JAMIA Open, 5(2), 2022, 1–11
https://doi.org/10.1093/jamiaopen/ooac030
Research and Applications

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Development and implementation of a prescription opioid registry across diverse health systems

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Precis: A population-based, prescription opioid registry was developed across 10 health systems in Texas, Minnesota, North Dakota, Wisconsin, Pennsylvania, Michigan, Colorado, Washington, DC, Virginia, Maryland, California, Oregon, and Massachusetts for years 2012–2018.

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Received 12 January 2022; Revised 21 March 2022; Editorial Decision 15 April 2022; Accepted 28 April 2022

ABSTRACT

Objective: Develop and implement a prescription opioid registry in 10 diverse health systems across the US and describe trends in prescribed opioids between 2012 and 2018.

Materials and Methods: Using electronic health record and claims data, we identified patients who had an outpatient fill for any prescription opioid, and/or an opioid use disorder diagnosis, between January 1, 2012 and December 31, 2018. The registry contains distributed files of prescription opioids, benzodiazepines and other select medications, opioid antagonists, clinical diagnoses, procedures, health services utilization, and health plan membership. Rates of

outpatient opioid fills over the study period, standardized to health system demographic distributions, are described by age, gender, and race/ethnicity among members without cancer.
Results: The registry includes 6 249 710 patients and over 40 million outpatient opioid fills. For the combined registry population, opioid fills declined from a high of 0.718 per member-year in 2013 to 0.478 in 2018, and morphine milligram equivalents (MMEs) per fill declined from 985 MMEs per fill in 2012 to 758 MMEs in 2018. MMEs per member declined from 692 MMEs per member in 2012 to 362 MMEs per member in 2018.
Conclusion: This study established a population-based opioid registry across 10 diverse health systems that can be used to address questions related to opioid use. Initial analyses showed large reductions in overall opioid use per member among the combined health systems. The registry will be used in future studies to answer a broad range of other critical public health issues relating to prescription opioid use.

Key words: EHR data, registry, prescription opioids, opioid use disorder

LAY SUMMARY
Prescription opioid use has played a large role in the opioid crisis over the last 2 decades. This article describes the development and implementation of a population-based prescription opioid registry using electronic health record and claims data from 10 diverse health systems in the United States. We also conduct descriptive analyses of opioid use trends over the study period of January 1, 2012–December 31, 2018. Patients who filled a prescription for an opioid, and/or had an opioid use disorder diagnosis in the study period are included in the registry. The registry contains several data domains: patient demographics, medications, including prescription opioids and benzodiazepines, clinical diagnoses, health procedures, health services utilization, health plan membership, and mortality. The registry includes 6 249 710 patients and over 40 million outpatient opioid fills. Descriptive analyses showed large reductions in overall opioid use per member among the combined health systems over the study period. The registry is a large, comprehensive data resource with a flexible data structure that can be leveraged in future studies to answer a broad range of critical public health questions relating to prescription opioid use. The design may be useful for other research teams developing similar data resources.

INTRODUCTION

The United States continues to face an opioid crisis,[1] and while prescription opioids do not drive recent steep increases in mortality,[2] they cause a considerable number of overdose deaths.[1,3,4] Although opioid prescribing has decreased nationally since 2012,[5,6] the morphine equivalents prescribed per person is 3 times the 1999 level.[7] In 2020, 9.3 million people older than 12 years misused prescription pain medications in the past year, making it the second most commonly misused drug after cannabis.[8] In 2020, 2.3 million people had a pain medication use disorder and 2.7 million people had an opioid use disorder (OUD).[9] Prescription opioid misuse is also a risk factor for heroin use.[10]

In response to the crisis, national and professional guidelines have outlined cautions about prescribing at high levels, to whom to prescribe, and how to manage long-term opioid treatment.[11] Critical questions remain about the prescribing environment that has changed quickly as the opioid crisis evolves. Studies that can leverage large population-level data are needed to address research priorities about opioid prescribing limits, opioid dose reductions, and use of medications for OUD.

Disease registries and robust electronic health record (EHR) data are cited as valuable resources to address critical research questions with high efficiency.[12] These data sources can be leveraged to increase our understanding of the impact of changing opioid use trends, and inform future research. Registries have been developed for various disease conditions, including chronic medical conditions,[13–15] and alcohol problems,[16] and the research team's prior work on a prescription opioid registry in a single health system.[17] To our knowledge, no study has established an EHR-based prescription opioid registry across multiple, diverse health systems with harmonized data and the ability to address current questions of prescription opioid use and OUD.

The goal of the overall project was to use EHR and insurance claims data to develop a prescription opioid registry across 10 diverse health systems with the ability to address important public health questions relating to opioid use, including questions of trends in use over time, reductions in opioid use and adverse events, opioid prescribing limits, and optimal length of buprenorphine treatment for OUD. It draws on our, and others, previous opioid research methodology and assumes that opioid fills represent use, a typical approach in studies based on pharmacy data.[18–20]

The objective of this article is to describe the development and implementation of the registry, the population it contains, and provide descriptive information on rates of opioid use from 2012 to 2018. The description of our methodological approach may be useful to other research teams and health systems in their efforts to study prescription opioid use and related problems.

MATERIALS AND METHODS

Setting

The opioid registry was developed in 10 health systems across several states: Baylor Scott and White, Texas; Essentia Health System, Minnesota, North Dakota, Wisconsin; Geisinger Health Systems, Pennsylvania; Henry Ford Health System (HFHS), Michigan; Kaiser Permanent Colorado; Kaiser Permanente Mid-Atlantic States, Maryland, Virginia, Washington DC; Kaiser Permanente Northern California (KPNC); Kaiser Permanente Northwest, Oregon; Kaiser Permanente Southern California; and Meyers Primary Care Institute/Fallon Health, Massachusetts (Table 1).

Table 1. Description of opioid registry sites

Site	Geographic area covered	Medication source[a]	Enrollment[b]	Tumor registry
Baylor Scott and White	Texas	Fills	Membership-based	None
Essentia Health System	Minnesota, North Dakota, Wisconsin	Orders	Utilization-based	Through December 31, 2018
Geisinger Health Systems	Pennsylvania	Orders/fills[c]	Membership and utilization-based	Through December 31, 2018
Henry Ford Health System[d]	Michigan	Orders	Utilization-based	Through December 31, 2018
Kaiser Permanente Mid Atlantic	Maryland, Virginia, Washington DC	Fills	Membership-based	Through December 14, 2018
Kaiser Permanente Northwest	Oregon	Fills	Membership-based	Through December 31, 2018
Kaiser Permanente Northern California	Northern California	Fills	Membership-based	Through December 31, 2017
Kaiser Permanente Southern California	Southern California	Fills	Membership-based	Through December 31, 2018[e]
Meyers Primary Care Institute/Fallon Health	Massachusetts	Fills	Membership-based	Through December 15, 2016

[a]The primary source for prescription medications is fills. Some sites capture only medication orders for some or all their registry patients.

[b]"Enrollment" refers to periods of time when the health system expects to have complete data for the patient. For most health systems, periods of enrollment are based on periods of paid membership. Other health systems serve patients who are not paid members and a utilization algorithm is used to determine periods of "proxy" enrollment. Finally, some sites serve a combination of these types of patients.

[c]For nonmember patients, orders and utilization-based enrollment algorithms are used; for member patients, fills and membership-based enrollment periods are used.

[d]Henry Ford Health System opioid registry includes data from January 1, 2014 to December 31, 2018. All other sites include data from January 1, 2012 to December 31, 2018.

[e]Tumor data for registry patients are included in the KPSC opioid registry. However, tumor data were not provided for other health plan members and therefore total denominator noncancer person time was not be determined.

The health systems are diverse, representing different geographic regions, patient populations, and delivery systems including primarily integrated delivery systems and health systems with mixed-model delivery systems (HFHS, Geisinger). The health systems are sites of the Health Systems Node of the National Drug Abuse Treatment Clinical Trials Network (CTN), which funded the project, and thus have established collaborative relationships that facilitated the development of the registry. Each health system has a Site Principal Investigator (PI) for the registry—this local investigator is an embedded researcher at their health system with expertise in local data structures and clinical environments.

Protocol

Protocol development was guided by prior work,[17] as well as other disease registries[13–15] and Agency for Healthcare Research and Quality guidelines for research registries.[21] KPNC, the lead site, collaborated with the local research team at each health system as well as consultants in the addiction field from the CTN to develop the approach. The protocol was approved by the National Drug Abuse Treatment CTN, and the KPNC Institutional Review Board (IRB) was the IRB of record for this multisite study.

Data sources

The primary data source was the Health Care Systems Research Network (HCSRN) Virtual Data Warehouse (VDW), a distributed data model which combines and harmonizes EHR, insurance claims, and mortality data across the participating health systems.[22] Programmers at each health system transform EHR and claim data elements from local data systems to a VDW standardized set of variable definitions, names, and codes. The VDW has been established for over 20 years, with rigorous harmonizing and quality assurance protocols. The common data structure allows for an efficient approach where health systems can exchange programming code developed at 1 health system and minimally adapt that code at other health systems to extract and analyze data.

Registry structure

The registry has a distributed data structure similar to the VDW, with a set of relational files that each represents a main content area (eg, opioid fills) (Figure 1). Records associated with the same patient are linked using a unique Study ID. The registry currently includes 18 patient-related files, 1 census-related file, 2 health plan person-time denominator files, and 5 lookup tables (Table 2). Patient-related files contain records linked to a specific individual (eg, opioid fills or diagnoses). The census-related file contains census information for each census tract in the health system's service area. The person-time denominator files include person-time of the system's underlying service population summarized by calendar month and stratified by gender, age, race/ethnicity, and cancer status. Lookup tables allow for elements like drug codes to be mapped to descriptions and strength. Files cover the following data domains: member-ship, mortality, provider-assigned diagnoses, OUD diagnoses, pharmacy fills/orders for opioids, benzodiazepines, gabapentin, "Z-drugs" (eg, zolpidem), antidepressants, procedures, providers, cancer diagnoses, and health care utilization. Files also contain created variables to support analyses (eg, person-time denominators). With a distributed structure, each health system maintains its own local version of the registry.

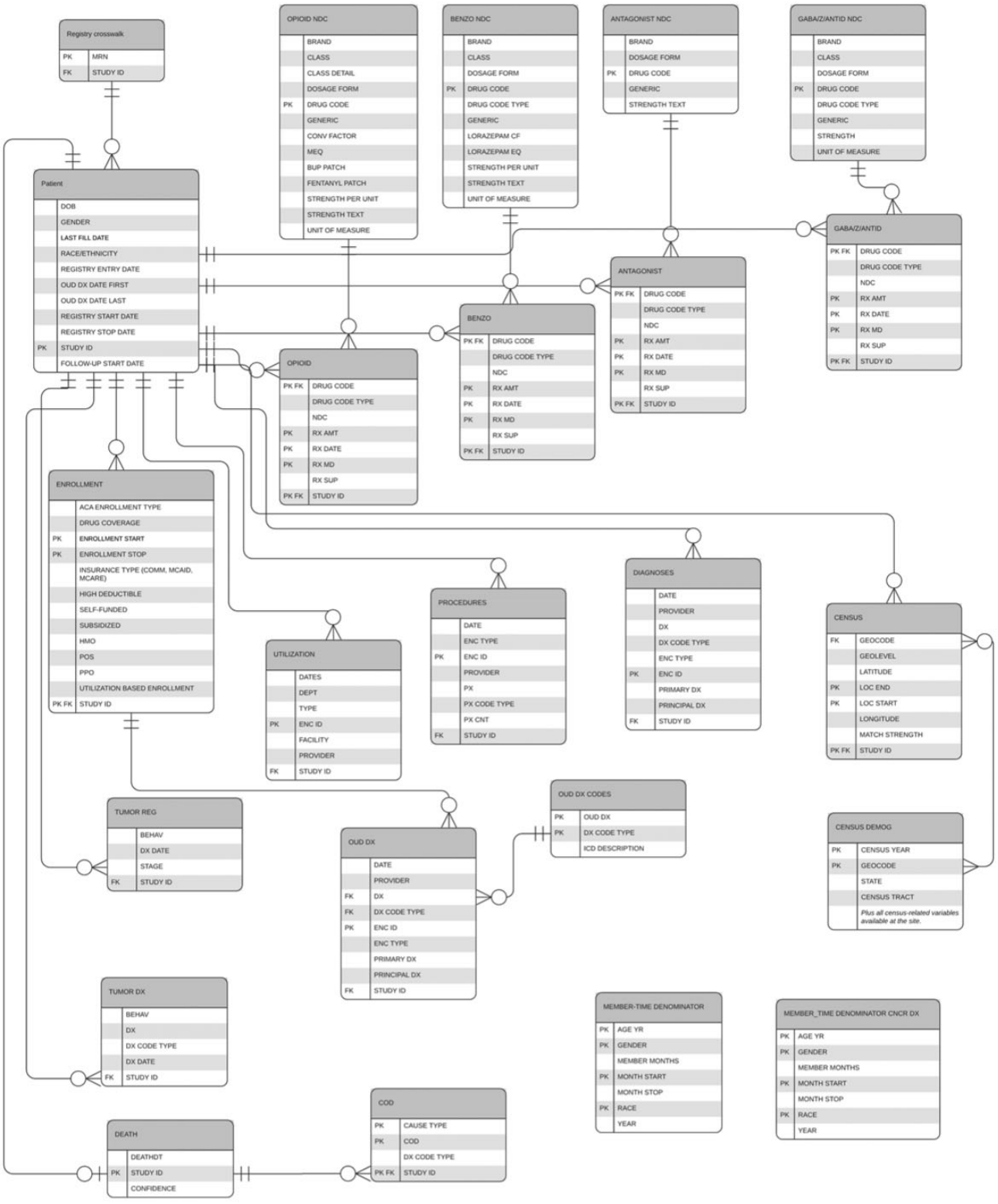

Figure 1. Opioid registry entity relationship diagram with selected variables shown.

Registry patients/inclusion criteria

Patients were included if, between January 1, 2012 and December 31, 2018, they had at least 1 outpatient opioid fill (or order at 3 of the mixed-model health systems) and/or an OUD diagnosis, and were 2: age 18 at the time of at least 1 opioid fill or OUD diagnoses. The registry's focus is on prescribed opioids (and includes all forms of buprenorphine), but patients with OUD were included to permit future studies of this patient group regardless of whether they had an opioid prescription. We defined the patient's registry entry date as the earliest of their first opioid fill or OUD diagnosis during the registry period.

Table 2. Description of opioid registry files

File	File type[a]	File description and notes
Benzodiazepine drug list	Lookup	List of benzodiazepine NDCs/DRUG_IDs
Benzodiazepine fills/orders	Patient	Benzodiazepine fills/orders[b]
Cancer diagnoses	Patient	Provider documented cancer diagnoses[c]
Cause of death	Patient	Causes of death
Census demographics	Census	Census data for all patient census tracts
Census locations	Patient	Census tract for each patient address during opioid registry period
Coverage	Patient	Medicare/Medicaid status of each subject in each month
Death	Patient	Known deaths and date of death for patients
Diagnosis	Patient	Provider documented diagnoses
Enrollment	Patient	Periods of enrollment in site health system
Gabapentin/Z-drugs/Antidepressant drug list	Lookup	List of gabapentin, Z-drugs, antidepressant NDCs/DRUG_IDs
Gabapentin/Z-drugs/Antidepressant fills/orders	Patient	Gabapentin, Z-drugs, antidepressant fills/orders[b]
Geocoded addresses for patients	Patient	Census block group of patient based on addresses
Member-time denominators (2 files)	Member-time	Member-time of the underlying population summarized by calendar month stratified by gender, age, race, and cancer status defined using (1) tumor or (2) cancer diagnosis data[d]
Opioid antagonist drug list	Lookup	List of opioid antagonist NDCs/DRUG_IDs
Opioid antagonist fills/orders	Patient	Opioid antagonist fills/orders[b]
Opioid drug list	Lookup	List of opioid NDCs/DRUG_IDs
Opioid fills/orders	Patient	Opioid fills/orders[b]
Opioid use disorder diagnoses	Patient	Opioid use disorder diagnoses
Opioid use disorder diagnosis codes	Lookup	List of ICD9/ICD10 codes for opioid use disorder
Patient[e]	Patient	One record with every patient, including demographic and other data
Procedures	Patient	Procedures
Study ID crosswalk	Patient	Crosswalk between patient ID used by site VDW and Study ID
Tumor	Patient	Tumors[f]
Utilization	Patient	Health services utilization (eg, visits, hospitalizations)

[a]"Patient" files include individual patient-level data (in the file's domain) for all persons from their observation start date until December 31, 2018. "Census" file includes census-related information for all census tracts. "Lookup" files include registry-related code sets. "Member-time" files include summarized person-time "at-risk," used as denominators. For most health systems member-time is based on periods of paid membership for all adult members of the health plan during the registry period. Other systems serve persons who are not members of their system and a utilization algorithm is used to determine periods of "proxy" membership. Finally, some sites serve a combination of these persons and use both membership- and utilization-based proxy membership to estimate member-time.

[b]Records represent outpatient medication fills at those sites with complete (or near complete) medication fill data for their member patients. Records represent prescriber orders at those sites with incomplete or no fill data.

[c]Cancer diagnoses. The primary use of this file is to censor patients at first cancer diagnosis within registry period or to identify if a person may be using opioids due to cancer pain. This file was used as a substitute for the Tumor file for those sites without a tumor file, and/or in combination with the Tumor file, and/or for sensitivity analyses.

[d](1) Member months had a status of "cancer" if they occurred after the member's first tumor date during the registry period. (2) Member months had a status of "cancer" if they occurred after the member's first cancer diagnosis during the registry period. Member time refers to the underlying population "at risk" for receiving opioid prescriptions. It includes persons who had opioid fills during the registry period as well as persons who did not have any opioid fills.

[e]Registry patients are all adults who had either an outpatient opioid fill/order and/or an opioid use disorder diagnosis between January 1, 2012 and December 31, 2018.

[f]Tumor records indicate all new tumors identified during the registry period. Some health systems do not have a cancer registry or tumor file. The primary use of this file is to censor patients at date of first tumor.

Registry files and data elements

We describe here the opioid fills, OUD, patient, and member-denominator files included in the registry since they are instrumental for entry into the registry and initial analyses of trends in opioid use. Each health system maintains their own set of files, containing data during the registry period (January 1, 2012–December 31, 2018) with the exception of one system which begins in 2014.

The opioid fills file contains a record for each outpatient opioid fill (or, at 3 sites, each order) during the registry period. For those sites using orders, all opioid orders—whether filled or not—are included. We excluded antitussives, anesthetics, antihistamines, antidiarrheals, and injectables. We include opioid formulations (including buprenorphine) used in the research team's prior research,[17–20] cross-referenced with the Centers for Disease Control and Prevention's (CDC) "Opioid NDC and Oral MME Conversion File".[23] Each record includes the date of the fill, the opioid's National Drug Code, a prescribing provider identifier, the amount dispensed, the day's supply and (when linked to the opioid lookup table), the type and form of opioid (eg, "hydrocodone" and "tablets"), strength per unit of the active opioid ingredient, and morphine milligram equivalent (MME) per unit. We calculated MMEs using Center for Medicare and Medicaid strength and conversion factors (Supplementary Appendix 1).[23]

The OUD diagnosis file contains a record for each OUD diagnosis during the registry period. The patient file contains one record for each person in either the opioid use file or the OUD diagnosis file, and includes demographic information and the patient's registry entry date. The patient file also includes an "observation start date" for each person that allows for a "look-back" period which is the latest of: (1) 1 year prior to the registry entry date; (2) the patient's

18th birthday; or (3) January 1, 2012. All other patient-related files (eg, service utilization, diagnoses, procedures) only include records for events occurring between the patient's observation start date and December 31, 2018.

The registry contains a summary member-time file with a record for every calendar month of the registry period with the number of members covered by the health plan during that month. These monthly denominator records are stratified by gender, age, race, and cancer-status, and are used to calculate rates of prescription opioid fills and MMEs in the underlying member-population served by the registry health systems. For health systems that offer health insurance, we defined the monthly denominators based on periods of paid enrollment ("membership") during the registry period; these patients have strong financial incentives to use that health care system. Two health systems used a utilization algorithm to determine denominator person-time because they regularly provide health care to persons for whom they do not provide insurance.[24,25] One site used paid enrollment to determine person-time for members and the utilization-based proxy for all other persons receiving care at their site.

Implementation and maintenance of the opioid registry

The opioid registry was implemented between September 2018 and May 2021, with a lead data scientist at KPNC and programmers at each participating health system. The overall registry team of site PIs, programmers, analysts, project managers, and consultants met biweekly to develop the data algorithms and data analytic strategies, troubleshoot data quality issues, and discuss initial findings of research questions. Each site had a site investigator with local knowledge to help put data, trends, and data anomalies into local context; these individuals also typically had content expertise in opioids, behavioral health, pharmacoepidemiology, addiction medicine, and biostatistics. In addition to related expertise among the site PIs, expertise from pain management and addiction medicine clinicians at each site was sought as needed.

The parent programming code was developed at the lead health system (KPNC) and then uploaded to a secure website for local programmers to access and implement at their health systems. Quality assurance procedures were iterative between each health system and KPNC. For each registry file, we generated a report with frequency counts and/or descriptive statistics that were reviewed by KPNC and the local health system for missing data and data anomalies. Five additional audit reports were run at each site after all files were created, which were reviewed by KPNC and the local health system. When possible, electronic chart review was conducted selectively to understand extreme outliers or missing data. All data anomalies were corrected as necessary. All code were written in SAS. Data elements were kept as granular as possible, and data cleaning minimized, to allow future studies flexibility regarding the format and structure of the data adapted to their own specific research questions. An overall data dictionary was developed. Although the data are maintained locally, bidirectional data sharing agreements were developed with each health system that allowed for quality-assurance activities, as well as approval for initial trend analyses.

Trends in opioid use from 2012 to 2018

Opioid prescribing guidelines and initiatives have focused primarily on noncancer patients, given that pain management for cancer patients has different clinical considerations. To describe trends in opioid prescribing among the noncancer population, we first extracted all opioid fills and associated MMEs from the registry opioid fill file, excluding fills after the date of a first malignant or metastatic tumor. Number of opioid fills and associated MMEs were summarized by calendar month into strata by patient age (at the time of the fill), gender, and race. Member-time denominators by calendar month, age, race, and cancer-status were extracted from the member-time files, and we retained only noncancer member-time strata. (Due to incomplete tumor data, 2 health systems used all opioid fills and all person-time for these analyses.) We calculated the opioid fills and total MMEs per member-month in each calendar month for the entire noncancer membership and by gender, age, and race groups. These rates measure overall opioids filled in the member population and therefore reflect both the amount of opioids received per patient and overall number of patients receiving opioids. We used direct standardization to standardize the rates to the gender, age and race/ethnicity distribution of the 2018 noncancer member population for all sites combined. When analyzing trends by demographic subgroups, the reference group for standardization was the 2018 population of that subgroup.

In addition, to understand the trends in noncancer use within the changing prescribing environment, we conducted interrupted time series (ITS) analyses treating the publication of the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain as an "intervention." The input dataset consisted of 1 record per month from January 2012 to December 2018. The dependent variable in the ordinary-least-squares model was the MMEs filled per member-month, standardized to the 2018 distribution of opioid registry members. Because preliminary inspection of the trend in MMEs per member-month indicated a possible change in slope beginning in 2014, we ran a sensitivity analysis using 2014, instead of 2012, as the starting date. We used SAS software Version 9.3 (SAS Institute Inc., Cary, NC, USA), and PROC AUTOREG to identify and adjust for any significant autoregressive terms.

RESULTS

Opioid registry patient characteristics

Across all 10 sites, the opioid registry included 6 249 710 patients, of whom 56% were women (Table 3), 35% were 18 to <40 years of age, 44% were 40 to <65, 16% were 65 to <80, and 5% were 2:80 years of age. Registry patients were diverse in terms of race/ethnicity, with 7% being Asian, 10% Black, 21% Hispanic, 9% other/unknown, and 53% white. In total, the registry captured over 40 million individual outpatient opioid fills.

Trends over time in outpatient opioid fills and MMEs

The number of prescription opioid fills and total MMEs per member-year declined between 2012 and 2018 (Figure 2). The decline in MMEs per member-year reflects both declines in the number of fills per member-year and in the MMEs per fill. The number of opioid fills increased from 0.714 per member-year in 2012 to 0.718 in 2013, and then declined from 0.718 in 2013 to 0.478 in 2018. MMEs per fill declined from an average of 985 per fill in 2012 to 758 in 2018. As a result, MMEs declined from 692 per member-year in 2012 to 362 in 2018. By December 2018, MMEs per member month were less than half of what they were in January 2012 (Figure 2). MMEs per member-month declined among both men and women, although declines were greater for women. By December 2018 the MMEs per member-month were approximately the same for both genders (Figure 3). Similar declines were seen in all

Table 3. Distribution of patients in opioid registry by demographics by site (n ¼ 6 249 710)

Characteristic	All sites (%)
Gender (% of site patients)	
Women	56.23
Men	43.76
Unknown	0.01
Age group (%)	
18 to <40	34.86
40 to <65	43.83
65 to <80	16.14
80þ	5.18
Race/Ethnicity (%)	
Asian	7.05
Black	10.30
Hispanic	20.50
Multiracial[a]	1.08
Native American	0.37
Other	0.39
Pacific Islander	0.47
Unknown	6.67
White	53.1

[a]Persons could be classified as "multiracial" if the primary race source at the site included multiracial as a category or allowed multiple different races to be specified.

age (Figure 4) and race/ethnicity groups (Figure 5). In particular, observed differences in MMEs per member-month by race/ethnicity were substantially less by the end of the study.

The ITS analysis examining the impact of the CDC Guideline using 2012 as the starting year indicated a statistically significant change in the trend in overall MMEs per member-month, with the postguideline trend having a steeper decline by 0.11 MMEs per month than the preguideline trend (Table 4). The ITS also indicated a downward shift in the postguideline trend of 0.72 MMEs per month, but this was not statistically significant (CI: −2.03 to 0.59). In the sensitivity analysis using 2014 as the starting date rather than 2012, we found no statistically significant changes in opioid use following the 2016 Guideline.

DISCUSSION

We developed and implemented an opioid registry representing 10 diverse health systems across the United States with a distributed data structure that includes patients with any prescription opioid use and/or OUD diagnosis. The registry contains over 6 million patients, diverse in terms of age, race, and gender, and over 40 million outpatient opioid prescription fills/orders. During the ongoing opioid-related public health crisis, this rich data source can be used to address critical questions of opioid prescribing.

Prescription opioid use declined steadily over the registry time period, beginning in 2012, measured by number of fills per member, MMEs per fill, and overall MMEs per member. Prescribers both reduced the number of prescriptions—fills per member-year declined by 33%— and the morphine-equivalents per fill (by an average of 23%). Combined, this resulted in overall reductions in opioid use per member-year by 48% over the registry period. These declining trends are consistent with national, Veteran's Health Administration (VA), and community health clinic data,[26–28] but at odds with a recent study using a large, national claims database of commercially insured and Medicare Advantage patients.[27] It is unclear why the contrasting findings, given a similarly insured population, although it is possible that the registry health systems were more nimble in changing opioid prescribing.

The decline in prescribing considerably predates the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain.[11] Findings do not indicate an additional impact of the CDC guidelines, contrary to a study by Bohnert et al[26] using national pharmacy data with 2012 as the first measurement year, but are consistent with a more recent analysis.[29] The measurement year makes a difference—we observed an association with CDC guidelines using 2012 as the initial measurement year, but not when using 2014 as the starting year, which we selected after observing that opioid use began a steeper decline in that year.

Physicians may have had concerns about prescribing opioids prior to 2016, and changed prescribing behavior. In addition, during the study time period health systems also implemented local prescribing initiatives,[28,30] which included reducing high dosages, additional criteria for initial prescriptions, and greater monitoring of high dose patients. Changes in acute and surgical pain treatment may also be reflected in decreased outpatient opioid use. Federal and state policies during the study period likely impacted trends, including: Centers for Medicare and Medicaid Services safety rules for opioid prescribing[31]; Food and Drug Administration risk evaluation and mitigation strategy on opioid prescriber education[32]; state prescription drug monitoring programs were implemented and integrated with health system EHRs; state limits on prescription duration, and; pain clinic regulations (eg, certification).

All demographic groups experienced a decline in opioid use, although some more modestly. Declines in use among women were greater than declines among men, which is important given past research showing older women have higher prevalence of long-term opioid use and that women are more likely to present with pain and be prescribed a pain medication.[20] Declines were seen in every age group, although steepest for the older age groups, even among those over 80 years of age, which may have positive implications for the risks of adverse events such as falls in the elderly. We also observed a narrowing of differences in opioid use among race/ethnicity groups, and in particular for Native American and white patients. Native Americans had considerably higher use than other race/ethnicity groups at the beginning of the study period and experienced the steepest decline over time.

Reasons for the convergence among the demographic groups cannot be determined with these data. Safer opioid prescribing efforts have focused on the highest dosage patients, which may translate into the steeper decreases observed here. Women typically use more health services, which present more opportunity for intervention (eg, tapering),[33] and they are also more likely to have coprescribing of benzodiazepines which may trigger greater scrutiny. Exploring the impact of reduced use in these patient subpopulations is an important research area, particularly with respect to patient outcomes such as functional status and pain. Few studies using large electronic datasets report trends in MMEs over this time period by age and gender, particularly with a population-based denominator, and to our knowledge none have done so by race and ethnicity. It will be important to continue to analyze these trends past 2018.

Observational data can be a key complement to traditional clinical trial and national survey data to address critical questions of the opioid crisis. Primary data collection is often not feasible given the considerable time and financial resources needed. Secondary data sources based on routinely collection health care data such as those used in the opioid registry, have significant advantages in reaching similar research goals given their large, diverse patient samples and

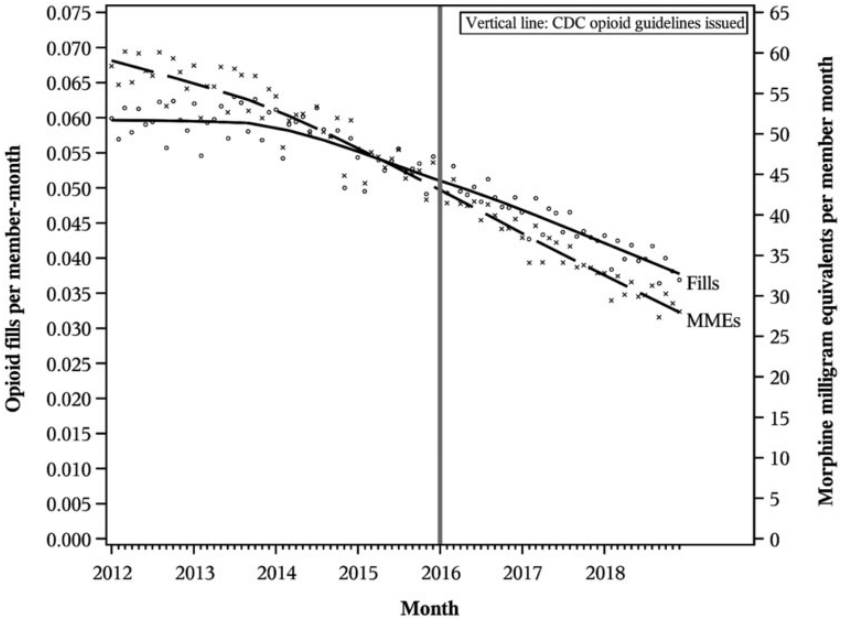

Figure 2. Outpatient opioid fills and morphine milligram equivalents per member-month by month, all opioid registry sites combined, 2012–2018.

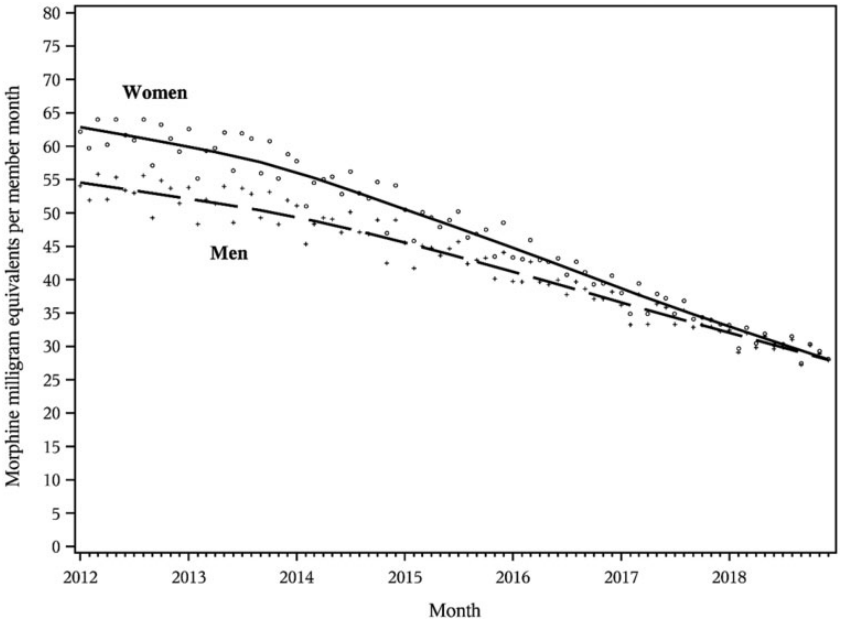

Figure 3. Outpatient morphine milligram equivalents filled per member-month by gender and month, all opioid registry sites combined, 2012–2018.

"real world" settings. The current registry uses EHR data, which can offer advantages over even some very large claims datasets, given the ability to access primary electronic data sources for data quality assessment or for focused auxiliary analyses, and their relatively greater depth compared with deidentified claims data.

Several elements facilitated the implementation of the registry, including a team with extensive expertise in analyzing EHR data. The team had experience running distributed code, conducting quality-assurance on EHR data, and using a common data model based on experience as members of the HSCRN. A critical piece is the involvement of an embedded Site PI at each health system with expertise in local data sources, and an understanding of the local clinical and operational context. A high level of trust among collaborators was also a key ingredient to successful implementation. Each site made important contributions to developing algorithms and in data interpretation—data were not simply aggregated together. A distributed model is employed because of the importance of local control and the preservation of data privacy, critical concerns of the health systems. The registry leverages existing and long-standing investments by the health systems to build and sustain electronic health care data—it is not a "plug and go" approach, but one that requires significant investment.

Limitations

The registry has limitations common to all observational studies relying on secondary data sources. Pharmacy fills may not capture actual

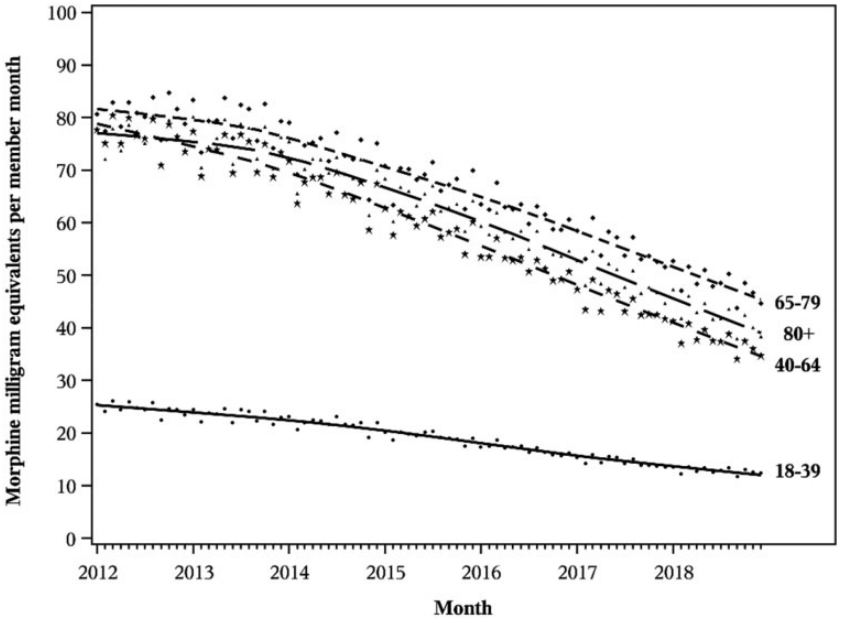

Figure 4. Outpatient morphine milligram equivalents filled per member-month by age group and month, all opioid registry sites combined, 2012–2018.

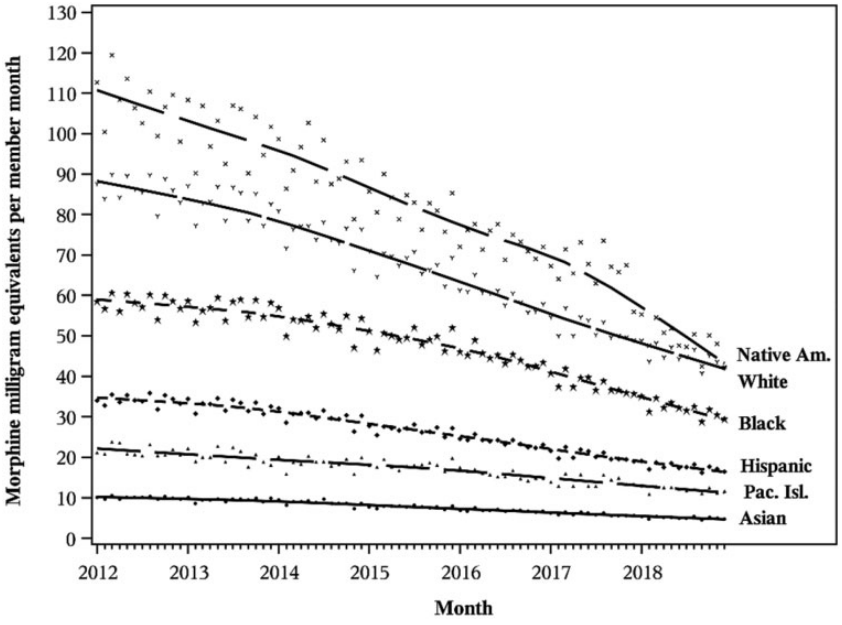

Figure 5. Outpatient morphine milligram equivalents filled per member-month by race/ethnicity and month, all opioid registry sites combined, 2012–2018.

Table 4. Interrupted time series analysis of change in morphine milligram equivalents per member-month after 2016 revised CDC opioid use guidelines, all registry sites combined

	Morphine milligram equivalents per member per month	
Interrupted time series model variable	Start year: 2012	Start year: 2014
Intercept	60.44 (59.00, 61.89)*	53.41 (52.66, 54.17)*
Preguideline expected trend	−0.33 (−0.38, −0.29)*	−0.40 (−0.45, −0.36)*
Postguideline shift	−0.72 (−2.03, 0.59)	−0.26 (−1.03, 0.51)
Postguideline change in trend	−0.11 (−0.19, −0.03)*	−0.04 (−0.09, 0.02)

*Significant at $P \leq .05$.

patient opioid consumption, and 3 sites used pharmacy order data, which may overestimate use. However, these data are typically used in pharmacoepidemiological research.[28] Illicit opioid use is not captured nor are prescriptions filled outside of the health systems without a claim. However, the large majority of patients fill their prescriptions within their health systems.[34] Identification of OUD is based on diagnoses recorded in the EHR as part of routine care, and individuals with higher service utilization may have more opportunity to be identified. Similar to other disease registries and some surveys, diagnoses in the EHR may not reflect when patient problems first emerged or recurred. OUD can be diagnosed in addiction medicine, psychiatry, and other inpatient and outpatient settings and the diagnostic criteria may be inconstantly applied across settings. In addition, OUD and other substance use disorder diagnoses can be underdiagnosed or not documented in the EHR due to concerns about patient privacy or to respond to patient requests. Findings may not generalize to other health systems or patient populations, although the structure and registry approach can be adapted to other systems. Finally, due to differences in organizational structure, 3 health systems define their membership denominator with a utilization algorithm rather than enrollment. Other studies have taken a similar approach.[24,25]

CONCLUSIONS AND FUTURE DIRECTIONS

Data from a multisite prescription opioid registry indicated a substantial reduction in opioid use over time due to both declines in the number of opioid prescriptions filled per member and in the MMEs per fill. This registry and the infrastructure to create it could be leveraged to respond to emerging knowledge gaps about the opioid crisis, such as key questions about prescribing limits, deprescribing, use of opioids for cancer, and the coronavirus disease 2019 pandemic impacts on opioid prescribing; indeed some of these analyses are currently planned as next steps. Although this infrastructure would require refreshing data over time and investments in data cleaning, local expertise, and scientific content knowledge to use effectively, it can be a valuable resource both to generate hypotheses and test them using observational methods. To our knowledge, a similar multisite resource using EHR data has not been described in the literature and we hope the methods described are useful for other teams interested in developing a similar resource.

FUNDING

This work was supported by the National Institute on Drug Abuse Clinical Trials Network and the National Institutes of Health HEAL Initiative under awards 3UG1DA040314 (Health Systems Node), UG1DA015815 (Western States Node), and UG1 DA013714 (Pacific Northwest Node). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or its NIH HEAL Initiative. Dr. Karmali received funding from The Permanente Medical Group for the Delivery Science Fellowship.

AUTHOR CONTRIBUTIONS

All authors who contributed to this article, and who are listed, meet all 4 criteria for authorship according to the ICMJE guidelines for authorship.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *JAMIA Open* online.

ACKNOWLEDGMENTS

We gratefully acknowledge Agatha Hinman for her assistance in preparing the article.

CONFLICT OF INTEREST STATEMENT

GTR has received research support on grants to Kaiser Permanente Division of Research in the past 3 years from Pfizer on topics unrelated to this study, and he and CIC, SEA, BA, JAB, RH, and JY have received support managed through their institution from the Industry PMR Consortium, a consortium of companies working together to conduct postmarketing studies required by the Food and Drug Administration that assess risks related to opioid analgesic use. RK completed nearly all her work on this article while a fellow at the Kaiser Permanente Northern California Division of Research and currently is a researcher at Mathematica. IB reports receiving royalties from UpToDate for content on incarceration and health. SEA has received research support on grants to the University of Massachusetts Chan Medical School in the past 3 years from Pfizer and GlaxoSmithKline on topics unrelated to this study.

DATA AVAILABILITY

The data underlying this article were extracted from the electronic health records at 10 study sites. Deidentified data are available upon reasonable request.

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