HHS Public Access

Author manuscript

J Behav Health Serv Res. Author manuscript; available in PMC 2016 October 01.

Published in final edited form as:

J Behav Health Serv Res. 2015 October ; 42(4): 540–553. doi:10.1007/s11414-014-9396-9.

Key Data Gaps Regarding the Public Health Issues Associated with Opioid Analgesics

Teresa D. Schmidt, MS[a], **J. David Haddox, DDS, MD**[b,c], **Alexandra E. Nielsen, MS**[a], **Wayne Wakeland, PhD**[a], and **John Fitzgerald, PhD**[b]

[a]Portland State University, Systems Science Graduate Program

[b]Purdue Pharma L.P

[c]Tufts University School of Medicine, Public Health & Community Medicine

Abstract

Most pharmaceutical opioids are used to treat pain and they have been demonstrated to be effective medications for many. Their abuse and misuse pose significant public health concerns in the United States. Research has provided much insight into the prevalence, scope, and drivers of opioid abuse, but a holistic understanding is limited by a lack of available data regarding key aspects of this public health problem. Twelve data gaps were revealed during the creation of a systems-level computer model of medical use, diversion, nonmedical use, and the adverse outcomes associated with opioid analgesics in the United States. Data specific to these gaps would enhance the validity and real-world applications of systems-level models of this public health problem, and would increase understanding of the complex system in which use and abuse occur. This paper provides an overview of these gaps, argues for the importance of closing them, and provides specific recommendations for future data collection efforts.

Background

Pharmaceutical opioids (morphine-like drugs) include opioid drug products indicated for use as analgesics, antitussives, antidiarrheals, and for the treatment of addiction. Opioid analgesics have been demonstrated to be effective medications for various acute and chronic pain conditions, including some cases of chronic non-malignant pain (CNMP),[1–4] and are used to treat millions of chronic pain sufferers in the United States.[5,6] At the same time, the abuse of opioid analgesics increased dramatically in the last decade, resulting in significant public health problems.[7] These medications are now among the most popular drugs for nonmedical use, second only to marijuana.[8,9] Adverse events associated with nonmedical use of opioid analgesics have increased significantly over the past two decades due to higher prevalence, frequency of use, and rates of initiation.[8,10,11] Overdose deaths in which

Teresa D. Schmidt, MS, tds@pdx.edu, phone: (509) 592-3588, fax: N/A
J. David Haddox, DDS, MD, Dr.J.David.Haddox@pharma.com, phone: (203) 588-7667, fax: (203) 588-6242
Alexandra E. Nielsen, MS, alexan3@pdx.edu, phone: (503) 349-3483, fax: N/A
Wayne Wakeland, PhD, wakeland@pdx.edu, phone: (503) 725-4975, fax: (503) 725-8489
John Fitzgerald, PhD, John.Fitzgerald@pharma.com, phone: (503) 343-5666, fax: N/A

Funding for this project was provided by Purdue Pharma L.P. Preliminary work that formed the basis for this manuscript was presented at the 72nd Annual Meeting of the College on Problems of Drug Dependence.

pharmaceutical opioids were detected outnumbered deaths involving heroin and deaths involving cocaine *combined* since 2001, and in 2007, outnumbered heroin-related overdose deaths by more than five times.[11]

The federal Food and Drug Administration (FDA) responded to the rise in opioid analgesic misuse and abuse by working with industry to develop a Risk Evaluation and Mitigation Strategies (REMS).[12] A REMS is designed to ensure that the benefits provided by a drug outweighs its risks.[13] Unfortunately, nonmedical use of pharmaceutical opioids has tended to resist government policy and regulation,[14] and prior research has found little evidence to suggest that many of the types of interventions required by REMS (e.g., medication guides) are effective in reducing the risk of medication misuse or abuse.[15]

To address this concern, a computer simulation was created to incorporate the full range of available data on use, misuse, and abuse of opioid analgesics into a systems-level model that would allow the user to evaluate the likely impact of several intervention alternatives.[16] System dynamics is a computer simulation methodology that describes a system in terms of stocks and flows which are governed by differential equations.[17,18] The system dynamics method is particularly well-suited for studying health care systems,[19] and has been successfully applied to public health phenomena such as the evaluation of policy options concerning cocaine prevalence[20,21] and health care reform.[22]

Despite much research into the prevalence, scope, and drivers of opioid misuse and abuse, application of system dynamics to this public health concern identified twelve specific gaps in available data that create significant limitations in understanding the inter-related phenomena modeled in a system dynamics approach. Advances in data collection are needed inform effective interventions to deter opioid misuse and abuse[15,23,24] and are critical for achieving a full understanding of the system of pharmaceutical opioid use and abuse in the United States. This paper provides an overview of gaps identified by the authors, argues for the importance of closing them, and provides specific recommendations for future data collection efforts.

Method

The creation of a system dynamics model of opioid analgesic use and abuse by Wakeland and colleagues[16] led to the identification of 12 gaps in available data. The model features the population dynamics of: (1) opioid analgesic treatment for CNMP, (2) medical use and abuse of opioid analgesics, (3) diversion of opioid analgesics for nonmedical use, (4) initiation of and frequency of nonmedical use among non-patients, and (5) the associated overdose deaths. Experts on chronic pain treatment, prescription drug abuse, and public health policy research provided instrumental feedback and guidance throughout the project by participating in a number of team meetings, presentations, and email conversations. Following its creation, the model was used to explore the likely effects of several policy intervention alternatives on opioid overdose deaths in the United States.

The full model contains 40 parameters, all warranting empirical support to establish validity and real-world applicability. The modeling team searched databases (e.g., PubMed,

PsychINFO) and federal and industry websites (e.g., CDC, DEA, RADARS® System), for empirical support for each parameter from early 2009 through 2011. Keywords included: opioids, opioid analgesics, (prescription) pain medications, chronic (noncancer) pain, pain treatment, supply, overdose, death, nonmedical use, misuse, abuse, dependence, and mortality rate. Guidance was periodically sought from panel members during team meetings or via email correspondence, which elicited additional insights and empirical references regarding various aspects of the model. Despite this expert consultation and intensive searching, some parameters lacked sufficient empirical support and, therefore, imposed potential limitations on the model's usefulness. More information regarding the model, parameters, and empirical support can be found elsewhere.[16]

Following the identification of areas where empirical support was limited, a list of data gaps was compiled and circulated within a network of colleagues, including all panel members and the research associates of one panel member. Colleagues were asked to: (1) identify any gaps that may have been filled in recent months, (2) suggest methods for addressing key gaps, and (3) identify which, if any, of the gaps seem likely to have limited relevance for informing policy interventions or improving understanding of the opioid analgesic system. Feedback and discussion with these colleagues resulted in the removal of what were termed "knowledge gaps"–those which reflect a need for future analyses on existing data–leaving only those gaps for which new data collection is needed. The following paragraphs summarize the data gaps that remained pertinent after this stage of refinement.

Results

Twelve data gaps (listed in Table 1) address data needs related to better understanding behaviors and effects of opioid analgesics, including the development of CNMP, therapeutic use, diversion, nonmedical use, and adverse outcomes. Each gap represents an opportunity to increase our understanding of the use, misuse, and abuse of opioid analgesics, and may inform the development of effective policy interventions to ameliorate the associated public health concerns.

1. Incidence of CNMP

Data on chronic pain incidence, or the rate at which individuals previously free from chronic pain develop it, are sparse. The Institute of Medicine estimates that about 100 million adult Americans live with chronic pain, and suggests that all Americans are at risk of developing chronic pain at some time in their lives.[25] Prevalence data, from the National Health and Nutrition Examination Survey (NHANES),[26] support an estimate of 29 million Americans aged 20 or older with chronic pain (defined as pain lasting three months or longer) during the period 1999–2002. However, NHANES' self-report data could have included transient pain conditions that resolved spontaneously or conditions for which no medical intervention was required, and some conditions causing frequent, recurrent pain may not have met the operational definition used in NHANES. Both of these limitations threaten the accuracy of the NHANES prevalence estimate, and data on prevalence cannot be used to derive an incidence rate. More information on the incidence of CNMP in the US population is needed

to better estimate the spread of CNMP and to indicate the extent to which it fluctuates over time.

2. Diagnosis Rate of CNMP

A similar data gap exists for the CNMP diagnosis rate. Research by Gureje and colleagues[27] at a primary care setting in Seattle, WA found that 11.2% of primary care patients who were previously free from chronic pain conditions (defined in this study as pain lasting six months or longer) were diagnosed with chronic pain during the year of the study. However, this analysis features only one care facility over a one-year period, and is limited to individuals already seeking medical care. A large proportion of self-reported chronic pain sufferers have been documented as not receiving medical diagnoses or treatment for chronic pain,[28] which point out the distinction between the incidence and diagnosis rate of CNMP. The difference between the number of individuals who develop CNMP each year and the number of individuals who are diagnosed with CNMP would indicate of the extent to which CNMP goes undiagnosed and possibly undertreated in the United States.

Data from insurance claims and managed care organizations are two resources for ascertaining the rate at which individuals are diagnosed with CNMP. Multiple proprietary databases contain insurance claims data, including MarketScan® Research Data, PharMetrix™, PharmaNet/i3, IMS Health® LRx, and SDI's Vector One®: Total Patient Tracker. However, these data provide a conservative estimate of the number of CNMP diagnoses per year, as some diagnoses do not generate insurance claims. The International Classification of Diseases (ICD-10) codes[29] for chronic pain are applied primarily for insurance claims purposes, and may not represent all aspects of the patient's condition or treatment.[30] Codes for CNMP may be recorded less consistently if a pain complaint is not the primary reason for a doctor visit and the physician does not prescribe opioids to treat pain. Further, with analysis of ICD codes, little information can be gleaned about severity, duration, or impact of persistent pain. Consequently, ICD-10 codes do not provide a reliable indicator of the incidence of CNMP diagnoses, and the apparent prevalence of CNMP (as evidenced by diagnosis rate) may be confounded with the opioid treatment rate. Further, people with pain, especially if comorbid with mental health or substance abuse, may be underrepresented in claims data since they may be more likely to be unemployed and uninsured due to these conditions.

3. Rate of Opioid Use to Treat CNMP

Data are needed on the fraction of individuals who receive opioid versus nonopioid treatments for CNMP. While opioid analgesics have been demonstrated to be effective medication for various CNMP conditions[1–4], there is less research on non-pharmaceutical treatments for chronic pain conditions. Chou and colleagues[15] call for more research on nonopioid treatments for CNMP, such as randomized trials that would evaluate opioid therapy against (and in combination with) behavioral therapy, multidisciplinary rehabilitation, or functional restoration. In addition to more information regarding the relative effectiveness of opioid and nonopioid treatments, data are needed on the opioid treatment fraction, or the number of diagnosed CNMP patients who do and do not receive opioid therapy. If measured before and after the implementation of prescribing regulations,

data on the opioid treatment rate would be an important indicator of the impact of those regulations on prescribers' choices of treatment.

4. Abuse-Related Opioid Consumption Rate among Those Treated for CNMP

People with substance-use disorders may abuse opioid analgesics during opioid treatment for pain.[31–33] Abuse of opioid analgesics, defined as the self-administered use of medication for a nonmedical purpose,[34] can manifest as patients consuming opioids more quickly than prescribed. While "over-consumption" of opioids is an imperfect indicator of abuse, as when patients escalate dosage due to inadequate pain treatment, it remained a criterion for having an opioid-use disorder in the newly-released Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).[35] Currently there are no data on the rate at which patients with opioid-use disorders over-consume medications or the amounts consumed in excess of medical need.

Pharmacy claims data provide one indication of consumption rates via records of multiple prescribers, multiple pharmacies, and early refills,[34–36] and proprietary insurance claim databases contain national-level data on many of the retail pharmacy transactions that are submitted to insurance companies. However, claims databases may not receive transaction information from all retail pharmacies[37] (e.g., when analgesics are purchased with cash, so no claim is generated) and may not always capture multiple prescribers, which limits their generalizability.

State prescription drug monitoring programs (PDMPs) are another source of individual-level data on pharmacy transactions within a given State. Multiple prescribers, pharmacies, and early refills are not captured by state PDMP databases, either, when prescriptions are filled in more than one State, and will not be unless and until faithful interoperability among the states is achieved. To that end, the National Association of Boards of Pharmacy has created a workable solution, NABP PMP InterConnect, which allows data from different state PDMPs to be consolidated into one report for clinical purposes (www.NABP.net/programs/pmpinterconnect/ nabp-pmp-interconnect). But neither PDMPs nor claims databases contain any information about adherence to prescribed regimen after a drug is dispensed.

Using early fills or refills as a proxy for "over-consumption" is problematic with either PDMP or claims databases, because early dispensing situations may also stem from misplacement, theft, travel situations, authorized dose escalation during titration or treatment of a transient pain flare, or compensation for under treatment, and may not indicate abuse. Cases of overconsumption can also be missed when patients delay refilling their prescriptions until the normal renewal would occur or if they obtain opioid medication through extra-medical routes. Because of these limitations, data continue to be sorely needed on the rate of abuse among patients with opioid-use disorders.

5. Average Amount Consumed per Event among Nonmedical Users

The amount of pharmaceutical opioids that are used nonmedically remains a critical and understudied indicator of the magnitude of prescription opioid abuse in the United States.[38] The National Survey of Drug Use and Health (NSDUH)[8] contains data regarding the frequency of use for a variety of different substances, including pharmaceutical opioids.

However, data about the amount taken per event of nonmedical use or per unit time are not routinely reported.

In addition to indicating the magnitude of prescription opioid abuse in the United States, information on quantities used among nonmedical users could inform the total nonmedical use demand and could allow for estimates of the impact of supply interventions, such as interdictions in supply chain theft[39] or prescription-drug take-back programs.[40] Addressing this gap would require measurement of the amount of pharmaceutical opioid taken per event (or per day, week, or another time unit) in conjunction with measurements of the number of nonmedical users and their frequency of nonmedical use.

6. Opioid Availability for Nonmedical Use

Another critical indicator of the magnitude of prescription opioid abuse is its availability to nonmedical users. Monitoring the total volume of opioid medication available for nonmedical consumption is hardly feasible, but estimates of the fraction of the U.S. population with access to these substances for nonmedical purposes is feasible and could serve as a useful proxy for availability. The Delaware School Survey and Monitoring the Future collect some data on perceived availability,[41–44] but these studies are limited to student populations.

Several proxy measures for accessibility of opioids for nonmedical use are collected by law enforcement. These include observations of opioid street price,[45] reports of theft or loss of controlled substances,[39] and the Automation of Reports and Consolidated Orders System (ARCOS),[46] a database maintained by the Drug Enforcement Administration (DEA) which tracks the volume of manufactured opioids sent to DEA registrants, such as physicians and pharmacies, and distributed by them. While there is no direct evidence whether a registrant's order is placed for illegitimate purposes, exceptionally large volumes of opioids, especially when dispensed directly through physician offices, are suspicious of diversion.[47] Data on street price, which is expected to reflect local changes in supply and demand, are also collected through the RADARS® System via a network of participating law enforcement officials,[45] and through online crowd sourcing.[48] Unfortunately, researchers currently do not have access to ARCOS data, and additional data on accessibility are needed to indicate the number of individuals with the opportunity to acquire opioids for nonmedical use. If followed over time, these data could be used to evaluate the impact of supply-focused interventions, and would also allow for the popularity/desirability of pharmaceutical opioids to be examined by comparing rates of accessibility to rates of nonmedical use.

As an extension, better data regarding the sources by which pharmaceutical opioids are accessible (e.g., friends and relatives, leftover prescriptions, dealers, etc.) would indicate the most prevalent/salient diversion routes, and perhaps those most warranting intervention. The NSDUH provides self-report data on direct sources of opioids for recent nonmedical use, but, with the exception of the categories involving "friends or relatives", the NSDUH does not elicit further information about where the nonmedical user's source acquired the opioids. (This may be justified, as it is questionable that a nonmedical user would know a dealer's or stranger's source.)

The NSDUH also does not measure the volume of drugs sourced by each route. For example, the most recent NSDUH report states that in 2011–2012, only 0.2% of nonmedical users indicated the Internet as the source for pain relievers most recently used nonmedically.[8] However, the DEA and other agencies have reported substantial volumes of opioid dosage units being diverted via the internet during 2009, primarily schedule III and schedule IV medications.[49] Variations over time in availability and amount diverted via these sources could also be used to indicate whether diversion mechanisms are responding as anticipated to supply-focused interventions.

7. Prevalence of Drug-Seeking Behaviors

In the 2011–2012 NSDUH surveys, approximately 82% of the nonmedical users who received their most recent supply of opioids for free from friends or relatives stated that their source had originally acquired the drugs from one doctor.[8] What remains unknown about this report is the nature of the relationships among the friends or relatives and the doctors, any of whom (sources or doctors) might be in a legitimate doctor-patient relationship or might be engaging in any of several illegitimate means of opioid acquisition or distribution.

Diversion of pharmaceutical opioids from their lawful purpose to illicit use occurs through a variety of routes including doctor shopping, illegal Internet sites purporting to be pharmacies, drug theft from various nodes in the supply/inventory chain (distributors, in-transit, pharmacies, nursing homes, hospitals, homes), prescription forgeries, unlawful prescribing by physicians, and pain-complaint fabrication.[50,51] Among the routes through which a doctor-patient relationship is implicated in opioid diversion, data appear to be most lacking on the number of individuals who masquerade as pain patients in order to acquire pharmaceutical opioids for nonmedical use or diversion. If collected over time, data on the prevalence of pain fabrication could serve as an indicator of the effectiveness of changes in clinical practice guidelines and policy interventions, such as those required by the FDA's REMS.[12]

8. Fraction of Diversion via Drug-Seeking People

In a complementary fashion, data are needed on the proportion of diverted pharmaceutical opioids that stem from drug-seeking people who fabricate or exaggerate pain behaviors and symptoms. Law enforcement officials assume that individuals who exaggerate or fabricate pain may be responsible for a disproportionate volume of diverted medication, compared to amounts obtained by other types of individuals who divert,[52] but this has not yet been directly measured. If captured, data on the fraction of diverted supply via drug-seeking people could be compared with fractions stemming from doctor shopping, prescription forgery, illicit prescribing, and other routes of diversion to identify those most warranting intervention. Ultimately, these data would provide substantial context allowing a more nuanced interpretation of the NSDUH findings about sources of pain relievers for nonmedical use.[8]

9. Amount Acquired via Doctor Shopping and Forgery

In addition to data on which groups of individuals are diverting, data are needed on the amount of pharmaceutical opioid medication–perhaps in morphine equivalents–acquired

through doctor shopping and forgery. Select individuals have been reported to acquire as many as thousands of extra pills via doctor shopping within a single year,[53] and while most cases of doctor shopping and prescription forgery may be less extreme, these methods likely constitute a significant diversion mechanism in the United States.[54]

Efforts to estimate the volume of supply of pharmaceutical opioids for nonmedical use should ideally be measured at the point of diversion. The volumes supplied via many 'organized-crime' diversion routes *are* measured at the point of diversion, through means such as DEA theft reports[39] and PDMP records of prescribers who are later proven to be involved in unlawful behaviors.[14] However, data are still needed on the amount of medication acquired through doctor shopping and forgery,[55] especially because doctor shopping cases that are identified by applying algorithms to pharmacy data[56] can be difficult to verify. Such data would indicate the extent to which these diversion routes are supplying nonmedical users, and would aid in the evaluation of policies and interventions that target diversion.

10. Amount Diverted/Retained via Drug-Seeking People

In measuring the amount of opioids diverted via doctor shopping and forgery, a finer detail that may be critically useful is the fraction of illegitimately acquired medication that is (a) diverted to others and (b) retained for personal nonmedical use. Data collected on the amount diverted and retained by doctor shoppers, prescription forgers, and drug-seeking people would indicate the extent to which these populations engage in illicit behaviors to supply themselves – likely in the case of individuals with opioid-use disorders – or to sell or share with others. These data would be useful for informing interventions, as it is likely that treatment programs for opioid-use disorders would be less impactful with individuals who engage in doctor shopping, forgery, or pain fabrication primarily to obtain a supply for illicit sale or trade.

11. Thwart Rate of Forgery and Doctor Shopping Attempts

Very little is known about the proportion of doctor shopping attempts and forged prescriptions that are thwarted by prescribers and dispensing pharmacists, or, conversely, what fraction of attempts are successfully completed. There is evidence of the fraction of people who engage in doctor shopping and forgery,[56–58] but evidence is lacking about the fraction of doctor shopping and forgery attempts that are thwarted versus those that are successful. Some of the research on PDMP effectiveness[15] will depend on data regarding the prevalence and incidence of doctor shopping and forgery, and on evidence that more attempts are being thwarted as a result of PDMP implementation, ongoing development, and interoperability among states. Therefore, state-specific data collection efforts are sorely needed to document the thwart rate of forgery and doctor shopping attempts.

12. Opioid Overdose and All-Cause Mortality Rates

The increase in overdose and all-cause mortality rates for individuals who use pharmaceutical opioids nonmedically is a critical indicator of the severity of the public health problems of nonmedical use as and unintentionally-problematic prescribing. However, cross-sectional as well as longitudinal data on opioid mortality remain severely

limited. Longitudinal data are available for the elevated mortality rate of many drug-using populations, such as heroin, cocaine, and methamphetamine users,[59] but the elevated mortality rates for medical and nonmedical users of pharmaceutical opioids remain unknown. Longitudinal data are also very much needed regarding four related mortality rates listed in Table 1, including overdose and all-cause mortality rates of individuals (a) with and without a history of opioid-analgesic treatment for CNMP, and (b) with and without a history of significant nonmedical opioid use, such as that associated with an opioid-use disorder.

In addition, current data collection procedures regarding opioid overdose deaths are often misleading. Fatalities in which opioids are detected are often described as “opioid deaths” in coroner and medical examiner reports, despite the frequent involvement of multiple drugs in these fatalities.[60,61] Consistent differentiation between “opioid deaths” (due to an opioid alone) and “polydrug deaths” (due to multiple drugs) would provide more detail and precision to estimates of overdose fatalities resulting from pharmaceutical opioids. Similarly, the benefits and risks of using opioids alone and in combination with other types of drugs for medical purposes could be examined more fully with data on the rates of overdose and all-cause mortality associated with opioid treatment for CNMP and acutely painful conditions.

Discussion and Research Recommendations

A comprehensive analysis of the benefits and risks of opioid analgesics requires better data in several areas. Measurements of incidence, severity, impact, diagnosis, and treatment rates (by use of opioids with or without other approaches) of chronic nonmalignant pain conditions would indicate the magnitude of CNMP as a public health problem and would also indicate the prevalence of non-diagnosis, under treatment, and inappropriate treatment. Information regarding the prevalence of fabricated pain complaints and the extent to which forgery, doctor shopping, and abuse-related opioid consumption occur could inform the development of alert systems among PDMPs, and could aid in the evaluation of their effectiveness. Data on the levels of nonmedical consumption, availability of opioids for nonmedical use, and the amounts diverted by various methods would identify the most salient diversion routes and points of intervention. Data characterizing the rates and precise causes of mortality of individuals who use pharmaceutical opioids medically and nonmedically are critical indicators of the public health risks of pharmaceutical opioids. Closing these gaps would provide a more complete understanding of the system of pharmaceutical opioid use and abuse in the United States, and would have many implications for practice and policy interventions.

Recommendations for Expanding Current Data Collection

Existing data come from a variety of sources, including federal agencies, proprietary systems, national organizations, academic institutions, industry, and state and regional government agencies. To represent as accurately as possible the U.S. population, many of the gaps identified here would most feasibly be addressed by national organizations or federal agencies. For example, the NSDUH collects data at a national scale and already

includes questions about the sources of various illicit drugs. This survey could be augmented to ask respondents about the degree to which they believe that pharmaceutical opioids are accessible for nonmedical use (Gap #6), through which source(s) they believe it to be accessible (Gap #10), and estimates of the amounts of drugs diverted through or obtained from various sources (Gap #10). Research on those seeking treatment for abuse of opioid analgesics could be expanded to assess the ease with which opioids have been available to them (Gaps #6) and the relative accessed through various sources (Gap #8). Other ongoing data collection efforts, such as those implemented by Monitoring the Future (MTF) and the National Epidemiologic Study of Alcohol and Related Conditions (NESARC) might also be augmented to address these gaps more definitively.

National-level data collection on nonmedical use could also be expanded to include the amount of pharmaceutical opioid taken per usage event (Gap #5). For example, if the NSDUH were to ask about the amount of drug used alongside its existing questions on the frequency of nonmedical use, the resulting data could be used to estimate the amount of nonmedical opioid consumption in the United States, in a fashion similar to Katz, Birnbaum, and Caster.[38] Such data over time could be used to estimate the impact of supply-focused interventions.

The US Standard Certificate of Death and corresponding instructions could be revised to indicate the option for poly-drug overdose as the primary cause of death, instead of implying that one drug must be selected as the cause. Death certificate revisions would best be accompanied by training in its use and regulatory changes that would encourage complete and detailed accounts of cause of death. This revision would allow for more granular data to be stored in the CDC's database and would allow for more detailed analyses.[62] Continuing education courses for medical examiners and coroners and their staff could improve attribution of cause of death when drugs with wide therapeutic indices, such as opioids, are detected alone or in combination with other licit or illicit drugs. These efforts would help to clarify the severity of problems associated with pharmaceutical opioids, and would assist in the estimate of overdose mortality rates (Gap #12).

Studies investigating the prevalence of chronic pain, such as those conducted by the World Health Organization[26] and the American Pain Society[28] might be augmented to investigate (a) the date of onset of pain conditions, (b) the date of chronic pain diagnosis, and (c) the date of onset of opioid treatment. Annually administered surveys, such as the CDC's NHANES could also be expanded to track new cases of CNMP. Given a representative sample of the US population, these additional measures could help to establish the incidence of CNMP (Gap #1) and the proportion of CNMP-suffering individuals who are diagnosed each year (Gap #2). If such studies were to collect a modest amount of demographic data, the data might also identify subpopulations that are especially at risk for CNMP. Data collection on treatment satisfaction could also indicate the number of people with CNMP who are treated satisfactorily with interventions other than opioid analgesics (Gap #3).

Rates of diagnosis (Gap #2) and treatment (Gap #3) might also be partly addressed through analysis of commercial, Medicare, and Medicaid claims databases, as insurance claims can indicate treatment durations and diagnoses for pain, as well as other conditions that are

likely to be associated with CNMP (e g., diabetic neuropathy). When coupled with estimates of the average duration of treatment for CNMP, information regarding CNMP incidence could be used to better anticipate the demand for CNMP-related medical care in future years.

Recommendations for Future Data Collection

Several national-level data gaps require systematic investigation. Measuring the fraction of CNMP patients who are treated with opioids versus nonopioid treatment options (Gap #3) requires physicians to record ICD-10 codes consistently for CNMP complaints, even when pain complaints are not the patient's primary reason for seeing a doctor and when physicians elect not to prescribe opioid therapy. While it may not be feasible for physicians to change their general diagnostic coding practices, it may be possible for a representative sample of physicians to adopt this practice temporarily in the context of a research study. It is also possible that more consistent use of electronic health records following incentives from the Centers for Medicare and Medicaid Services will aid in capturing more detail about chronic pain.

Clinical practice guidelines or quality indicators relating to diagnosing and managing CNMP may also improve data collection. Even with more consistent application of newer, pain-specific diagnosis codes, much detail is lacking (e.g., severity, impact, duration, temporal variation), which may necessitate further codes or revision of existing codes to capture this important information. In addition, longitudinal research – such as a recent study on heroin addicts[63] – would be necessary to estimate the mortality rates associated with medical and nonmedical pharmaceutical opioid use (Gap #12). These projects might stem from initial efforts via MTF or NESARC.

Self-report studies may be the only feasible strategy for addressing some gaps: the prevalence of drug-seeking in the United States (Gap #7), the fraction of opioid diversion from drug-seeking individuals (Gap #8), and the amount of abuse-related opioid consumption among CNMP patients with use disorders (Gap #4), would almost certainly need to stem from questioning a representative sample of people presenting for pain care about their pain conditions and abuse behaviors. Similarly, the thwart rate of doctor shopping and forgery attempts (Gap #11), the amount acquired (Gap #9) and the amount retained for personal use versus diverted for sale or sharing purposes (Gap #10), would require the collection of self-report data from a large and representative sample of individuals who fill prescriptions or attempt to fill them, or perhaps even from a representative sample of pharmacies that would actively record refusals to dispense. Even if collected, there would be limitations to these data, as people being treated for CNMP are not likely to be forthcoming about their abuse of medications. Assuring anonymity and accuracy in this context would be both essential and challenging.

Limitations

To the best of the authors' knowledge, the twelve gaps identified in this article have persisted despite the significant amount of research that has been done regarding the prevalence, scope, and drivers of misuse and abuse of opioid analgesics. These critical gaps

in data collection efforts impact our understanding of the complex system of pharmaceutical opioid use and abuse in the United States, as well as our ability to ameliorate the risks associated with pharmaceutical opioids.

As our understanding of this complex system develops, it is likely that additional gaps will become apparent. The data gaps included here were drawn entirely from the list of parameters needed to support research to construct a systems-level dynamic model of opioid pain treatment, diversion, and misuse. From this lengthy list, parameters were chosen which: (1) to the best of authors' knowledge lacked empirical support, (2) seemed feasible to address in future data collection efforts, and (3) were arguably relevant to inform policy interventions or improve understanding of the opioid analgesic system. It is likely that additional gaps exist outside the boundaries of the dynamic model and further that these gaps are also critical for understanding and intervening within the pharmaceutical opioid system. Even for those aspects of the problem where data is available, evidence suggests that there is tremendous variation in the routes of diversion,[64] routes of administration,[65] and nonmedical use patterns along cultural,[66,67] geographical,[44] and temporal lines.[68]

Conclusion

To better understand the dynamics of the use and abuse of opioid analgesics and to create a more robust model for simulating various policy interventions, more data are needed regarding: (a) the incidence, diagnosis, and opioid treatment rates of CNMP, (b) the typical rate of abuserelated consumption among people with opioid-use disorders, (c) the typical accessibility to opioids for nonmedical use and the amounts taken per nonmedical use event, (d) the prevalence of drug-seeking behaviors and the fraction of diverted supply they render, (e) the thwart rate, retention/diversion fraction, and amount acquired in doctor shopping and prescription forgery attempts, and (f) the overdose and all-cause mortality rates for medical and nonmedical users of pharmaceutical opioids. Among these gaps, several appear to require entirely new studies to be designed, and many would require a reliance on self-report data of unlawful activities, which would likely be subject to self-report bias. The prevalence of drug-seeking, the frequency with which doctor shopping and prescription forgery go undetected, and the typical amounts taken per nonmedical use event are several examples of critical data on the pharmaceutical opioid system that are cannot be obtained by direct observation.

Despite challenges associated with data collection for many of these gaps, several could be addressed by highly feasible adjustments to existing data collection efforts. Questions about availability and dosage levels of opioids for nonmedical use could be added to regularly-implemented national surveys. Data gaps on CNMP diagnosis and treatment could be addressed by expanding future investigations on the *prevalence* of chronic pain to include dates of pain onset and opioid treatment. Existing longitudinal datasets, such as MTF, could potentially be expanded to provide a longer-term cohort study that could help to estimate overdose and all-cause mortality rates associated with medical and nonmedical use of pharmaceutical opioids.

Many of the gaps described in this article represent opportunities to achieve a more holistic understanding of the system of medical use, nonmedical use, diversion, and adverse outcomes associated with pharmaceutical opioids. Research to address these gaps would assist in the development, implementation, and evaluation of interventions at various points in the system of pharmaceutical opioid use and abuse in the United States.

Implications for Behavioral Health

Many of the gaps described in this article represent opportunities to achieve a more holistic understanding of the system of medical use, nonmedical use, diversion, and adverse outcomes associated with pharmaceutical opioids. Research to address these gaps would assist in the development, implementation, and evaluation of interventions at various points in the system of pharmaceutical opioid use and abuse in the United States.

Acknowledgments

The authors also appreciate the significant contributions from Howard Chilcoat, Ph.D., Aaron Gilson, Ph.D., Dennis McCarty, Ph.D., and Lynn Webster, M.D., who provided valuable insight into the organization of the manuscript and the relevance of its contents. Additional support was provided from NIDA grant number 5R21DA031361-02.

Disclosures

Wayne Wakeland, PhD, Teresa Schmidt, MA, and Alexandra Nielsen, BS, were compensated through a research grant to Portland State University funded by Purdue Pharma L.P. John Fitzgerald, PhD is a full-time employee of Purdue Pharma L.P. J. David Haddox, DDS, MD is a full-time employee of Purdue Pharma L.P. and receives no compensation from Tufts University.

References

1. Furlan AD, Sandoval JA, Mailis-Gagnon A, et al. Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects. Canadian Medical Association. 2006; 174(11):1589–1594.
2. Whittle SL, Richards BL, Husni E, et al. Opioid therapy for treating rheumatoid arthritis pain. Cochrane Database of Systematic Reviews. 2011; 11 Available at: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003113.pub3/pdf/standard.
3. Noble, M.; Treadwell, JR.; Tregear, SJ., et al. The Cochrane Collaboration. Long-term opioid management for chronic noncancer pain. In: Noble, M., editor. Cochrane Database of Systematic Reviews. Chichester, UK: John Wiley & Sons, Ltd; 2010. Available at: http://doi.wiley.com/10.1002/14651858.CD006605.pub2. [Accessed February 10, 2013]
4. Eisenberg E, McNicol E, Carr DB. Opioids for neuropathic pain. Cochrane Database of Systematic Reviews. 2006; 3 Available at: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006146/pdf/standard.
5. Caudill-Slosberg MA, Schwartz LM, Woloshin S. Office visits and analgesic prescriptions for musculoskeletal pain in US: 1980 vs. 2000. Pain. 2004; 109(3):514–519. [PubMed: 15157714]
6. Governale, L. [Accessed March 9, 2013] Outpatient Prescription Opioid Utilization in the U.S., Years 2000–2009. 2010. Available at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndLifeSupportDrugsAdvisoryCommittee/UCM220950.pdf.
7. Volkow ND, McLellan TA. Curtailing diversion and abuse of opioid analgesics without jeopardizing pain treatment. Journal of the American Medical Association. 2011; 305(13):1346–1347. [PubMed: 21467287]
8. [Accessed February 26, 2013] Substance Abuse and Mental Health Services Administration. Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings. 2013.

Available at: http://www.samhsa.gov/data/NSDUH/2012SummNatFindDetTables/NationalFindings/NSDUHresults2012.pdf.

9. Alford DP, Livingston EH. Misuse of Opioid Medication. Journal of the American Medical Association. 2013; 309(19):2055–2055. [PubMed: 23677318]
10. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. Journal of the American Medical Association. 2008; 300(22):2613–2620. [PubMed: 19066381]
11. Centers for Disease Control and Prevention (U.S.), National Center for Injury Prevention and Control (U.S.). [Accessed March 4, 2013] Unintentional drug poisoning in the United States. 2010. Available at: http://www.cdc.gov/HomeandRecreationalSafety/Poisoning/brief_full_page.htm.
12. Food and Drug Administration. [Accessed May 3, 2013] Extended-release (ER) and long-acting (LA) opioid analgesics risk evaluation and mitigation strategy (REMS). 2013. Available at: http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm163647.htm.
13. Leiderman DB. Risk management of drug products and the U.S. Food and Drug Administration: Evolution and context. Drug and Alcohol Dependence. 2009; 105:S9–S13. [PubMed: 19307069]
14. Fishman SM, Papazian JS, Gonzalez S, et al. Regulating opioid prescribing through prescription monitoring programs: Balancing drug diversion and treatment of pain. Pain Medicine. 2004; 5(3): 309–324. [PubMed: 15367312]
15. Chou R, Ballantyne JC, Fanciullo GJ, et al. Research gaps on use of opioids for chronic noncancer pain: findings from a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. Journal of Pain. 2009; 10(2):147. [PubMed: 19187891]
16. Wakeland W, Nielsen A, Schmidt TD, et al. Modeling the Impact of Simulation Educational Interventions on the Use and Abuse of Pharmaceutical Opioids in the United States: A Report on Initial Efforts. Health Education & Behavior. in press.
17. Forrester, JW. Industrial dynamics. Cambridge, Mass: M.I.T. Press; 1961.
18. Sterman, J. Business dynamics: systems thinking and modeling for a complex world. Boston: Irwin/McGraw-Hill; 2000.
19. Sterman JD. Learning from evidence in a complex world. American Journal of Public Health. 2006; 96(3) Available at: http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2005.066043.
20. Homer JB. A system dynamics model for cocaine prevalence estimation and trend projection. Journal of Drug Issues. 1993 Available at: http://psycnet.apa.org/psycinfo/1993-43867-001.
21. Homer JB. Projecting the impact of law enforcement on cocaine prevalence: a system dynamics approach. Journal of Drug Issues. 1993; 23:281–281.
22. Milstein B, Homer J, Hirsch G. Analyzing national health reform strategies with a dynamic simulation model. American Journal of Public Health. 2010; 100(5) Available at: http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2009.174490.
23. Dasgupta N, Kramer ED, Zalman M-A, et al. Association between non-medical and prescriptive usage of opioids. Drug and Alcohol Dependence. 2006; 82(2):135–142. [PubMed: 16236466]
24. Fischer B, Manzoni P, Rehm J. Comparing Injecting and Non-Injecting Illicit Opioid Users in a Multisite Canadian Sample (OPICAN Cohort). European Addiction Research. 2006; 12(4):230–239. [PubMed: 16968998]
25. Institute of Medicine (U.S.). Relieving pain in America a blueprint for transforming prevention, care, education, and research. Washington, D.C: National Academies Press; 2011. Committee on Advancing Pain Research C. Available at: http://site.ebrary.com/id/10520732. [Accessed February 23, 2013]
26. Hardt J, Jacobsen C, Goldberg J, et al. Prevalence of Chronic Pain in a Representative Sample in the United States. Pain Medicine. 2008; 9(7):803–812. [PubMed: 18346058]
27. Gureje O, Simon GE, Von Korff M. A cross-national study of the course of persistent pain in primary care. Pain. 2001; 92(1):195–200. [PubMed: 11323140]
28. Roper Starch Worldwide. Chronic pain in America: Roadblocks to relief. American Academy of Pain Medicine, American Pain Society, Janssen Pharmceuticals. 1999

29. World Health Organization. International statistical classification of diseases and related health problems. Geneva: World Health Organization; 1992.
30. Strom BL. Data validity issues in using claims data. Pharmacoepidemiology and Drug Safety. 2001; 10(5):389–392. [PubMed: 11802582]
31. Edlund MJ, Steffick D, Hudson T, et al. Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. Pain. 2007; 129(3):355–362. [PubMed: 17449178]
32. Martell BA, O'Connor PG, Kerns RD, et al. Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. Annals Internal Medicine. 2007; 146(2): 116–127.
33. Weisner CM, Campbell CI, Ray GT, et al. Trends in prescribed opioid therapy for non-cancer pain for individuals with prior substance use disorders. Pain. 2009; 145(3):287–293. [PubMed: 19581051]
34. Katz N, Panas L, Kim ML, et al. Usefulness of prescription monitoring programs for surveillance —analysis of Schedule II opioid prescription data in Massachusetts, 1996–2006. Pharmacoepidemiology and Drug Safety. 2010; 19(2):115–123. [PubMed: 20014166]
35. Hasin DS, O'Brien CP, Auriacombe M, et al. DSM-5 Criteria for Substance Use Disorders: Recommendations and Rationale. American Journal of Psychiatry. 2013; 170(8):834–851. [PubMed: 23903334]
36. Sullivan MD, Edlund MJ, Fan MY, et al. Risks for possible and probable opioid misuse among recipients of chronic opioid therapy in commercial and medicaid insurance plans: The TROUP Study. Pain. 2010; 150(2):332. [PubMed: 20554392]
37. Lee, JH.; Kuyateh, F.; Mehta, H. [Accessed August 27, 2012] Department of Health and Human Services, Public Health Service, Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology. Serious Adverse Events. 2008. Available at: http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM234301.pdf.
38. Katz NP, Birnbaum HG, Castor A. Volume of prescription opioids used nonmedically in the United States. Journal of Pain and Palliative Care Pharmacotherapy. 2010; 24(2):141–144. [PubMed: 20504136]
39. Joranson DE, Gilson AM. Drug Crime Is a Source of Abused Pain Medications in the United States. Journal of Pain Symptom Management. 2005; 30(4):299–301. [PubMed: 16256890]
40. Gray JA, Hagemeier NE. Prescription drug abuse and DEA-sanctioned drug take-back events: characteristics and outcomes in rural Appalachia. Archives of Internal Medicine. 2012; 172(15): 1186–1187. [PubMed: 22733245]
41. Center for Drug and Alcohol Studies. The Delaware School Survey: Alcohol, Tobacco, and Other Drug Abuse Among Delaware Students. 2011 Available at: http://www.udel.edu/delawaredata/Pages/level03/delschsurv.htm.
42. Center for Drug and Alcohol Studies. Delaware School Survey: Alcohol, Tobacco & Other Drug Abuse Among Delaware Students. 2010 Available at: http://www.udel.edu/delawaredata/Files/2010StateReport.pdf.
43. Center for Drug and Alcohol Studies. Delaware Secondary School Student Assent and Survey instructions. 2011 Available at: http://www.udel.edu/delawaredata/Files/DSS/225793-13%20secondary%20back%20from%20s.pdf.
44. Johnson LD, O'Malley PM, Bachman JG, et al. Monitoring the Future: National Results on Adolescent Drug Use: Overview of Key Findings, 2012. University of Michigan Institute for Social Research. 2013
45. Severtson SG, Bartelson BB, Davis JM, et al. Reduced Abuse, Therapeutic Errors, and Diversion Following Reformulation of Extended-Release Oxycodone in 2010. Journal of Pain. 2013
46. US Department of Justice (USDOJ). [Accessed August 31, 2013] Drug Enforcement, Drug Enforcement Administration. ARCOS: Automation of Reports and Consolidated Orders System. Available at: http://www.deadiversion.usdoj.gov/arcos/index.html.
47. Scott R. Testimonry Before the United states House of Representatives Hearing on the Growing of Prescription Drug Diversion. 2011

48. Dasgupta N, Freifeld C, Brownstein JS, et al. Crowdsourcing Black Market Prices For Prescription Opioids. Journal of Medical Internet Research. 2013; 15(8):e178. [PubMed: 23956042]
49. Inciardi JA, Surratt HL, Cicero TJ, et al. Prescription drugs purchased through the internet: Who are the end users? Drug and Alcohol Dependence. 2010; 110(1):21. [PubMed: 20227199]
50. Rigg KK, March SJ, Inciardi JA. Prescription Drug Abuse & Diversion: Role of the Pain Clinic. Journal of Drug Issues. 2010; 40(3):681–702. [PubMed: 21278927]
51. Trescot AM, Boswell MV, Atluri SL, et al. Opioid guidelines in the management of chronic non-cancer pain. Pain Physician. 2006; 9(1):1. [PubMed: 16700278]
52. Inciardi JA, Surratt HL, Kurtz SP, et al. Mechanisms of prescription drug diversion among drug-involved club-and street-based populations. Pain Medicine. 2007; 8(2):171–183. [PubMed: 17305688]
53. Kraman P. Drug abuse in America: prescription drug diversion. Council of State Governments. 2004 Available at: http://www.csg.org/knowledgecenter/docs/TA0404DrugDiversion.pdf. Published in 2004.
54. Califano JA. Under the counter: The diversion and abuse of controlled prescription drugs in the US. National Center on Addiction Substance Abuse at Columbia University. 2005 Available at: http://buysafedrugs.info/uploadedfiles/section5.pdf.
55. Gilson AM, Ryan KM, Joranson DE, et al. A reassessment of trends in the medical use and abuse of opioid analgesics and implications for diversion control: 1997–2002. J Pain Symptom Management. 2004; 28(2):176–188.
56. Cepeda MS, Fife D, Chow W, et al. Assessing Opioid Shopping Behaviour. Drug Safety. 2012; 35(4):325–334. [PubMed: 22339505]
57. Colliver, JD.; Kroutil, LA.; Dai, L., et al. Misuse of prescription drugs: data from the 2002, 2003 and 2004 national surveys on drug use and health. Rockville, Md.: Dept. of Health and Human Services, Substance Abuse and Mental Health Services Administration, Office of Applied Studies; 2006. Available at: http://www.samhsa.gov/data/prescription/toc.htm.
58. Manchikanti L, Cash KA, Damron KS, et al. Controlled substance abuse and illicit drug use in chronic pain patients: An evaluation of multiple variables. Pain Physician. 2006; 9(3):215–225. [PubMed: 16886030]
59. Brecht M-L, Huang D, Evans E, et al. Polydrug use and implications for longitudinal research: ten-year trajectories for heroin, cocaine, and methamphetamine users. Drug and Alcohol Dependence. 2008; 96(3):193–201. [PubMed: 18329825]
60. Cone EJ, Fant RV, Rohay JM, et al. Oxycodone involvement in drug abuse deaths: a DAWN-based classification scheme applied to an oxycodone postmortem database containing over 1000 cases. Journal of Analytical Toxicology. 2003; 27(2):57–67. [PubMed: 12669998]
61. Cone EJ, Fant RV, Rohay JM, et al. Oxycodone involvement in drug abuse deaths. II. Evidence for toxic multiple drug-drug interactions. Journal of Analytical Toxicology. 2004; 28(4):217–225. [PubMed: 15189671]
62. Jones CM. Frequency of Prescription Pain Reliever Nonmedical Use 2002–2003 and 2009–2010. Archives of Internal Medicine. 2012; 172(16):1265–1267. [PubMed: 22733257]
63. Hser Y-I, Huang D, Chou C-P, et al. Trajectories of Heroin Addiction Growth Mixture Modeling Results Based on a 33-Year Follow-Up Study. Evaluation Review. 2007; 31(6):548–563. [PubMed: 17986707]
64. McCabe SE, Boyd CJ. Sources of prescription drugs for illicit use. Addictive Behaviors. 2005; 30(7):1342–1350. [PubMed: 16022931]
65. McCabe SE, Boyd CJ, Teter CJ. Subtypes of nonmedical prescription drug misuse. Drug and Alcohol Dependence. 2009; 102(1):63–70. [PubMed: 19278795]
66. Havens JR, Oser CB, Leukefeld CG, et al. Differences in prevalence of prescription opiate misuse among rural and urban probationers. American Journal of Drug and Alcohol Abuse. 2007; 33(2): 309–317. [PubMed: 17497554]
67. Young AM, Havens JR. Transition from first illicit drug use to first injection drug use among rural Appalachian drug users: a cross-sectional comparison and retrospective survival analysis. Addiction. 2012; 107(3):587–596. [PubMed: 21883604]

68. Martins SS, Keyes KM, Storr CL, et al. Birth-cohort trends in lifetime and past-year prescription opioid-use disorder resulting from nonmedical use: results from two national surveys. Journal of Studies on Alcohol and Drugs. 2010; 71(4):480–487. [PubMed: 20553656]

Table 1

List of Key Data Gaps

1	Incidence of CNMP
2	Diagnosis rate of CNMP
3	Rate of opioid use to treat CNMP
4	Abuse-related opioid consumption rate among those treated for CNMP
5	Average amount consumed per event among nonmedical users
6	Opioid availability for nonmedical use
7	Prevalence of drug-seeking behaviors
8	Fraction of diversion via drug-seeking people
9	Amount acquired via doctor shopping and forgery
10	Amount diverted/retained via drug-seeking people
11	Thwart rate of forgery and doctor shopping attempts
12	Rates of overdose and all-cause mortality among select classes of nonmedical users