.2 to 1.3
Cannabinoids	0.1	0.1 to 0.2	0.1	0.1 to 0.2	0.1	0.1 to 0.2	<0.1	0.0 to 0.02	46 (0.04)	0.0 to 0.1

*NHAMCS did/does not distinguish between new and continuing prescriptions.
NAMCS, National Ambulatory Medical Care Survey; NHAMCS, National Hospital Ambulatory Medical Care Survey.

to monitor their use of these combined medications.[35] Additionally, since older patients are more likely to have frequent healthcare visits to address health problems than their younger counterparts,[36] the older average age of the patients could be due to more frequent visits. The issue lies in the observed increased likelihood of older adults being prescribed high-risk medications while receiving more frequent healthcare visits.[36 37]

In our analyses, females were more likely than males to be given opioids alone (57.1% vs 42.9%, respectively) and more likely to have a coprescription of opioids and a high-risk medication (59.0% vs 41.0%, respectively). This finding is consistent with previous studies that have described sex differences in opioid prescribing[31 38–40] and chronic pain.[37] Importantly, females have also been shown to use healthcare more than males which could help explain these findings,[38–40] though ED visits involving opioid-related problems (eg, opioid poisoning, opioid dependence) tend to be by male patients.[5 6]

Patient visits characterised by an opioid prescription and a high-risk medication (n=25 021) were more likely to be older, female, white and using private and/or Medicare insurance mechanisms compared with patient visits with an opioid prescription only (n=80 699). There are two additional disparities worth discussing.

First, visits where race was marked 'Non-Hispanic White' made up a larger proportion of visits with opioids plus high-risk medications than visits with opioids alone. This is consistent with findings from other studies.[35 39 40] One possible explanation for this difference is the medicalisation of drug use in the white population specifically.[41–44] It is also possible that the lower proportion of coprescriptions with high-risk medications for Black patients is indicative of a resistance among practitioners to treat symptoms out of unfounded concerns of drug misuse.[25 45–47] Indeed, the undertreatment of pain in Black patients is well documented.[48–50]

Second, Medicare visits included a smaller proportion of visits involving opioids only (19.8%) compared with visits involving opioids plus a high-risk drug (25.4%). This finding could be due to the fact that the Medicare population is older than those using Medicaid or private insurance.[51–53] Our other findings from this study show that visits with older adults more frequently had an opioid and a high-risk medication. Medicare Part D (2006) might also explain our observation, as Medicare became the largest payor for opioid prescriptions after implementation.[54] There is also literature to support higher rates of this type of coprescribing among those with public insurance compared with private insurance or no insurance.[55]

Understanding the reasons for age, race and insurance differences among patients who are coprescribed an opioid and high-risk medication requires further investigation, as do interventions to reduce coprescribing risk. Provider-level interventions currently in practice include education about ways to reduce high-risk prescribing[56] and EMR flags to signal a high-risk prescribing situation.[57–62]

A key strength of our study included the large sample size of our study population and rigorous sampling methods (eg, sampling weights, multistage probability sampling) for NAMCS and NHAMCS. These lead us to believe that the study population (ie, NAMCS and NHAMCS visits) and source population (ie, total number of ambulatory and ED visits in the USA) are demographically, clinically and geographically representative of care received by Americans.

There are also limitations to this work. First, NAMCS and NHAMCS transitioned from paper to electronic records in 2012, which may have affected how patient data were recorded and could have influenced results.[25] Additionally, these data sets count patient visits, not individual patients, so individuals could be counted more than once, and we cannot parse out the risk of patients receiving prescriptions from multiple clinicians. The most recent NAMCS data available were in 2016 and it is unclear whether and how prescribing practices may have changed since that time, especially given there has been a heightened awareness of the risks of opioid prescribing in recent years.[36 58] This study is also unable to comment on how doses, days of supply, illicit versus prescription use of, and/or indications of opioids and/or high-risk drugs have changed over time for individual patients. This is particularly important to note in combination with the aforementioned limitation of the data sets only reporting

Table 3 Opioid prescription only versus opioid prescription+high-risk medication for selected demographic variables, combined sample (n=105 720)

n (%)	Opioid prescription only (n=80 699)	95% CI	Opioid prescription+high-risk medication (n=25 021)	95% CI	P value
Sex					
Female	46 067 (57.1)	56.7 to 57.4	14 772 (59.0)	58.4 to 59.7	<0.0001
Male	34 632 (42.9)	42.6 to 43.3	10 249 (41.0)	40.4 to 41.6	
Age, mean (SD)					
Overall	46.6 (18.4)	46.5 to 46.8	50.87 (16.6)	50.7 to 51.1	<0.0001
Age (groups)					
18–29	17 576 (21.8)	21.5 to 22.1	2784 (11.1)	10.7 to 11.5	<0.0001
30–39	14 803 (18.3)	18.1 to 18.6	3971 (15.9)	15.4 to 16.3	
40–49	14 790 (18.3)	18.1 to 18.6	5059 (20.2)	19.7 to 20.7	
50–59	13 735 (17.0)	16.7 to 17.3	5668 (22.7)	22.1 to 23.2	
60–69	9094 (11.3)	11.1 to 11.5	3963 (15.8)	15.4 to 16.3	
70–79	6035 (7.5)	7.3 to 7.7	2262 (9.0)	8.7 to 9.4	
80–89	3826 (4.7)	4.6 to 4.9	1136 (4.5)	4.3 to 4.8	
90+	840 (1.0)	1.0 to 1.1	178 (0.7)	0.6 to 0.8	
Race and ethnicity					
Non-Hispanic Black	14.7	14.4 to 14.9	11.7	11.3 to 12.1	<0.0001
Non-Hispanic White	53.9	53.6 to 54.3	64.8	64.2 to 65.4	
Non-Hispanic 'Other' race*	2.7	2.6 to 2.8	2.2	2.0 to 2.3	
Hispanic	9.2	9.0 to 9.4	7.3	7.0 to 7.6	
Missing	19.5	19.3 to 19.8	14.0	13.6 to 14.5	
Geographical region					
South	25 708 (31.9)	31.5 to 32.2	6114 (24.4)	23.9 to 25.0	<0.0001
Midwest	16 259 (20.2)	19.9 to 20.4	3556 (14.2)	13.8 to 14.6	
West	13 814 (19.6)	19.3 to 19.9	3466 (13.9)	13.4 to 14.3	
Missing†	11 467 (14.2)	14.0 to 14.5	9652 (38.6)	38.0 to 39.2	
Northeast	11 451 (14.2)	14.0 to 14.4	2233 (8.9)	8.6 to 9.3	
Health insurance					
Private	23 792 (29.5)	29.2 to 29.8	7769 (31.1)	30.5 to 31.6	<0.0001
Medicare	15 945 (19.8)	19.5 to 20.0	6346 (25.4)	24.8 to 25.9	
Missing	13 815 (17.1)	16.9 to 17.4	4119 (16.5)	16.0 to 17.0	
Medicaid	13 631 (16.9)	16.6 to 17.2	3508 (14.0)	13.6 to 14.5	
Self-pay	9767 (12.1)	11.9 to 12.3	2150 (8.6)	8.3 to 9.0	
Other	1911 (2.4)	2.3 to 2.5	550 (2.2)	2.0 to 2.4	
Worker's compensation	1115 (1.4)	1.3 to 1.5	452 (1.8)	1.6 to 2.0	
No charge (ie, charity care)	723 (0.9)	0.8 to 1.0	127 (0.5)	0.4 to 0.6	

*'Other' race includes Asian, American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander and multiracial.
†Region not collected for National Ambulatory Medical Care Survey (NAMCS) from 2012 to 2016.

visits, not patients; a patient weaning off of an opioid, for example, will likely be seeing practitioners frequently and will be receiving new prescriptions (tapering doses) frequently, and these data sets could capture this patient multiple times with opioid prescriptions at each visit.[59 63] Likely more frequently, though, patient visits with the same patient receiving the same opioid prescription month after month are captured in the data. Lastly, study findings have limited generalisability outside of contexts in the USA.

CONCLUSIONS

US adult medical visits have featured the coprescription of opioids and high-risk medications at a proportion higher than 15% over the last two decades. This is

concerning. This study advances the current state of knowledge in understanding risky prescribing situations involving opioids by identifying key settings (ie, outpatient clinics), contexts (ie, prescription refills/continuations) and demographic groups (ie, older females), in which these situations are occurring. Trends should continue to be studied and updated with newly released data to assess whether ongoing interventions and efforts to reduce high-risk coprescribing are effective. New and existing targeted and evidence-based interventions should be implemented and then evaluated to improve patient safety and reduce excess coprescribing.

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Contributors KS conducted the data analysis, contributed to manuscript writing, organised study meetings, conceptualised study design and prepared the manuscript for submission. AZ constructed the study tables, contributed to manuscript writing and contributed to subject matter expertise. MKA provided study and clinical oversight, contributed to manuscript writing and helped conceptualise the study design. JS, JSM and DK provided critical feedback on manuscript drafts, and clinical and health services subject matter expertise. KS obtained the data for this study from publicly available NAMCS and NHAMCS data sets provided by the CDC and NCHS. KS is the guarantor of this work and accepts full responsibility for the study.

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