Defining Gaps between Information Needs and Readiness: Assessing Opioid Use Disorder Risk in Patients Considered for Long-Term Opioid Treatment

by

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The following individuals read and discussed the dissertation submitted by student Meenakshi Mishra, and they evaluated the student's presentation and response to questions during the final oral examination. They found that the student passed the final oral examination.

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DEDICATION

I would like to dedicate this work to my parents, Mr. Jag Mohan Misra and Mrs. Amarawati Misra, who encouraged me to pursue my dreams and nurtured my spirituality and curiosity, leading me to undertake and complete this journey.

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ABSTRACT

Patients on prescription opioids for pain can develop opioid use disorder (OUD) from extended use. Such patients are at increased risk for opioid overdose deaths contributing to the national opioid crisis. The CDC's opioid prescribing guidelines has recommendations for the primary care providers (PCPs) to consider OUD risk before and periodically during ongoing prescribing of long-term opioids for patients with chronic, non-cancer pain. However, the process is relatively complex, requiring PCPs to integrate disparate patient-specific data from multiple sources. Further, recent initiatives and plans to address opioid misuse and use disorder require that data be computable to meet the triple aim of improving practice, enabling research and informing policy.

This work is a novel attempt to incorporate PCPs' knowledge and experience into a framework for defining the gaps between information needs of the PCPs and readiness of the electronic health record (EHR) for assessing patients' OUD risk. The gap analysis framework incorporates provider experience from real-world challenges of caring for complex and stigmatized conditions. This work also extends the current data readiness frameworks to include the computability construct. Findings from this work will be used to inform future informatics project to improve access to better data for OUD risk assessment. This framework can be used for other complex conditions and help standardize practice that is otherwise susceptible to variability and bias.

SUMMARY

Background

Long-term opioid therapy (LTOT) for patients with chronic pain is associated with an increased risk of misuse, Opioid Use Disorder (OUD), diversion, and overdose. OUD is associated with considerable morbidity and mortality and increased social and healthcare costs. Primary Care Providers (PCPs) manage most patients with chronic pain and prescribe about half of all prescription opioids. The CDC guidelines call for PCPs to consider OUD risk before prescribing and periodically during ongoing prescribing of long-term opioids for patients with chronic, non-cancer pain. However, the process is relatively complex, requiring PCPs to integrate disparate patient-specific data from multiple sources. The challenge of accessing data needed for evidence-based OUD risk assessment at the point of care has not been sufficiently explored. Informational interviews with PCPs suggest that required data for OUD risk assessment are often missing, incomplete, or buried in unstructured notes, challenging risk assessment. Moreover, providers often use their experience when deciding a patient's overall OUD risk. Consequently, efforts to apply CDC recommendations for OUD risk assessment and referral to treatment have led to ad-hoc work with the potential to increase provider burden and introduce bias.

Objectives

In this dissertation work, I had three aims: 1) increase our understanding of the task and barriers to OUD risk assessment for chronic non-cancer pain in the primary care setting, 2) identify and achieve consensus on the information needs of PCPs for performing this task in the real world primary care setting, and 3) assess the readiness of EHR to address the PCPs information needs.

Methods

For Aim 1, I used a qualitative approach, literature review, and stakeholder interview to identify the barriers to evidence-based opioid prescribing and risk assessment in potential and active LTOT patients for chronic non-cancer pain in the primary care setting. For Aim 2, I used a mixed method approach that combined literature review, stakeholder input, and a Delphi survey. Aim 3 was also achieved using a mixed method approach. I determined the documentation practice for high-ranking OUD concepts and factors from the Delphi survey and mapped them to the existing standard terminologies and tools. Next, I determined the availability and quality of data for the high-ranked structured OUD concepts and factors by extracting them from an academic medical center's research data warehouse (RDW) for adult patients on LTOT for nonmalignant, non-end-of-life pain between 2018 and 2019. I conducted a manual chart review to determine the completeness and correctness of the high-ranked structured OUD concepts and factors.

Results

Aim 1: Barriers to evidence-based OUD risk assessment in patients with chronic pain exist at many levels. Many sociotechnical factors affect the actual practice of opioid risk assessment in the primary care setting. Most recommendations in the guidelines are backed by weak evidence and are expert opinions at best. As a result, providers often assess risk based on their knowledge and experience. Assessing OUD risk requires integrating many different types of patient-specific factors, often inconsistently documented in the EHR. The reason for inconsistent documentation includes the strong stigma attached to many of these factors, which has the potential to harm patient-provider trust and affect insurance coverage for potentially beneficial treatments.

Aim 2: Using a modified Delphi survey, I achieved consensus on 34 patient-specific OUD risk factors and concepts that are highly useful for providers to make OUD risk assessments for their patients. These factors and concepts span eight biopsychosocial domains: 1) aberrant drug-related behaviors, 2) substance use, 3) medication, 4) psychiatry, 5) socioeconomic,6) demographics, and 7) medical comorbidity. Providers report that genetic factors, such as being positive for gene polymorphism associated with substance use disorder, are not useful for OUD risk decision-making in the real world. Most of the high-risk factors are also mentioned in the CDC guidelines. Nearly half of the 34 highly useful OUD risk concepts and factors comprise of aberrant drug-related behaviors (ADRBs) that often exist as unstructured data. Through open response survey items, I identified that social support constructs potentially play a role in OUD risk assessment decisions.

Aim 3: I assessed the availability of all 34 highly useful OUD risk concepts and factors for aim three. I developed "computability" as a data quality construct, using the concepts of "definability," "structure," and "standards, "to determine computability for each of the 34 high-ranked data element. Nearly 80% of OUD risk factors and concepts have clear definitions, with the remaining 20% needing additional patient and local practice context. Thirty percent are computable because these have clear definitions, are documented in structured fields, and have standard codes. Approximately 41% of the OUD risk factors and concepts are potentially computable and can be derived from two or more structured data or captured using standard and validated tools in an electronic health record flowsheet. Three of the 14 potentially computable data OUD risk concepts and factors require establishing temporality to resolve concurrency issues. Just one-third of the high-ranked concepts can currently be represented using standardized healthcare terminology. Percentage sensitivity (s) and positive predictive value (PPV) of all 10 computable concepts are: history of non-fatal overdose (s=0, PPV = undefined), current substance use disorder (s=50, PPV=100), alcohol

use disorder (s=100, PPV=100), hazardous situation due to opioid use (s=77.8, PPV=100), history of substance use disorder (s=72.7, PPV=100), illicit drug use (s=66.7, PPV=100), showing symptoms consistent with withdrawal (s=8.3, PPV=100), suicide ideation (s=0, PPV=0), history of suicide attempt (s=0, PPV=undefined), history of childhood physical, emotional or sexual abuse (s=0, PPV=undefined).

Discussion

Triangulating patient-specific biopsychosocial risk factors from diverse information sources is ideal for making an informed OUD risk assessment. Identifying and improving access to patient-specific factors that drive OUD risk and prescription opioid treatment decisions in the real world are vital to improving the current practice of OUD risk assessment. OUD risk factors and concepts having standard workflow for collection for all patients in the primary care setting, like alcohol use, have higher sensitivity. Standard workflow for collecting OUD risk factors and concepts for all patients treated with opioids will result in better data availability at the point of care for decision-making. In the electronic health record, providers are more likely to document data for opioid "withdrawal" in unstructured notes than in a structured data field, such as the encounter diagnosis or problem list. In addition, providers are less likely to capture historical diagnoses in a structured field, especially those with associated stigmas, such as suicide ideation or attempts and a history of childhood sexual, physical, or mental abuse. These findings suggest that establishing a standard workflow for high-ranked OUD risk factors will improve their availability for decision-making. For OUD risk concepts with considerable stigma and the potential to affect patient-provider trust, it is crucial to adopt appropriate information gathering and retrieval techniques to have better data for triangulation and decision-making. It is worth noting that all ten theoretically computable OUD risk factors and concepts have a high degree of specificity and positive predictive value

and are less likely to flag a patient falsely for the OUD risk factor.

Based on the results from the Delphi survey, there is a need to develop a social support construct for this patient population. Many elements of social support align with the standard social determinants of health (SDoH) that are increasingly collected in healthcare settings. However, some concepts that emerged from this work, e.g., patient-provider trust, patient activation, and patient self-efficacy, are not typically assessed or recorded. Increasing the assessment and capture of such concepts may be valuable for OUD risk decision-making and any other clinical context where such constructs may influence care and adherence to medical recommendations.

Conclusion

Through this work, I developed a generalized approach to assessing PCP's information needs and EHR's data readiness for OUD risk assessment. Most OUD risk assessment and stratification methods use algorithms based on OUD risk factors; however, these methods currently fail to account for EHR data readiness and clinical knowledge and experience, which is often complex and diverse. This work is a novel attempt to incorporate real-world provider knowledge and experience into a framework for defining the gaps between information needs and readiness for complex conditions with considerable stigma. The work also extends the current data readiness framework to include the computability construct. Standard and computable data are prerequisites for generating local practice-based evidence and integrating it with external research-based evidence. However, a generalized methodology to develop standard and computable data to enable the learning health system and evidence-based care is not currently available.

We need better quality data for clinical decision support, research and policies. The findings from this work will help prioritize future informatics projects to improve data quality for highly useful OUD risk factors and concepts needed for risk assessment in the primary care setting. The information needs and readiness assessment pipeline can be used to improve data readiness for other complex clinical decisions requiring real-world context.

Figure 1. Research Framework for Dissertation

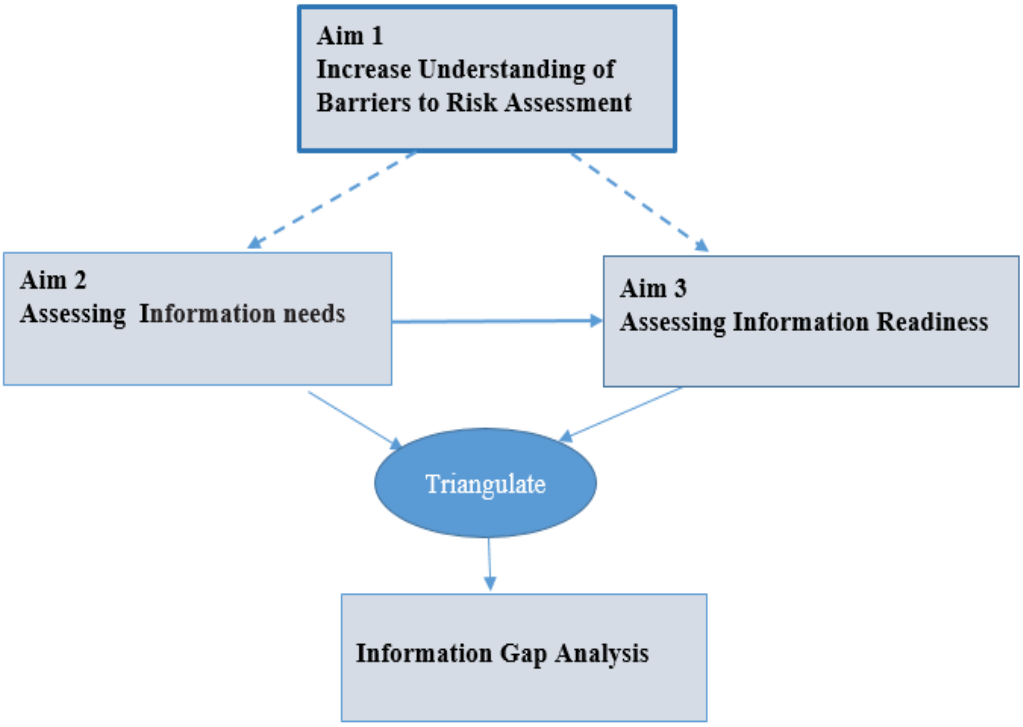


Figure 1 represents the research framework for the three aims. The data from aim 1 informs aim 2 and 3, while that from aim 2 supports aim 3. The final step is the triangulation of findings from aim 1, 2 and 3 to conduct an information needs and readiness gap analysis and propose future work.

CHAPTER ONE: BACKGROUND

The Problem - Prescription opioids and the U.S. overdose crisis: An overview of various system-level policies

The lifetime odds of dying from an accidental opioid overdose are among the top ten leading causes of death in the United States.(1) Drug overdose deaths involving prescription opioids increased almost five times between 1999 and 2017, leading to the national opioid crisis.(2) Misuse of opioids is common among patients with chronic pain treated with prescription opioids.(3) According to the 2017 National Survey on Drug Use and Health (NSDUH), approximately 21 to 29 percent of patients who receive prescription opioids for chronic pain misuse them, and 8 to 12 percent develop opioid use disorder (OUD). OUD is a disease characterized by an uncontrolled urge to seek and consume opioids without regard to harmful consequences and hazards to self. Patients with OUD have a higher chance of dying from an overdose. The economic burden from chronic pain and opioid misuse runs into billions of dollars.

Though there is insufficient evidence regarding the efficacy of opioids for long-term chronic pain(4-8), a significant percentage of the U.S. population lives with chronic pain, 11% to 40% (9, 10), and opioids continue to be a viable treatment option for some. Since prescription opioids have a role in the national opioid crisis, any future efforts to reduce harm from these drugs must be informed by lessons from the past. I will identify the significant events that shaped the current overdose death epidemic and determine the effectiveness of former laws, regulations, and policies in addressing the growing problem.

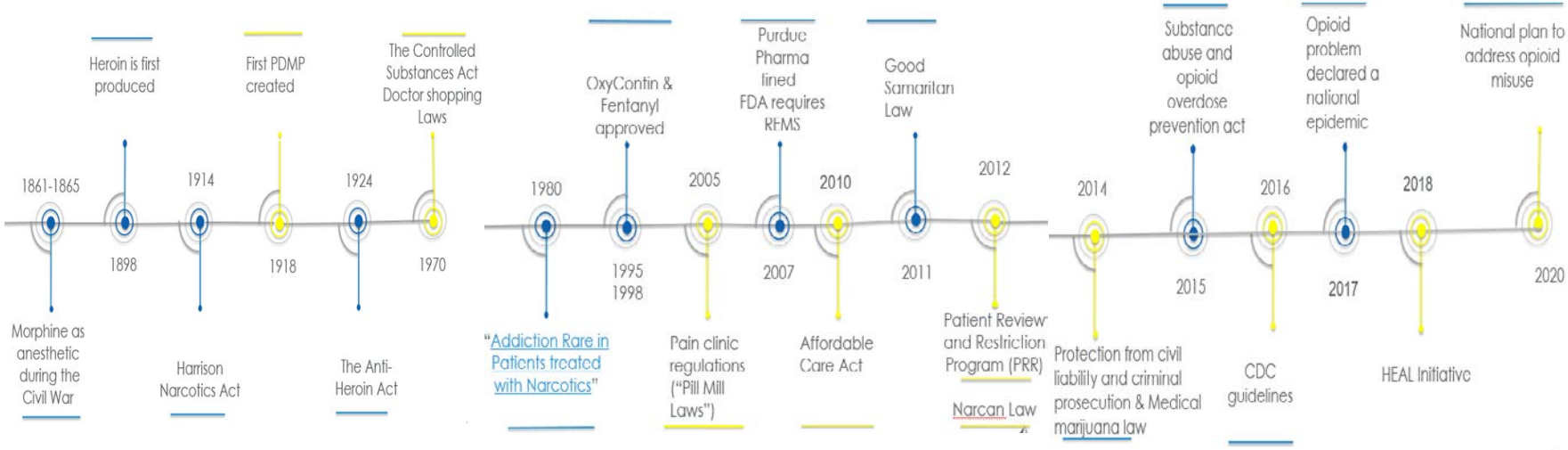


Figure 1.1 Significant events, laws, regulations, and policies that shaped the use of prescription opioids

Significant events, laws, regulations, and policies that shaped the use of prescription opioids

Figure 1.1 is a timeline of significant events, laws, regulations, and policies shaping the use of prescription opioids and the current opioid crisis. Morphine was first used as an anesthetic during the civil war in the mid-nineteenth century. This was followed by the manufacture of Heroin from morphine for use as an analgesic at the turn of the twentieth century. The Harrison act of 1914 regulated and taxed the production and distribution of opiates. The first prescription drug monitoring program (PDMP) was established in 1918 in New York to monitor the prescription of cocaine, codeine, heroin, morphine, and opium. The discovery of the addictive nature of Heroin led to the 1924 anti-Heroin act, which prohibited the import and use of opium to synthesize Heroin. Two landmark events led to the increased use of natural and synthetic opioids for treating chronic non-cancer pain. The first was the publication of a letter to the editor in the New England Journal of Medicine by Porter et al., titled "Ad*diction Rare in Patients Treated with Narcotics,*" and the second was the decision by the U.S. Department of Veterans Affairs (V.A.) to regard pain as the "fifth vital sign." Increased use of prescription opioids over the subsequent years parallels the steep increase in death from overdose involving prescription opioids. Consequently, many laws and regulations were instantiated to address the growing epidemic.

Numerous system-level programs, procedures, and statewide policies aim to detect and prevent misuse, abuse, diversion, and overdose of prescription opioids. Among them are prescription drug monitoring programs (PDMP), insurer and pharmacy benefit manager strategies for prevention of OUD, state Laws and regulations, clinical guidelines, Naloxone distribution programs, procedures for storage and disposal, and patient and provider education. Understanding the effectiveness of these interventions is vital for informing future policies.

PDMP is a state-run program requiring state pharmacies to submit all information on prescriptions for controlled substances electronically to a central office. State PDMP programs are limited in terms of their data's accuracy, accessibility, and interpretability.(11) The PDMP programs operate under different regulatory agencies, collect different data types, require data to be updated at different intervals, and allow access to different groups of people. The data are stored in an electronic database that can be accessed by authorized personnel, prescribers, and pharmacists. Authorized personnel can access a patient's controlled drug history by accessing the PDMP database, which can alert providers and pharmacists of patient “doctor shopping” to access more opioids. PDMP has been cited as a promising state-level intervention to inform opioid prescription and patient risk. Evidence suggests that providers' use of PDMP leads to reduced opioid prescriptions (12-14) and opioid-related deaths.(15, 16) Prescribers are more likely to detect prescription drug abusers and “doctor shoppers” (patients seeking opioids from multiple prescribers) when PDMP use is mandatory than when the use of the PDMP is voluntary.

The objective criteria for drug-seeking behavior using the PDMP data include >= 4 opioid prescriptions from >= 4 providers. However, "many patients have multiple prescribers because of poor primary care access, visits to the Emergency Departments (E.D.) for acute exacerbations of pain, and conditions requiring visits to multiple specialists." There is a need to determine what data values in the PDMP, when considered alongside complete clinical encounters, should prompt intervention from the physician.(17)Insurer and pharmacy benefit manager strategies include the Patient Review and Restriction (PRR) program. PRR essentially restricts a Medicaid recipient to a designated provider and pharmacy for prescription and dispensing of prescription opioids following a review and determination that a patient utilizes more healthcare services than is medically necessary. No studies have looked at the effectiveness of PRR in reducing opioid misuse or opioid-related disorders.

However, there is evidence that PRR reduces health plan expenditure and patient use of controlled substances.(18)

State legislations include pain clinic regulations, Good Samaritan laws, and "doctor-shopping" laws.

- More commonly known as "pill mill" laws, pain clinic regulations impose state oversight on pain clinics, including routine inspections, requirements for those who practice within them, and civil and criminal penalties when violations occur. Eleven states have pain clinic laws – Louisiana being the first state to enact one in 2005 and Wisconsin being the most recent state to pass in 2016. The states with so-called pill mill laws are Louisiana, Georgia, Florida, Alabama, West Virginia, Wisconsin, Tennessee, Texas, Ohio, Mississippi, and Kentucky. The states, however, vary in terms of the requirements under this law. Enhanced enforcement and implementation of pill mill laws have no overall effect on overdose deaths from prescription opioids.(19)
- The Good Samaritan Law (GSL) was initially passed in 1959 to protect physicians from liability when providing voluntary care under emergencies outside the hospital. Since then, the law has been extended to non-physicians and bystanders. Nurses, police officers, firefighters, emergency service professionals, and even bystanders who provide emergency care, in good faith, to people at the scene of an accident are exempted from civil liabilities in case of adverse outcomes from the care provided. In 2011, GSL was extended to 911 callers seeking Emergency Medical Service for an overdose. The callers are exempted from arrest for possession of drugs. States with GSL in place have decreased overdose death rates compared to prior years.(19) Some of it may be due to changes in bystander behavior and willingness to call 911 for an overdose

case; however, though E.D. visits have increased, it is concurrent with an increase in the number of opioid uses.(20) In other words, GSL laws have not affected the opioid use behaviors of people with OUD.

- Laws commonly known as "doctor-shopping laws" require that patients must not withhold from their physicians any information about receiving a controlled substance prescription from other healthcare providers. In some states, these laws make it a felony crime for a patient to withhold relevant opioid prescription history or to falsify symptoms. Specific laws in each state vary slightly, but the Uniform Narcotic Drug act of 1932 and the Uniform Controlled Substances Act of 1970 cover this topic thoroughly. Additional regulations in 23 states specify that information patients provide to a practitioner during "doctor shopping" is not protected under the standard doctor-patient privilege. Peer-reviewed literature on the effectiveness of this law is non-existent.

Various healthcare, state, and federal organizations have issued guidelines for prescribing opioids to adult patients with chronic non-cancer pain. These guidelines aim to provide access to safe and effective chronic pain treatment while reducing misuse, abuse, addiction, diversion of prescription opioids, and opioid-related overdose and death. Most guidelines, including the most recent CDC guidelines for safe opioid prescribing, agree on closely monitoring the patients for risk from prescription opioids. Risk assessment activities with a broad agreement between different guidelines include i) conducting a physical exam, pain history, past medical history, and family/social history; ii) conducting urine drug testing, when appropriate; iii) considering all pain treatment options, weighing benefits and risks of opioid therapy, and prescribing long-term opioids only when alternative treatments are ineffective; iv) starting patients on the lowest effective dose of prescription opioids; v)

implementing pain treatment agreements; vi) monitoring pain and treatment progress with documentation; vii) using greater vigilance with higher doses; viii) using safe and effective methods for discontinuing opioids (e.g., tapering, making appropriate referrals to medication-assisted treatment, substance use specialists, or other services); and ix) using data from Prescription Drug Monitoring Programs (PDMPs) to identify past and present opioid prescriptions at initial assessment and during the monitoring phase. However, these guidelines are implemented with variable consistency at the local level. Opioid prescribing policies have led to a decrease in the mean opioid prescribed dose; however, these policies have also been associated with increased use of heroin and non-prescribed opioid analgesic.(21)

Naloxone distribution programs, Overdose Education, and Naloxone Distribution (OEND) have followed close on the heels of the passage of the Narcan (Naloxone) law of 2012, which protects a person from civil liability and criminal prosecution for processing and administering Naloxone to a person experiencing an opioid overdose. These programs reduce overdose mortality and the rate of adverse events.(22) However, the impact of Narcan on decreasing misuse of opioids and OUD is unclear.

Safe storage and disposal of opioids have been promoted through community-sponsored events such as “drug take-back” to ensure the safe disposal of unused controlled medications. Educating patients about the safe storage and disposal of opioid medication can limit diversion; however, many patients do not receive adequate education from their prescribers or pharmacies and do not follow proper do’s and don’ts of sharing, storage, and disposal. (23, 24)

Educating patients and providers about the risks and proper management of prescription opioids can potentially change patient and provider behavior. The substance abuse and opioid overdose prevention act of 2015 initiated continuing education requirements for practitioners

regarding pain and opioid management. High-risk prescription opioid prescribing decreases when providers participate in pain management educational programs.(25) However, patient education requires much work. Analysis of public survey data from the National Survey on Drug Use and Health (NSDUH) 2015 – 2019 (Figure 1.2) suggests that access to prescription pain relievers from secondary sources (from a source other than a prescription from a doctor) is higher in adults between the ages of 18 and 25 years than other age groups. Friends and family are frequent sources of pain relievers in this age group. Education intervention and risk counseling in this younger population may reduce opioid misuse. Very few studies have evaluated the role of patient and provider education in reducing prescription opioid misuse.

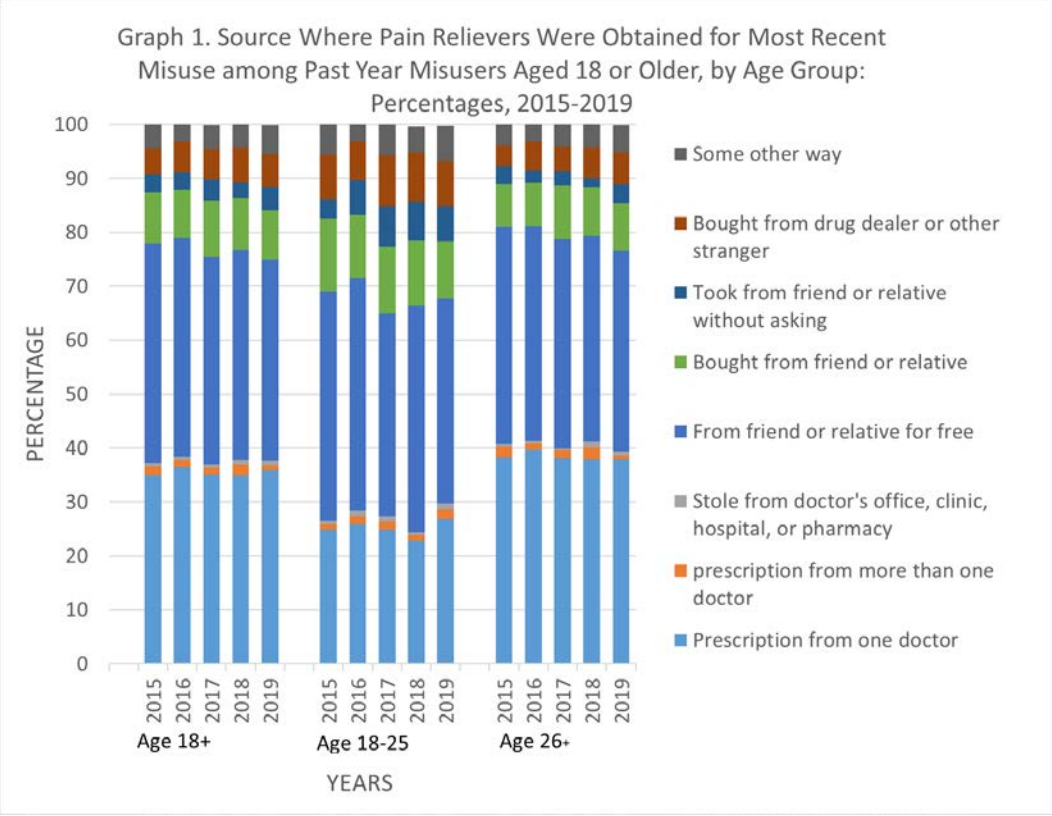


Figure 1.2 Sources of pain relievers for most recent misuse among the past year misusers aged 18 or older (Data sources in Appendix A)

There is considerable variability in how various programs, laws, and guidelines are implemented in different states and healthcare organizations. Some studies have reported temporal associations between policy implementation and reduction in opioid prescription (26, 27) and opioid-related overdoses.(27) However, there is no substantial evidence that the presence of policy reduces opioid misuse.(27) Barriers to robust assessment and evaluation of health policies include "lack of baseline data and comparison groups, inadequate statistical testing, small sample sizes, self-reported outcomes, and short-term follow-up."(28) The need for better data to understand the opioid epidemic has led to the CDC project, "Modernizing the Infrastructure for Capturing Drug Death Data and Enhancing Research on Opioid Poisoning using Death Certificates' Literal Text Field," to improve interoperability in sharing mortality data.

More recently, the Helping End Addiction Long-term (HEAL) initiative requires efforts from the scientific community to develop better interventions and treatments for opioid misuse and use disorder. The National Plan to Address Opioid Misuse by the National Safety Council calls the prescriber and medical community to increase research efforts in pain and addiction treatment and continue to evaluate and update the CDC guidelines for safe prescribing of opioids. However, we need better quality data to address the triple aim of improving care, enabling research, and informing policies.

At first glance, the various system-level policies, programs, and guidelines may seem to address the overdose death crisis involving prescription opioids, as there has been a decreasing national trend in overdose deaths involving prescription opioids between 2017 and 2019, barring the recent spike during the Covid pandemic (2). However, there is a simultaneous rise in overdose deaths from synthetic opioids, which warrants further investigation. Analyzing the intended and unintended consequences of the complex dynamics of all opioid-related policies and interventions is beyond the scope of this research project.

There is clearly a role that prescribers and the healthcare community play in addressing the opioid crisis, and the need for better quality data is vital to understanding and improving the practice of pain management and OUD treatment.

Evidence-based OUD risk assessment and timely intervention are essential to address the ongoing opioid crisis; therefore, this research identifies the barriers to guideline-concordant OUD risk assessment practice that can be bridged using informatics solutions. Additionally, a generalized methodology is needed to improve the quality of data for OUD risk assessment to evaluate and update the practice. This research defines the gaps between the information needs of PCPs for the real-world practice of guideline-concordant OUD risk assessment and the readiness of EHR to address those needs to guide future informatics efforts to bridge the gaps.

CHAPTER TWO: AIM 1 - UNDERSTANDING THE GUIDELINE CONCORDANT OUD RISK ASSESSMENT TASK AND BARRIERS

The Role of Informatics in Implementing Guidelines for Chronic Opioid Therapy Risk Assessment in Primary Care: A Narrative Review Informed by the Socio-technical Model

Abstract

The economic burden from chronic pain and opioid use disorder runs into billions of dollars. Patients on prescription opioids for chronic non-cancer pain (CNCP) are at increased risk for OUD and overdose. By adhering to the Centers for Disease Control and Prevention (CDC) opioid prescribing guidelines, primary care providers (PCPs) can potentially reduce patient harm. This narrative review examines the guideline-concordant risk assessment in a sociotechnical context to highlight the complexity of the task and identify barriers that can be addressed through informatics intervention. I used three frameworks: Cabana, Sociotechnical Model for Health Information Technology (ST-HIT), and Promoting Action on Research Implementation in Health Services (PARiHS), to extract system-level barriers and facilitators for guideline-concordant OUD risk assessment from 35 peer-reviewed articles.

Keywords

Practice guidelines, implementation science, sociotechnical context

Introduction

Approximately 16 million people worldwide and 2 million Americans live with OUD, defined as "a problematic pattern of opioid use leading to clinically significant impairment or distress." (29-31) OUD is associated with considerable morbidity and mortality, with individuals with OUD at a ten times higher risk for mortality than the general population.(32) In 2019, prescription opioids were involved in approximately 20% of the deaths from a drug

overdose in the U.S., contributing significantly to the nation's opioid crisis. The economic burden of chronic pain and OUD runs into billions of dollars annually.(33, 34) In 2017, the cost of reduced quality of life from OUD and lost life due to fatal overdose was estimated to be close to 1.02 trillion dollars.(35)

The risk of developing OUD is especially high for patients experiencing chronic pain. Roughly 21 to 29 percent of patients prescribed opioids for chronic non-cancer pain misuse opioids, and between 8 and 12 percent develop OUD.(36) Primary care providers (PCPs) manage most chronic pain patients and prescribe about half of all prescription opioids.(37) Managing complex and diverse chronic pain patients on long-term prescription opioids for non-cancer pain requires balancing treating pain and preventing addiction and overdose. To provide clinicians with guidance in caring for this complex population and reduce patient harm, the CDC has developed safe opioid prescribing guidelines.(38) Implementation of these guidelines has been challenging, and adherence by PCPs is low.(39, 40)

The CDC guidelines for prescribing opioids to adult patients with chronic non-cancer pain recommend that the PCPs assess the risk for OUD and appropriately refer them for treatment.

Systems View of Opioid Prescribing in Primary Care

Nearly 20% of the visits in primary care involve three or more chronic conditions, with pain being one of the most common reasons for visits. Figure 2.1 is a systems view of opioid prescribing and guideline-concordant risk assessment for chronic non-cancer pain in primary care. It illustrates the interplays between various social and technical components when assessing the risks of using prescription opioids for chronic non-cancer pain. Chronic pain is defined as pain lasting >90 days or beyond the time of normal tissue healing. A PCP, when considering opioid medication for chronic pain, needs to contextualize the evidence-

based guidelines with patient-specific data to make evidence-based, patient-centered decisions.

Intended Workflow and Process

The PCP must incorporate information from multiple sources to weigh the risks vs. benefits of prescription opioids for patients with chronic pain. Ideally, the PCP should do the following risk assessment tasks per CDC guidelines (Figure 2.1):

1) Use validated screening tools to detect OUD and misuse
2) Review patients' medical history for OUD risk factors and aberrant drug-related behaviors, "a range of anomalous patient behaviors involving prescribed opioid medication suggestive of patient's opioid misuse and possibly a substance use disorder."(41) Specifically, a prescriber should look for a history of overdose, present or past substance use disorder, and the presence of mental health conditions. A high total dose of opioids and concurrent benzodiazepine use increase the risk for overdose.
3) Check for unexpected urine drug screening (UDS) result
4) Check the PDMP for patient's use of multiple prescribers and pharmacies to get prescription opioids

However, Physicians underutilize UDS, written Opioid Use Agreements (OUA), and Prescription Drug Monitoring Programs (PDMP).(42-46) Moreover, there are variabilities in how providers perform risk assessments and interpret OUD risk for their patients.(43) Evidence that guidelines concordant OUD risk assessment improves patient outcomes is mostly meager and inconclusive due to variability in risk assessment practice. There is a need to understand the barriers and facilitators for guideline-concordant OUD risk assessment to

improve adherence and standardize the practice.

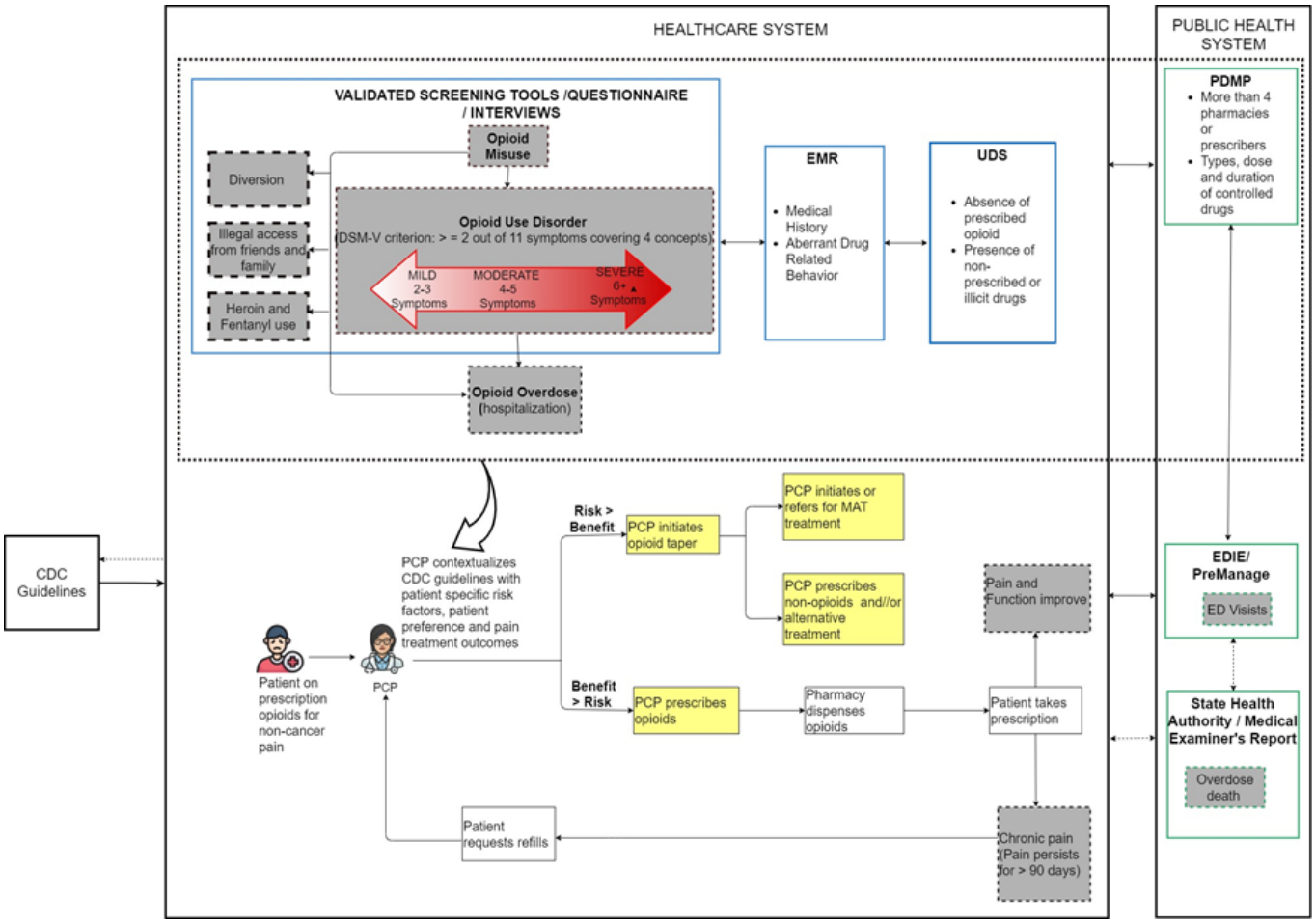


Figure-2.1. Systems view - Interplays between clinical tools, processes, and information systems in the primary care setting. Grey boxes: outcomes; Yellow boxes: clinical decisions; Information systems: EHR, PDMP, PreManage (a collective ambulatory platform that can receive data from Emergency Department Information Exchange (EDIE)), State Health Authority; Clinical decision tools/test: CDS (Clinical Decision Support); risk assessment tools, UDS (Urine Drug Screening

Methods

I searched for articles on barriers to guideline-concordant OUD risk assessment in the PubMed and Scopus databases. Initially, I used the search term - "((CDC guidelines) AND ((((chronic pain) NOT (cancer)))) AND (opioid analgesic)) AND ((barrier) OR (challenges))" to look for relevant articles. However, just two out of the six articles were found to be relevant. More articles were identified by reviewing the references of the two original articles and using Scopus. I also expanded the search to include systematic reviews and review articles on each risk assessment information source mentioned in the CDC guidelines (validated screening tools, PDMP, urine drug screening, and aberrant drug-related behaviors). Finally, 35 articles were used for barrier analysis in this narrative review.

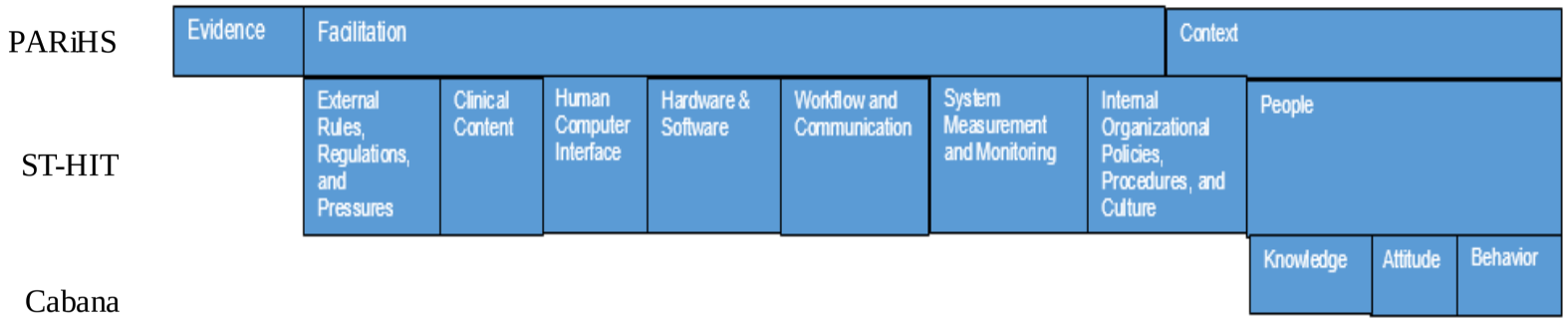
The CDC guidelines comprise the best available evidence from research and require successful implementation and adoption to reduce patient harm. Hence, I used frameworks that explored implementation and adoption barriers to guidelines/evidence. I used 14 constructs from three frameworks, the sociotechnical model for health information technology (ST-HIT), Cabana, and Promoting Action on Research Implementation in Health Services (PARiHS), for thematic extractions and synthesizing the findings for barriers and facilitators.(47-49) Figure 2.2 shows all 14 constructs used for extracting themes for barriers to guideline-concordant OUD risk assessment. The ST-HIT model by Sittig and Singh (2010) has eight constructs that play a role in the successful design, development, implementation, use, and evaluation of health information technology. These include: 1) hardware and software, 2) clinical content, 3) human-computer interface, 4) people, 5) workflow and communication, 6) internal organizational features (e.g., policies, procedures, and culture), 7) external rules and regulations, and 8) measurement and monitoring. The Cabana framework by Cabana et al. (1999) is a behavioral framework for adherence to guidelines and includes three constructs: 1) knowledge, 2) attitude, and 3) behavior. The PARiHS framework by

Kitson et al. (1998) is an implementation framework that uses three constructs to improve the translation of research findings to healthcare practice: 1) evidence, 2) context, and 3) facilitation. All 14 constructs from the three frameworks helped explore barriers and facilitators for guideline-concordant OUD risk assessment.

It is important to note that there is a fair amount of overlap between the three frameworks (Figure 2.2). The knowledge, attitude, and behavior constructs from the Cabana framework overlap with the people construct from the ST-HIT framework, which overlaps with the context construct from the PARiHS framework.

Similarly, several constructs from ST-HIT, external rules, regulations and policies, internal organizational policies, procedures and culture, clinical content, hardware and software, system measurement and monitoring, workflow and communication, and human-computer interface overlap with the facilitation construct from the PARiHS framework. The evidence construct from the PARiHS framework allows exploring barriers due to the quality of evidence and clarity of recommendations in the guidelines. The degree of overlap between all 14 constructs ensures rigor during thematic extraction.

Figure 2.2. Overlap between the constructs from ST-HIT, Cabana, and PARiHS frameworks



Results

I identified 22 barriers and 8 facilitators for guideline-concordant risk assessment using the 14 constructs from the three frameworks. Significant barriers and facilitators are summarized below. Table 2.1 in the supplementary material references all barriers and facilitators.

Barriers

- Weak Evidence
    i. Most recommendations in guidelines are supported by weak evidence.
    ii. No widely used risk assessment tool accurately predicts or identifies misuse in the pain population.
    iii. Applying the OUD diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) for patients on long-term prescription opioids for chronic pain under medical supervision has proven to be complicated.
- Poor Facilitation
    4. Poor Human-Computer Interface
        iv. Poor PDMP-EHR interface – non-intuitive display.
        v. Inadequate Software and Hardware
        v. Lack of standards for PDMP integration into EHRs results in poor usability and decreased usage
    5. Poor Clinical Content
        vi. Variable and inconsistent documentation of opioid misuse and abuse in the EHR due to the potential for patient harm from the associated stigma
        vii. Variations in the use of validated screening tools and their documentation in the EHR

viii. Inconsistent and unsystematic documentation of aberrant drug-related behaviors

- Variable Context

6. Variable Context - Patient

ix. Fear of stigma

x. Existing comorbidities challenging alternate pain treatments

xi. Lack of provider trust

7. Variable Context – Primary Care Provider

xii. Lack of visit time

xiii. Short continuity of care

xiv. Emotional burden, inadequate resources, and a lack of trust between patient and provider

xv. Difficulty obtaining non-opioid pain treatments for patients

xvi. Difficulty justifying opioid wean for patients who are stable on chronic opioid use

xvii. Unfavorable Attitude – Younger providers feel less confident, find pain management stressful, and are worried about dependence

xviii. Knowledge gaps - Providers find the treatment of chronic pain challenging and desire additional training and referral support.

8. Variable Context – Practice

xix. Unavailability of comprehensive, multimodal pain care

9. Difficult Measuring & Monitoring

xx. Inconsistent use of terminologies and ICD codes for problem opioid use

xxi. Varying definitions of long-term opioid therapy, with 41 unique variations across 34 studies.

xxii. Lack of outcome measures to evaluate the impact of risk assessment that are meaningful to primary care providers

Facilitators

- Strong Facilitation

1. Supportive Organizational Policies, Procedures, and Culture
    i. Standard risk assessment policy
    a.Mandatory PDMP reviews
    b.Random urine drug test
    ii. Access to a collaborative team for opioid taper
    iii. An organizational culture that embraces educational interventions and audit and feedback processes
    iv. Academic detailing" models and a team-based approach to care with physician assistant care managers
2. Clear Protocol for Measurement and Monitoring
    v. Development of a risk-assessment algorithm and risk-stratified monitoring guidelines
3. Human-Computer Interface
    vi. EHR innovations, like the *EHR dashboard*, facilitate communication
4. Workflow and communication
    vii. A patient registry with the regular dissemination of reports to PCPs increases adherence to guidelines
5. Improving provider knowledge

viii. Educating providers leads to improved knowledge and confidence to manage patients on long-term prescription opioids per guidelines and increased screening practices.

Discussion

The intent of the CDC guidelines is not to be used as rigid rules and caution providers to include context and patient values when making risk vs. benefit decisions. However, the guidelines have been used out of context without considering patient-level factors, leading to patient harm. The recommended ceiling dose of 90 morphine milligram equivalents (MME)has been used as a hard limit by some payers and providers, leading to unintended consequences. Patients have been discharged from practice or abruptly tapered without appropriate weaning or OUD treatment.(39)

In the study by Setnik et al., PCPs assigned most patients to low risk for misuse, abuse, and diversion despite aberrant behaviors and abnormal urine drug testing.(50) Patient's medical history, patient interview, and history of treating/knowing the patient, were the three most frequent information sources used by physicians for assessing a patient's risk, with medical history used 84.9% of the time. Questionnaires or validated screening tools were used less frequently (21.5%). History of treating/knowing the patient also influenced risk assessment and low-risk assignment. The latter indicates provider bias or a type 2 decision process that is not well understood. It is not clear to what extent this factor underestimates the actual risk. There is a role for education to improve primary care providers' adherence to CDC guidelines and reduce variability in the risk assessment practice.

Providers, especially younger providers, need adequate education and training to improve their confidence in caring for patients with chronic pain on prescription opioids.

Requiring primary care providers to take continuing medical education credits for pain management and establishing a team-based approach to pain management with audit and feedback will help boost provider confidence and facilitate guideline-concordant risk management.

However, many factors besides education may lead to variability in opioid misuse and OUD risk assessment practice. Notably, eight out of twelve recommendations in the CDC's safe opioid prescribing guidelines are weak and supported by Type 4 evidence. Type 4 evidence is mainly derived from clinical experience using case studies, clinical examples, or observational studies with limitations. Also, the most widely used screening tools do not accurately predict or detect opioid misuse and the DSM-V criteria are difficult to apply to the chronic pain population. In the absence of weak evidence and inadequate tools and diagnostic criteria, primary care providers may use their experience to determine patients' risk for opioid misuse and use disorder.

Data in Electronic Health Records (EHRs) offer tremendous opportunities to identify at-risk patients and guide patient management.(51, 52) However, variation in documentation practices and difficulties identifying opioid use due to inconsistent opioid use terminologies makes it challenging to identify risk and implement appropriate intervention.(53, 54) Most providers are reluctant to clearly and unequivocally document problem opioid use in the patient's chart due to the potential for patient stigmatization and damaging patient-provider trust. Evidence suggests that the prevalence of opioid misuse/abuse varies considerably when estimated using the ICD codes.(55) Attempts to determine the baseline prevalence of problematic opioid use behavior has suffered from inconsistent terminologies and documentation of opioid misuse and abuse. There is wide variation in the estimation of problematic opioid use behavior in patients with chronic pain, 0% - 50% ,(56) making it challenging to inform clinical and policy decisions and implement and measure interventions.

Adopting de-stigmatizing vocabularies and tools that enhance patient-provider communication and trust are needed. National Institute for Drug Abuse (NIDA) also acknowledges the need for de-stigmatizing language and provides resources to guide its use in healthcare delivery.(57)

In 2013, a multidisciplinary group of academic, industry, clinical, public health, and regulatory experts in pain and addiction -the Analgesic, Anaesthetic, and Addiction Clinical Trials Translation, Innovation, Opportunities, and Networks (ACTTION) – was called by the Abuse Liability Evaluation for Research, Treatment, and Training (ALERTT), a public, private partnership to develop consensus-based definitions for misuse and abuse and related events (MARE) for use in clinical trials. The MARE definitions incorporated behaviors necessary for evaluating new pain therapeutics' misuse and abuse potential in clinical trials. These terms can be adapted for care delivery and policies after substituting the more stigmatizing "addiction" and "abuse" words for "use disorder" and "misuse" or "use other than prescribed, respectively."(57, 58)

Additionally, "Chronic Opioid Therapy" (COT), also called "Long Term Opioid Therapy" (LTOT), has been variably defined in the literature. Clinical guidelines define LTOT as the "use of opioids on most days for more than three months." A systematic review by Karmali et al. found "41 unique variations of definitions of LTOT across 34 studies.(59) The definition of LTOT differed by the follow-up time, cumulative duration of opioid use for LTOT, the time points used to define LTOT, and consistency of opioid use." The inconsistent definition has made it difficult to determine the prevalence of LTOT and the risk factors associated with the transition from short-term to long-term opioid therapy. Considering that terms like COT or LTOT are essential for understanding risk factors for misuse and OUD from long-term use and that these terms will constitute the denominator for quality measures

for the risk assessment process, they must have a consistent definition. The most recent CDC resource for quality improvement and care coordination defines LTOT as ≥ 60 days' supply of opioids within a quarter and provides an alternative definition in case determining days is too difficult (Note: If determining days' supply is too difficult, an alternative is to define it as at least two consecutive opioid prescriptions in a quarter.).(60)

Inconsistent use and documentation of standardized screening tools for assessing function and opioid risks are problematic and affect EHR data quality. Just 26% of providers report using patient assessment tools before treatment. In response to a survey question regarding the EHR documentation of medication contract, pain assessment, functional assessment, discussion of risks and benefits, and trial of non-opioid medications, the percentage of providers who reported "*always*" finding these in EHR was 41, 38, 4, 37, and 61 respectively.(61) The insufficient documentation of guideline-specific requirements makes it hard to evaluate its effectiveness in reducing risk and improving outcomes. Integrating standard screening tools in EHR may enhance their utilization and subsequent documentation, enabling guideline adherence.

Further, the low-frequency use of screening tools as an information source is poorly understood. CDC guidelines support the use of screening tools to identify patients' risk for abuse before initiating opioids and monitoring for misuse and abuse during opioid treatment. Most validated screening tools for predicting or detecting misuse and abuse have limited accuracy. Still, when data from the screening tool is enhanced with EHR data, PCPs can better distinguish the low-risk and high-risk populations.(62, 63) However, the data in EHR needs to be findable or accessible to triangulate and make decisions about patients' OUD risk. There is a need to systematically assess and improve the quality of opioid risk data in the

EHR to enable a more accurate and timely estimation of patients' opioid misuse and abuse risk.

Barriers to implementing CDC guidelines exist at many levels. Besides knowledge and information gaps, many system-level factors are significant obstacles to guideline-concordant risk assessment. Internal policies play substantial roles in adherence to risk assessment tasks. Standardized opioid prescribing and monitoring policies improve guideline-concordant risk assessment.(64-66) Random urine drug tests and mandatory PDMP reviews can potentially lead to timely detection of high-risk behavior and addiction, prompting timely intervention, like decreasing the monthly dispense of opioids and benzodiazepines.(67, 68) Lack of time and training are significant barriers to guideline adherence.(61, 69, 70) Development of a risk-assessment algorithm and risk-stratified monitoring guidelines improve adherence to guidelines.(64) Also, team-based pain management practice and an organizational culture that supports education and academic detailing are conducive to evidence-based pain care and risk assessment. (64, 71) Non-collaborative opioid taper increases patient risk.(39) "Organizational culture that embraces educational interventions and audit and feedback processes increases guideline adherence.(72, 73)

Developing interoperability standards for integrating PDMP data in EHR and improving the display of data needed for risk assessment will improve OUD risk assessment at the point of care. Creating a registry of patients on long-term prescription opioids for chronic non-cancer pain and using EHR dashboards to disseminate risk assessment reports to providers will make it easier to follow up on missed opportunities to track and monitor patients.

Additionally, patient preference and comorbidities may drive treatment decisions and affect adherence to CDC guidelines. Protecting patients from opioid-related harm is the top priority for PCPs.(74) Providers also fear damaging patient-provider trust and causing patient

harm from the associated stigma of use disorder diagnosis. The stigma of use disorder diagnosis can make patients susceptible to discrimination regarding jobs, housing, insurance coverage, and even potentially beneficial treatments. A standard risk assessment protocol and formal opioid treatment agreement with general patient expectations may reduce the risk of damaging patient-provider trust.

Informatics interventions hold promise to bridge knowledge and information gaps. Educational and training tools for PCPs can improve translating guidelines to practice. Interoperable information systems and well-designed human-computer interfaces can facilitate risk assessment tasks at the point of care. Patient registries and EHR dashboards can improve cross-team communication and workflow. However, many risk assessment activities and associated diagnoses carry a considerable social stigma.

The risk factors in patients with chronic non-cancer pain on long-term prescription opioid treatment are dynamic and need continuous monitoring. They can change with "disease progression, tolerance, changes in pain quality, mental health, comorbidities, other drug therapies or drug interactions, and changes in the patient's lifestyle."(75) When data from a validated opioid misuse screening tool is enhanced with the EHR data, PCPs can better differentiate the low-risk and high-risk populations.(76-78) There is a caveat: the EHR data should be accessible and findable at the point of care. There is a need to identify a minimum set of data that inform patients' risk from prescription opioids and improve its documentation in the EHR, using standard terminologies and vocabularies.

Furthermore, the impact of risk assessment on patient outcomes is not well understood. Improving data quality of patient outcomes, such as function, quality of life, misuse, OUD, and death, can better inform future policies and guidelines.

Conclusion

There are many barriers to evidence-based risk assessment, and solutions may require a multilevel and multi-pronged approach. Informatics interventions can address the sociotechnical challenges of assessing patients' risk for OUD. Decision support tools that personalize the recommendations in the guidelines for a specific patient and propose appropriate interventions will free up time to discuss treatment and risk prevention options with patients. Educational and shared decision support tools that help patients and providers make mutually acceptable pain treatment and opioid tapering plans and de-stigmatizing vocabularies for use in the delivery of substance use care will help strengthen patient-provider trust. We also need to standardize terminologies for opioid risk outcomes and chronic pain, integrate validated risk assessment tools in EHR and enable access and better display of patient's PDMP data within EHR. We also need to develop interoperability standards for better integration of PDMP data in the EHR.

Variable OUD risk assessment practice and documentation due to associated stigma had led to poor EHR data quality. PCPs need better access to patients' OUD risk data. There is a need to identify and improve the documentation of OUD risk factors to better understand their roles in prevention and treatment and to enable guideline-concordant OUD risk assessment. Improving the data quality of patient-specific risk factors and opioid-related outcomes is critical for enhancing practice and strengthening evidence.

Chapter Two - Supplementary Material

Table -2.1. Thematic extraction of barriers and facilitators using the 14 constructs of the selected frameworks

DIMENSIONS	SYSTEM COMPONENT	SUMMARY
EVIDENCE[c]	CDC guidelines	Most guideline recommendations are supported by weak evidence, type 3 or type 4. Regarding identifying and predicting misuse and diagnosing OUD, no widely used risk assessment tool accurately predicts or identifies misuse, and applying DSM-V criteria to CNCP patients on LTOT has proven difficult.(39, 79).
EXTERNAL RULES, REGULATIONS, and PRESSURES[a]/ CONTEXT[c]	External rules and pressures	A provider's ability to taper is influenced by the patient's insurance coverage, medical contraindications of non-opioid alternatives, difficulty justifying opioid weaning for patients who are stable on chronic opioid use, type of patient's insurance coverage, and patient-provider trust.(39, 80, 81)
CLINICAL CONTENT[a]/ CONTEXT[c]	EHR	Many factors affect the quality of patient-specific risk data in the EHR, influencing the risk assessment process. The stigma

		associated with opioid addiction may have led to variable and inconsistent documentation of opioid misuse and abuse in the EHR.(82) There are variations in the use and documentation of screening tools in the EHR.(61) Aberrant drug-related behaviors, used as indicators of misuse, are inconsistently and unsystematically documented in the EHR.(83)
INTERNAL POLICIES, PROCEDURES and CULTURES[a]/ CONTEXT[c], FACILITATION[c]	Organizational policies, procedures, and culture	Internal policies play significant roles in adherence to risk assessment tasks. Standardized opioid prescribing and monitoring policies improve adherence to guidelines.(64-66) Random urine drug tests and mandatory PDMP reviews can potentially detect high-risk behavior and addiction even in low-risk patients and decrease the monthly dispense of opioids and benzodiazepines.(67, 68) Lack of time and training are significant barriers to guideline adherence.(61, 69, 70) Development of a risk-assessment algorithm and risk-stratified monitoring guidelines improve adherence to guidelines.(64) Organizational culture that embraces

		educational interventions and audit and feedback processes increase guideline adherence.(72, 73) Non-collaborative opioid taper increases patient risk.(39) "Academic detailing" models and a team-based approach to care with physician assistant care managers increase adherence to guidelines.(64, 71)
HUMAN-COMPUTER-INTERFACE[a]/ FACILITATION[c]/	EHR	A patient registry with the regular dissemination of reports to PCPs increases adherence to guidelines.(64)
	PDMP	Difficulty accessing the PDMP and acquiring patient medication history information within the PDMP, due to its non-intuitive display are significant barriers to its use.(84) Also, the lack of standards for PDMP integration into EHRs results in poor usability and decreased usage.(85) Increased interoperability and good human-computer interfaces can facilitate risk assessment and improve adherence.
PEOPLE[a]/ KNOWLEDGE[b]/ ATTITUDE[b]/ BEHAVIOR[b]/	PCPs	Providers find the treatment of chronic pain challenging and desire additional training and referral support.(61) Educating providers leads to improved knowledge and confidence

CONTEXT[c]		to manage COT patients per guidelines and increased screening practices.(86-88) Some PCPs are reluctant to manage prescription opioids for CNCP patients.(89) A patient's risk level is determined based on trust and a history of knowing the patient.(90, 91) Physicians underutilize Urine Drug Screens (UDS), written Opioid Use Agreements (OUA), and Prescription Drug Monitoring Programs (PDMP).(42-46) Variabilities exist among providers in the interpretation of opioid risks.(43)
	Patients	Patient's preference for tapering off opioids influences the provider's ability to taper.(80) Patients with OUD are often not diagnosed and referred for treatment, partly due to the stigma attached to diagnosis and treatment.(92)
WORKFLOW and COMMUNICATION[a]/ FACILITATION[c]	Workflow	Implementing workflow protocol improves adherence to best practices(93); EHR innovations, like the *EHR dashboard*, facilitate communication and increase guideline adherence(64, 94)

CONTEXT[b]	Organizational structure/Practice type	The unavailability of comprehensive, multimodal pain care may limit guideline adherence(39)
MEASURING AND MONITORING[a]/ FACILITATION[c]	Outcome measures	There is a need for clinically relevant outcome measures for risk assessment activities.(95)
	Standard terminologies and codes	Measuring outcomes is challenging due to inconsistent use of terminologies and ICD codes for problem opioid use and varying definition of LTOT, with 41 unique variations across 34 studies.(55, 59, 82)

Note: a- dimension from ST-HIT framework; b – dimensions from Cabana framework; c – dimension from PARIHS framewok

CHAPTER THREE: INTRODUCTION TO THE INFORMATION NEEDS AND READINESS FRAMEWORK FOR COMPLEX AND STIGMATIZED CONDITION

The national plan to address the opioid crisis requires efforts from the prescriber and medical community to continually evaluate and update the CDC guidelines for prescribing opioids for chronic pain and standardize the practice.

However, barriers to guideline-concordant OUD risk assessment for patients on long-term opioid treatment for chronic non-cancer pain have led to variable practice. Real-world guideline-concordant OUD risk assessment is challenging due to a lack of clarity and interpretability and the inability to apply them to a complex patient population.(96) PCPs often use their experience to integrate patients' risk data from multiple sources and determine patients' OUD risk. There is an opportunity to replace the current variable risk assessment approach with one that incorporates evidence from real-world delivery of care.

Access to better quality data at the point of care holds promise to bridge gaps between evidence and practice of OUD risk assessment. We need to identify a minimum data set that alerts PCPs of patients' OUD risk to implement an early intervention. We must understand PCPs' information/data needs to identify patients at risk for OUD and address the challenges to EHR data readiness to meet the PCPs' information needs.

Incorporating provider experience in data need and readiness assessment framework

One of the challenges to using CDC recommendations for OUD risk assessment is timely access to contextual and high-quality data for complex clinical decisions in the real world. Clinical decision-making for complex disease, OUD, and heterogeneous chronic pain populations is contextual and partly driven by provider experience. Variable OUD risk assessment practices have led to racial and ethnic health inequities.(97) Standardizing OUD risk assessment practice requires access to data that meet the information needs of clinicians at the

point of care. I developed a systematic approach to assess and improve the quality of opioid risk data in the EHR to enable a more accurate and timely estimation of patients' opioid misuse and abuse risk.

A primer to evidence-based practice and practice-based evidence cycle

The evidence-based practice incorporates the best evidence, provider experience, and patient values. It has been proven to improve patient outcomes (98); ideally, "best evidence" should integrate "research-based evidence" with "practice-based evidence," which results from real-world delivery of care.

Figure 3.1. Integrating evidence-based practice and practice-based evidence for improving local practice and informing external policies

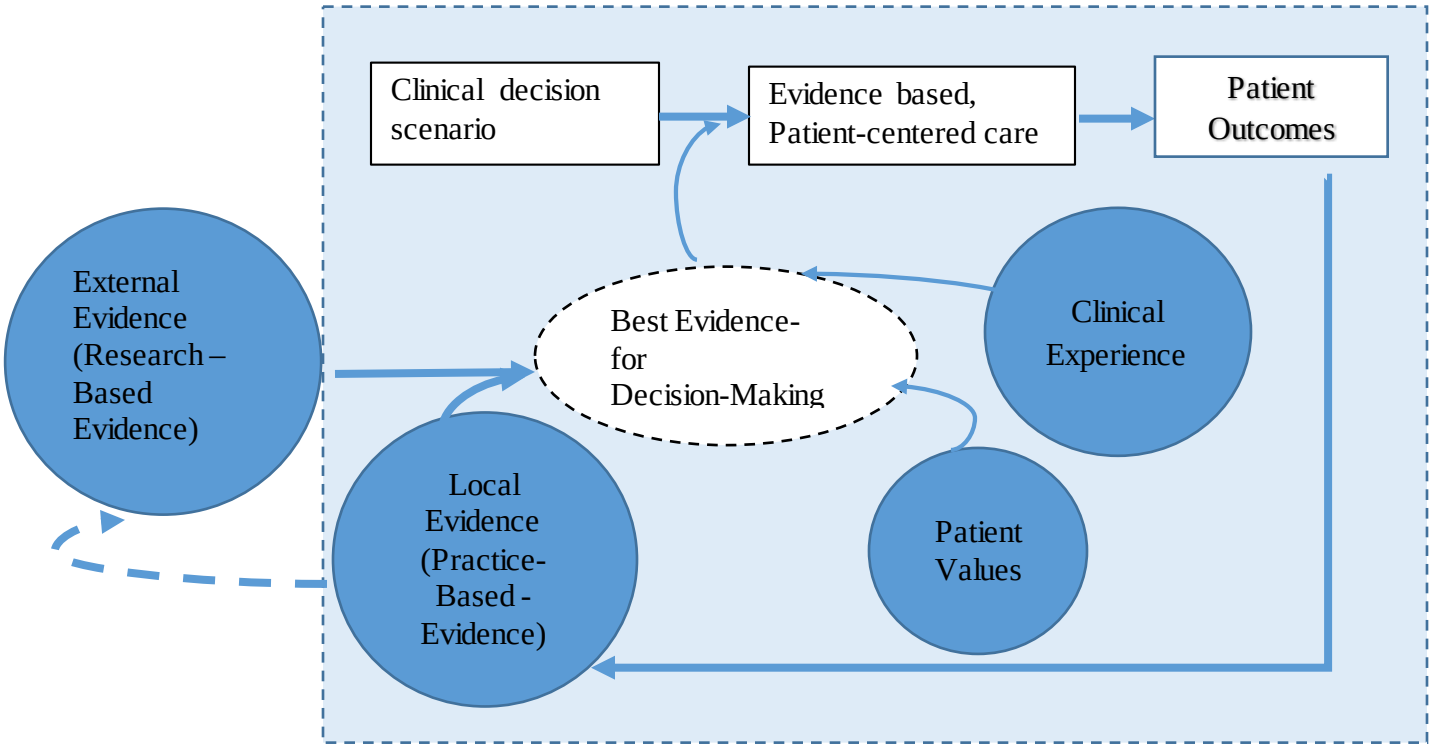


Figure 3.1 displays that both, research-based and practice-based evidence, have roles in improving local practice and informing external policies. However, practice-based evidence requires good quality EHR data and an informatics infrastructure that supports the ability to transform data into knowledge, knowledge to practice, and practice into analyzable data. Such a cycle is characteristic of Learning Health Systems (LHS). It can potentially improve local practice, inform external research-based evidence, and contribute to generalizable knowledge.(99) Standard and computable data are essential for LHS. The availability of adequate data to enable, measure, and improve best practices is of utmost importance, especially when the evidence is weak and the patient population is highly heterogeneous. As a result, we need a generalized approach to improving EHR data quality for complex real-world decision-making.

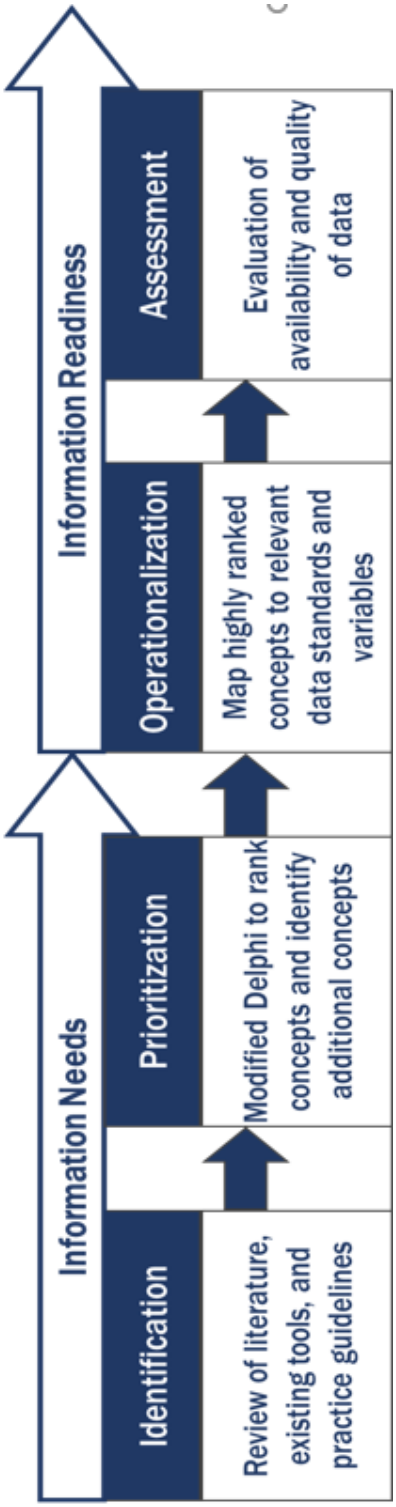
Given the importance of good quality data for OUD surveillance and referral for treatment, I sought to develop a systematic approach to identify the gaps between the information needs and readiness for determining OUD risk in patients on LTOT for chronic non-cancer, non-end-of-life pain.

Figure 3.2 is a framework for assessing the gaps between the information needs and readiness. The framework has two phases – 1) PCPs' information need assessment and 2) EHR's data readiness assessment. The first phase informs the method for the second phase. Each phase has two steps. Steps in information need assessment include i) identification and ii) prioritization. Steps in information readiness assessment include i) operationalization and ii) data quality assessment. Since provider experience plays an essential role in OUD risk assessment, in the absence of clear guidelines and substantial evidence, it is vital to incorporate their voice in gap analysis. I used a modified Delphi survey for identifying and prioritizing the information needs of PCPs. In the identification step, I conducted an extensive literature search of peer-reviewed articles. I elicited stakeholder input to identify a set of OUD risk factors and concepts that

potentially help real-world OUD risk assessment in a population with chronic non-cancer pain. For prioritizing the risk factors for the data readiness phase, I conducted a modified Delphi survey of PCPs in various healthcare settings to achieve consensus on "highly useful" OUD risk factors and concepts. The goals of the identification and prioritization phase of the gap assessment process were to generate a highly curated list of OUD risk factors for the survey and to achieve consensus on OUD risk factors and concepts that are "highly useful" for OUD risk decision-making in the real world.

The data readiness phase of the gap assessment framework consists of operationalization and quality assessment steps. I used the guidance of a PCP to determine how each of the "highly useful" OUD risk factors and concepts is operationalized in actual practice and mapped them to standard terminologies and tools. I developed the "computability" construct to determine the accessibility of "highly useful" OUD risk factors and concepts. The correctness and completeness of all computable OUD risk factors were determined to assess data quality gaps that can be addressed through informatics solutions. Data needs and readiness assessments were Aims 2 and 3 of my research project.

Figure 3.2. Framework for Gap Assessment between Information Need and Readiness



CHAPTER FOUR: AIM 2. THE MODIFIED DELPHI PROCESS TO ASSESS PRIMARY CARE PROVIDERS' INFORMATION NEEDS - Step 1. Identification & Step 2. Prioritization

Delphi Methodology to Achieve Consensus on Information Needs of Primary Care Providers to Assess Opioid Use Disorder Risk in Patients on Long-Term Opioids for Chronic Pain

Abstract

The purpose of this study was to achieve consensus from primary care providers (PCPs) on useful patient information to assess opioid use disorder (OUD) risk in patients on long-term opioid therapy (LTOT) for chronic nonmalignant, non-end-of-life pain. A modified Delphi-style survey was conducted to get consensus and rank patient information considered useful by PCPs for determining their patients' OUD risk. Out of 57 OUD risk concepts and factors across nine bio-psycho-social domains included in the survey, we achieved consensus on 33 as "very or extremely useful", three as "moderately or slightly useful", and one as "not useful". Many of the high-ranked OUD concepts are also mentioned in the CDC guidelines. Nearly half of the thirty-three "very" or "extremely" useful information consists of aberrant drug-related behaviors (ADRBs) that often exist as unstructured data. The results from this work will help prioritize future informatics projects in making these data elements more accessible at the point of care.

Introduction

The economic and healthcare cost of opioid use disorder (OUD) in the United States runs into billions of dollars.(100) Patients on prescription opioids for chronic pain are at increased risk for developing OUD,(36) increasing their risk for overdose and suicide.(101) In the United States, the majority of care for patients at risk of developing OUD is provided by primary care providers (PCPs).(102, 103) One of their most important responsibilities is identifying at-risk patients and enabling the delivery of appropriate care, including referrals to specialists. A

specific recommendation for PCPs, provided by the Center for Disease Control (CDC) is to screen patients on long-term opioid therapy (LTOT) for potential opioid use disorder (OUD), where LTOT is defined as the use of opioids on most days for >3 months.(38)

However, determining which LTOT patients are at risk for developing OUD is challenging. In general, LTOT patients and chronic pain patients are a complex and variable population, often with extensive medical histories. Additionally, OUD is a highly variable condition with a broad range of severity and presentation. Identifying and addressing OUD risk in patients on LTOT in the primary care setting has proven difficult due to limited time and specialized knowledge. While several guidelines and tools exist to assist providers in identifying at-risk patients, most of these tools fail to address the real-world complexities described earlier.

One of the main challenges of implementing these guidelines and tools in the primary care setting is difficulty in finding and accessing pertinent information in the EHR. Many of the required data are fragmented across multiple encounters, health care providers, or even entirely separate systems. Additionally, many of these concepts may either be missing or stored as unstructured data like free text documentation in progress notes, making retrieving relevant information at the point of care challenging. In applying existing guidelines and risk assessment tools for patients on opioids for chronic pain, PCPs must develop and implement their own approaches to finding and synthesizing multiple types of patient-specific information from various sources to determine their patients' OUD risk. These challenges made it difficult not only for PCPs to conduct OUD risk assessments but also make it difficult to deploy or develop screening tools or clinical decision support tools, which almost always rely on the availability of accessible, computable data.

To improve the identification and subsequent treatment of patients with or at risk for OUD, we must bridge the gap between guideline-based care and what is feasible, given the current

limitations of EHRs and the data they contain. Improving access to patient information that aids clinical decision-making can reduce provider burden. While one option would be to improve the structured entry of risk factors for developing OUD while on LTOT, this approach would add to providers' already substantial documentation burden.

An alternative would be to use current clinical practice and workflow to guide appropriate informatics interventions. Specifically, suppose the information needs of practicing PCPs can be codified. In that case, we can prioritize data collection and extraction and develop automated tools that rely on these data rather than those less likely to be available without increasing the documentation burden.

Therefore, there is a need for consensus on the relative usefulness of various factors in assessing OUD risk for this complex patient population to improve their availability at the point of care. Though various biopsychosocial and behavioral factors have been associated with OUD, it is unclear which factors are weighed more by the PCPs when determining OUD risk for patients on LTOT for chronic, nonmalignant, non-end-of-life pain. Our objective, therefore, was to determine the high-ranking information needs of PCPs to practice evidence-based care for complex patients.

In summary, current recommendations and tools for OUD risk assessment in LTOT populations reflect the expert opinion and scientific evidence. Still, they do not consider the reality of primary care and limited data availability within EHRs. PCPs who routinely manage patients on LTOT have unique insight into what factors might predict the development of OUD. We, therefore, employed a consensus-based approach to determine relevant information needs by asking PCPs from diverse care settings to state the relative usefulness of different patient-level concepts for assessing OUD risk in patients on opioids for chronic pain. The findings from this work are intended not to replace but to complement existing knowledge and evidence. The

insight gained may improve how recommendations can best be implemented in primary care settings to decrease provider burden, more reliably identify patients at risk for OUD, and improve the quality of care for this patient population.

Methods

In this study, I used a modified Delphi process to reach a consensus on high-ranking patient-specific information needed by PCPs to determine patients' risk for developing OUD while on long-term opioid therapy.

The Delphi Process

Initially developed by the RAND group in the 1950s, the Delphi process has been extensively used in studies requiring expert consensus in situations with contradictory or insufficient information.(104) The Delphi process consists of iterative survey rounds of subject matter experts to gain consensus on a particular subject. The first survey round is usually qualitative to collect diverse perspectives/opinions on a topic of interest. In this modified Delphi process, the qualitative survey round, done as a first step to collect various views on a topic (in this case – helpful OUD risk factors and concepts), has been replaced by a literature review and expert input. The literature review and stakeholder input constitute the identification step of my information need assessment phase.

Following an extensive literature review to identify candidate OUD risk factors and concepts, a purposive sample of PCPs who regularly care for patients on long-term opioid treatment were asked to participate in two rounds of the Delphi survey. The two Delphi survey rounds comprise the prioritization step of my information need assessment phase.

Method Step 1. Identification - Literature search and stakeholder input

Opioid Use Disorder (OUD) is another term for addiction and evolved from prior terms like dependence and abuse. People with addiction may misuse opioids. Opioid misuse or abuse does not necessarily result in addiction, but opioids are highly addictive, and the risk increases with misuse and abuse.(105)

Since the terminology of OUD evolved over the years and misuse and abuse are risk factors for OUD, I started my literature search with broader search terms, like "opioid-related disorders," to collect as many OUD risk factors as possible. I conducted a literature search to identify risk factors for opioid misuse, abuse, addiction, and opioid use disorder studied explicitly in patients on long-term opioid therapy (LTOT) for chronic, non-cancer pain. The search term was developed in consultation with Andrew Hamilton, a health science education and research librarian at Oregon Health & Science University.

Inclusion criteria – Adult patients on long-term opioid analgesics for chronic non-cancer pain with opioid misuse, addiction, and opioid use disorder.

PubMed search string

(((("Stress, Psychological"[Mesh]) AND ("Chronic Pain"[Mesh])) OR (((((("Analgesics, Opioid/adverse effects"[Mesh] OR "Analgesics, Opioid/poisoning"[Mesh] OR "Analgesics, Opioid/toxicity"[Mesh])) OR ("Analgesics, Opioid" [Pharmacological Action])) AND (("Drug Misuse"[Mesh]) OR ("Substance-Related Disorders"[Mesh]))) OR ("Opioid-Related Disorders"[Mesh]))) AND ((((("Chronic Pain"[Mesh]) AND ((((("Analgesics, Opioid/adverse effects"[Mesh] OR "Analgesics, Opioid/poisoning"[Mesh] OR "Analgesics, Opioid/toxicity"[Mesh])) OR ("Analgesics, Opioid" [Pharmacological Action])) AND (("Drug Misuse"[Mesh]) OR ("Substance-Related Disorders"[Mesh]))) OR ("Opioid-Related Disorders"[Mesh]))) AND ((Adult* and child* and advers* and (event* or traum*)) OR ("Adult Survivors of Child Adverse Events"[Mesh]))) OR (((((((("Analgesics, Opioid/adverse effects"[Mesh] OR "Analgesics, Opioid/poisoning"[Mesh] OR "Analgesics, Opioid/toxicity"[Mesh])) OR ("Analgesics, Opioid" [Pharmacological Action])) AND (("Drug Misuse"[Mesh]) OR ("Substance-Related Disorders"[Mesh]))) OR ("Opioid-Related Disorders"[Mesh])) AND (risk*)) AND ("Chronic Pain"[Mesh])) OR (((((((("Analgesics, Opioid/adverse effects"[Mesh] OR "Analgesics, Opioid/poisoning"[Mesh] OR "Analgesics, Opioid/toxicity"[Mesh])) OR ("Analgesics, Opioid" [Pharmacological Action])) AND (("Drug Misuse"[Mesh]) OR ("Substance-Related Disorders"[Mesh]))) OR ("Opioid-Related Disorders"[Mesh])) AND ("Chronic Pain"[Mesh])) AND ("Sociological Factors"[Mesh])) OR ((("Risk"[Mesh]) AND ((((("Analgesics, Opioid/adverse effects"[Mesh] OR "Analgesics, Opioid/poisoning"[Mesh] OR "Analgesics, Opioid/toxicity"[Mesh])) OR ("Analgesics, Opioid" [Pharmacological Action])) AND (("Drug Misuse"[Mesh]) OR ("Substance-Related Disorders"[Mesh]))) OR ("Opioid-Related Disorders"

[Mesh])))) AND ("Chronic Pain"[Mesh])))))

Two internal medicine physicians, M.P. & J.R., provided feedback on the collected OUD risk factors and behaviors. The revised list was used to create items for the survey. Items were discarded if deemed not applicable to the primary care setting.

Method Step 2. Prioritization – The Delphi survey

Recruitment and participation

Since this work aimed to consider the reality of care delivery in various primary care settings and incorporate unique insights of PCPs managing LTOT patients, I sought input from a more comprehensive network of PCPs. A purposive sample of PCPs was invited to participate. Delphi participants are also called experts for being the subject matter experts on the topic under study. An expert for this study was defined as a PCP who manages patients on opioids for chronic nonmalignant, non-end-of-life pain. Three levels of experts were identified in the survey: level 1, defined as a PCP who *occasionally* manages noncancer chronic pain patients on opioids; level 2, defined as someone who *routinely* manages noncancer chronic pain patients on opioids; and level 3, defined as someone who has *participated in research* in the area of opioid prescribing *and/or policy development* at the local, regional or national level. PCPs working in diverse care settings were invited to participate in the survey. I contacted PCPs working in internal medicine, family medicine, and the women's health clinics at Oregon Health and Science University (OHSU) to participate in the survey. I also invited PCPs working in rural and community clinics through the Oregon Rural Practice Research Network (ORPRN) and Federally Qualified Health Centers (FQHC) through Central City Concern (CCC) in Oregon. The sampling methodology sought to ensure adequate representation and a diverse perspective. I identified the primary contacts at each clinic mentioned above and requested them to send the link to the first round of

the Qualtrics survey. The links were sent out as group emails. I collected the email addresses of first-round participants for subsequent survey distribution.

Delphi structure and administration

Two rounds of the Delphi survey were conducted using the OHSU QualtricsXM platform. In the first round of the survey, I asked participants to rank the usefulness of each of the 57 OUD risk concepts when assessing their patients' risk. The ranking was done on a 5-point Likert scale ranging from "Not useful" to "Extremely useful". A score of 1 was assigned to "not useful", 2 to "slightly useful", 3 to "moderately useful", 4 to "very useful", and 5 to "extremely useful". A single open-ended question was also asked to collect any additional OUD risk concepts not included in the survey. I collected basic participant information regarding their training, certification, years of practice, and care setting. Sixty-two PCPs opened the survey in round one; however, ten did not meet the "expert" criteria to progress with the survey, and five were excluded from the analysis due to incomplete data. 47 PCPs participated in round one and 38 in round two surveys. The overall response rate in the second round was 80%.

In round two, I provided each participant with the median response for each OUD risk item and the individual participant's answer from round one for reference. The participants were requested to reflect and reevaluate their responses.

Analysis

Since nine first-round participants did not respond to the second-round survey, I tested if the responders, participants who completed both rounds, differed significantly from non-responders, who completed round one but not two. I used round one data to conduct Fisher-exact and Chi-square tests on categorical data (professional training, PCP type, continuing education credits for pain in the past two years (CME), expert levels, practice setting, expert level, and years of practice). Wilcoxon Rank Sum and Kruskal-Wallis tests with Bonferroni correction were done

on the ordinal data (survey item response).

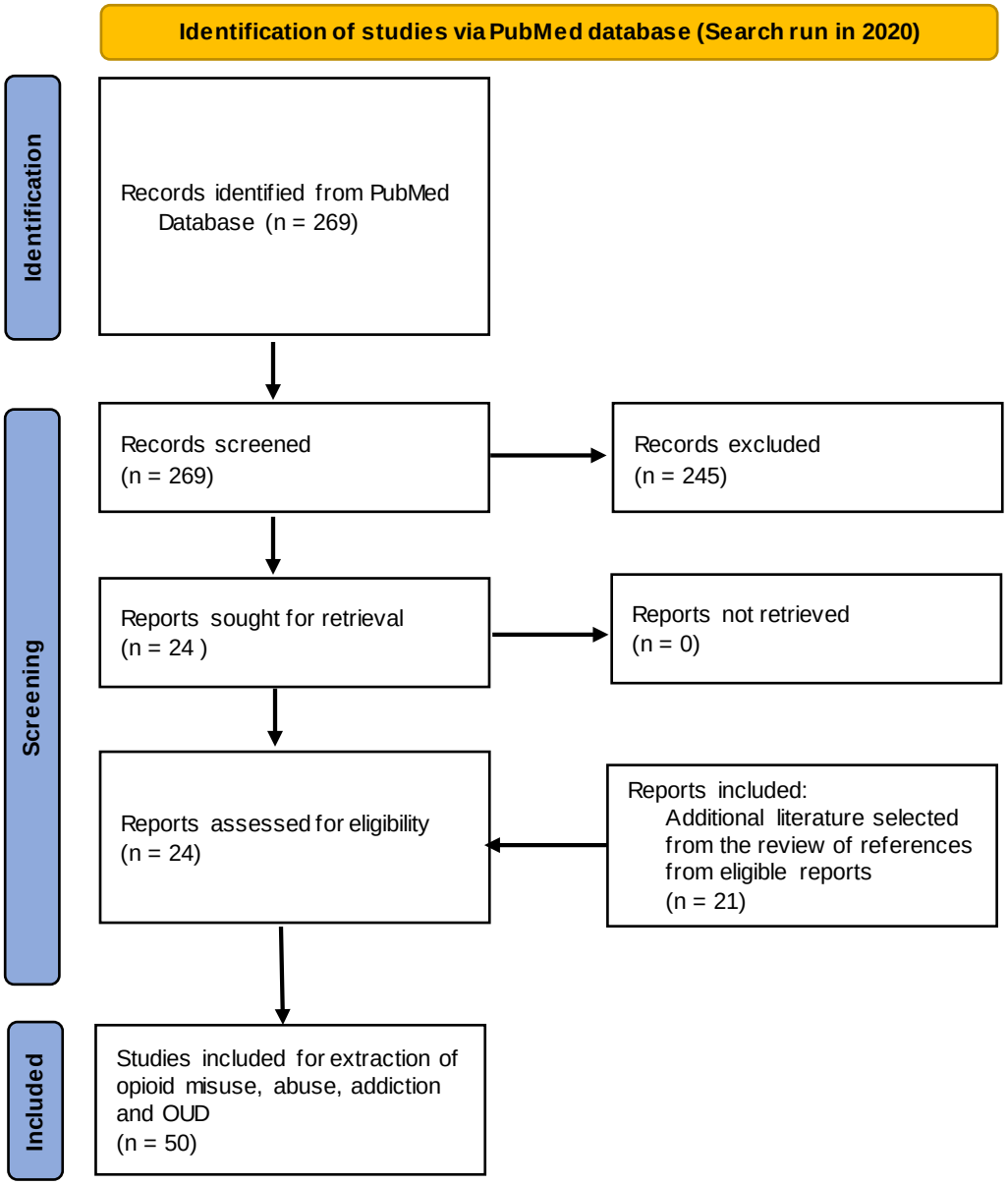
I computed the descriptive statistics (measures of central tendency - mean and median, and dispersion - standard deviation and interquartile range) to determine the relative rank and stability of consensus for each survey item. The five-point Likert scale was collapsed to three-point to determine consensus on the level of usefulness of an item on the survey. For this study, consensus on the usefulness of an OUD concept or factor was determined to have reached when ≥75% of the participants agreed that the item was one of the three: - very or extremely useful, slightly or moderately useful, or not useful. The final ranking of all concepts in the survey was based on their mean score in round two. I also analyzed the open-ended response from survey participants for themes for additional OUD risk factors.

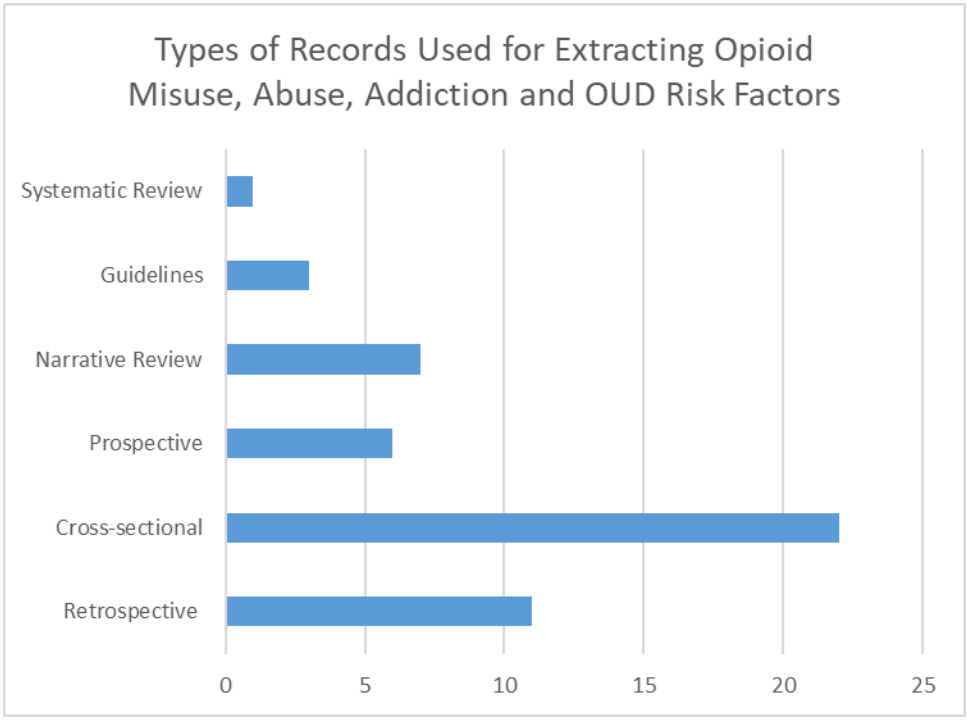
Results

Result Step 1. Identification - Literature search and stakeholder input

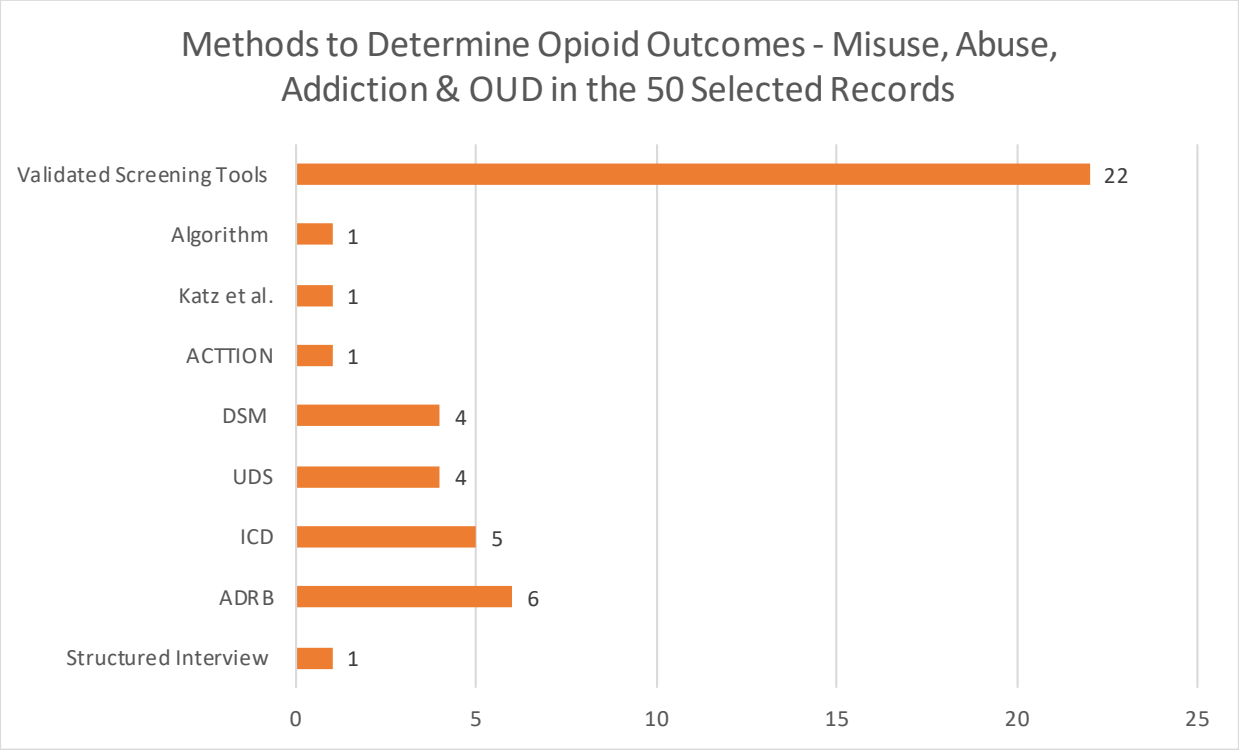
The search strategy yielded 269 articles or records. Figure 4.1 is the flowsheet for identifying and selecting articles to extract opioid misuse, abuse, addiction, and OUD risk factors. I also included secondary literature, such as review articles and official guidelines for extracting the risk factors. Finally, I identified 50 records/articles that covered risk factors for opioid misuse, abuse, addiction, and OUD in the population of interest (patients on long-term opioid analgesics for chronic non-cancer pain). Table 1 in the appendix details all 50 records for extracting the risk factors.

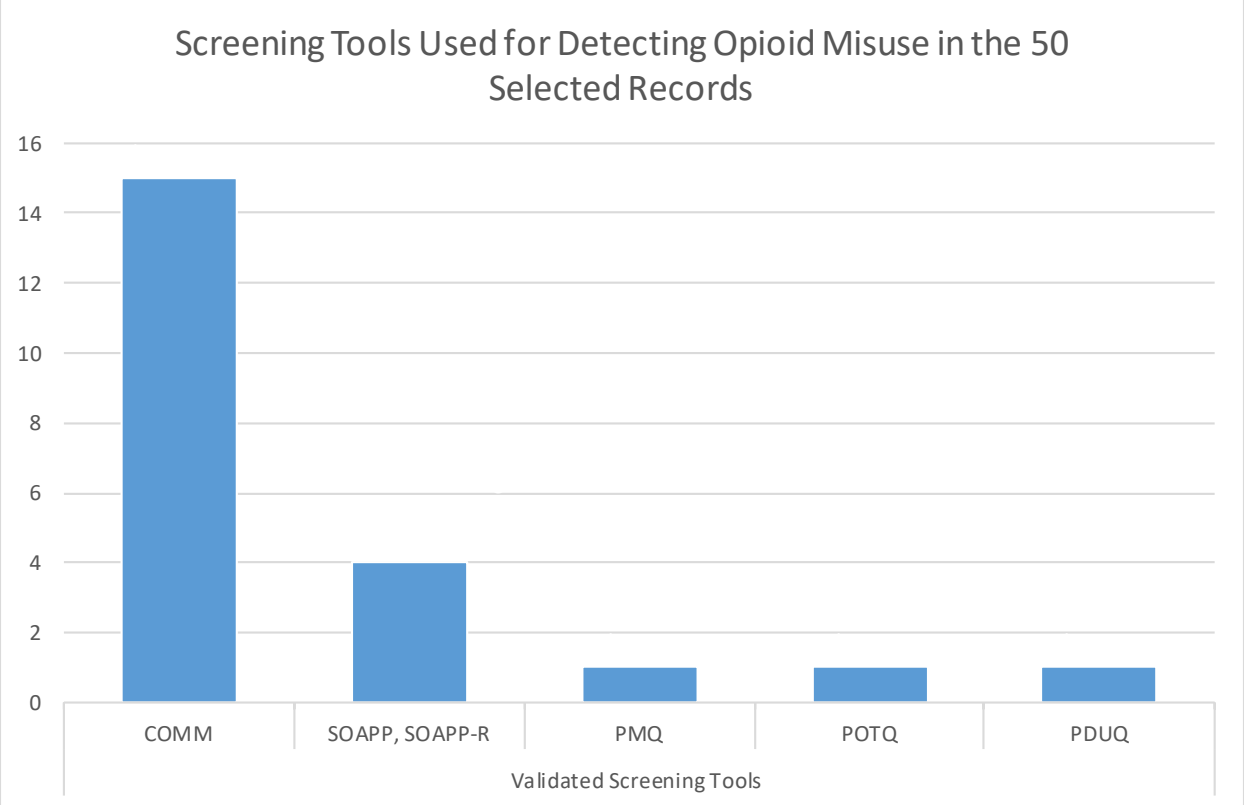
Figure 4.1. Flow diagram of PubMed search and literature selection for extracting opioid misuse, abuse, addiction, and OUD risk factors





Most records were cross-sectional (n=22) and retrospective (n=11) studies. It is important to note that there were variabilities in how the outcomes of misuse, abuse, addiction, and OUD were defined and measured in these studies. Most studies determined prescription opioid misuse or abuse using validated screening tools. A few studies used aberrant drug-related behaviors (ADRBs), unexpected Urine Drug Screening (UDS) results, International Classification of Diseases (ICD) codes, and criteria for misuse, abuse, and opioid use disorder specified in the diagnostic and statistical manual of mental disorders (DSM) to determine opioid-related harm. There were variabilities in the types of screening tools used to determine opioid misuse. Current Opioid Misuse Measure (COMM) and Screener and Opioid Assessment for Patients with Pain (SOAPP) were the most widely used tools.


Methods to Determine Opioid Outcomes - Misuse, Abuse, Addiction & OUD in the 50 Selected Records
Validated Screening Tools
22
Algorithm
1
Katz et al.
1
ACTTION
1
DSM
4
UDS
4
ICD
5
ADRB
6
Structured Interview
1
0
5
10
15
20
25


Screening Tools Used for Detecting Opioid Misuse in the 50 Selected Records
16
14
12
10
8
6
4
2
0
COMM
SOAPP, SOAPP-R
PMQ
POTQ
PDUQ
Validated Screening Tools

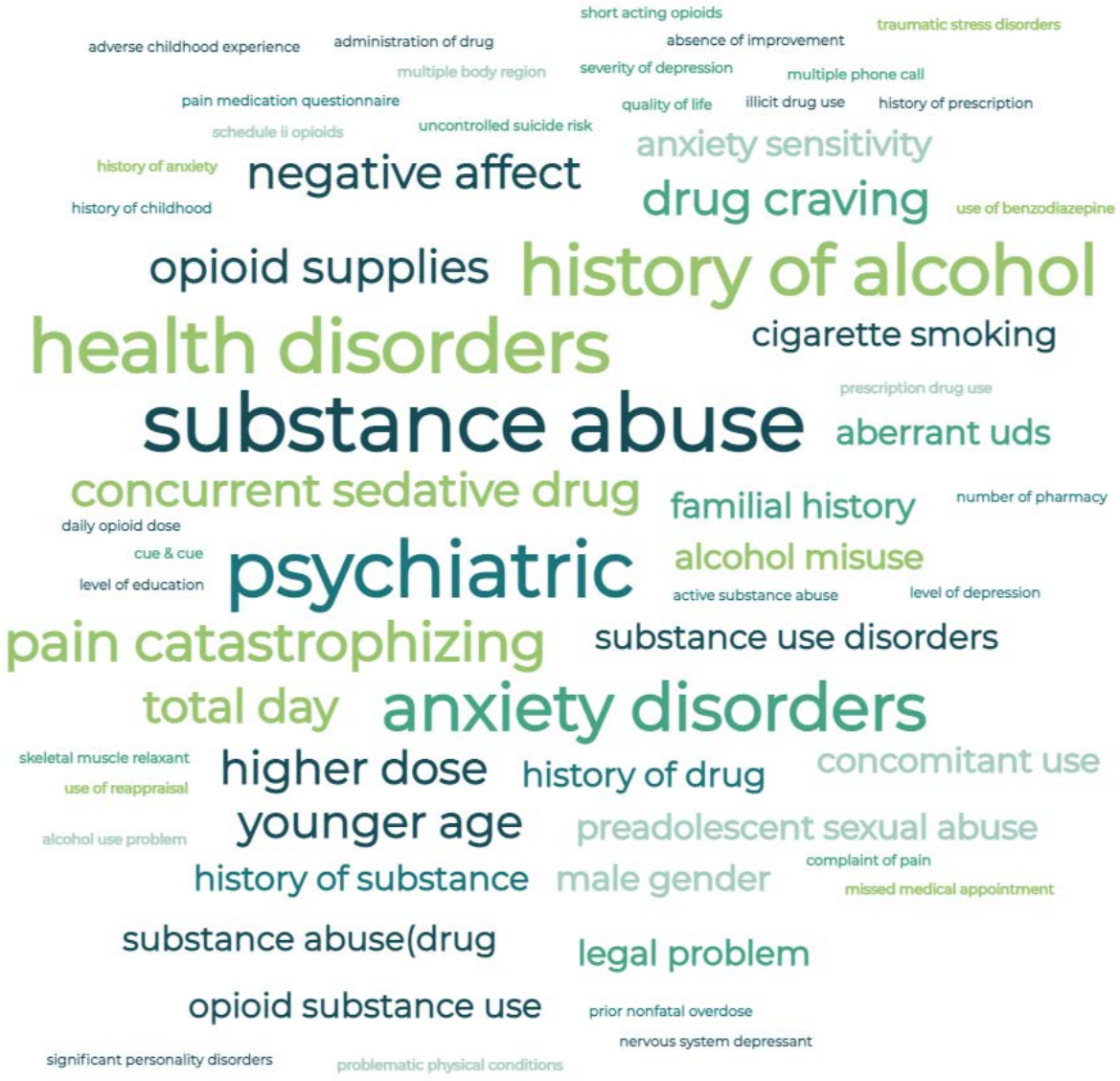
I extracted 102 risk factors for opioid misuse, abuse, addiction, and OUD from the 50 final records/articles (Appendix – Table 2). Figure 4.2 on the next page is a word cloud of all risk factors from the 50 studies. Risk factors in larger fonts appeared in more articles than risk factors in smaller fonts. The risk factors span various biopsychosocial domains. Substance abuse and psychiatric conditions were the top two risk factors for opioid misuse, abuse, addiction, and OUD. Younger age, a higher dose of prescription opioids, history of substance abuse, alcohol use, cigarette smoking, drug craving, concurrent sedative drug, anxiety disorder and substance use disorder, aberrant urine drug screening results, family history of substance use, male gender and preadolescent sexual abuse are also among the top risk factors for the outcomes of interest. Many of these factors are also mentioned in the CDC guidelines for safe opioid prescribing for adults with non-cancer chronic pain.

Two primary care providers, MP and JR, helped to select risk factors for prescription opioid misuse, abuse, addiction, and opioid use disorder to include in the Delphi survey. Table 3 in the Appendix has all 57 risk factors selected for the Delphi survey. The two PCPs selected risk factors that can be easily interpreted and screened in a primary care setting. Though beneficial for addiction research, risk factors like impulsivity, negative affect, attentional bias towards drug-related cues, and cue-elicited craving are not easy to measure and interpret in a primary care setting. So these were excluded from the final list. Two risk factors, traveling long distances for pain care and Kratom use, were added to the selected list of 57 risk factors based on the advice of the two PCPs, MP and JR.

Ultimately, I finalized 57 OUD risk concepts and factors across nine biopsychosocial domains for the Delphi survey. There were 16 items from aberrant drug-related (ADRBs), ten from substance use, eight from psychiatric, eight from pain and function, five from medication, five from socioeconomic, two from demographic, two from comorbidity, and one from genetic

domains.

Figure 4.2. Word cloud of opioid risk factors from the literature search



Result Step 2. Prioritization – The Delphi survey

Almost three-quarters of the Delphi participants were medical doctors or doctors or osteopathic medicine. Our expert group had an equal representation of internal and family medicine providers (Table 4.1). Most experts practiced in academic healthcare centers, but a

Table 4.1. Participant characteristics for the two rounds of the Delphi survey

Participant information	Round 1 n(%)	Round 2 n(%)	P value[a]
Professional Training			**0.01 (<0.05)**
MD /DO	34(74.5)	30(78.9)	
PA	7(14.9)	5(13.2)	
NP	3(6.4)	3(7.9)	
Other	2(4.3)	0(0)	
PCP type			0.92
IM	19(40)	16(42)	
FM	28(60)	22(58)	
Pain management CME in the past 2 years	25(53.2)	21(55.3)	0.71
Board-certified geriatrician or routinely see patients more than 65 years of age	24(51.1)	21(55.3)	0.29
Type of healthcare setting[b]			0.60
Academic health center	35(74.5)	30(78.9)	
Community health clinic	12(25.5)	9(23.7)	
Women's health clinic	3(6.4)	3(7.9)	
Rural clinic	7(14.9)	5(13.2)	
Other	1(2.1)	1(2.6)	
Expert level			0.15
Level 1	15(32)	12(32)	
Level 2	21(45)	15(39)	
Level 3	11(23)	11(29)	
Years of practice[c]			0.34
0-5	13(30)	11(31)	
6-10	14(32)	8(22)	
11-15	2(5)	2(6)	
16-20	5(11)	5(14)	
21-25	4(9)	4(11)	
>25	5(11)	5(14)	

a: A two-sided Fisher's Exact Test was performed for all categories except for PCP type and Expert level, where the Chi-square test was performed
b: Participants allowed more than one selection
c: Missing data for years in practice: 4 in Round1 and 3 in Round2

quarter also practiced in community health clinics and nearly one-tenth in rural and women's health clinics. Most experts were in the level 2 category, though levels 1 and 3 were well

represented. Almost half of the experts received CME credits for pain management education in the past two years. Around two-thirds of the survey participants had been in medical practice for ten years or less and around one-tenth for greater than 25 years. The non-responders mainly were MD/DO and 'other' licensed professionals (licensed qualified mental health counselors, naturopathic doctors) with less than ten years of practice and expert levels 1 and 2. Almost half had CME dedicated to pain management in the last two years. Responders and non-responders differed significantly (p-value <0.05) in their median score for three survey items – age < 45 years, heavy smoking, and pain condition with no evidence of benefit from prescription opioids. After Bonferroni correction, however, no significant differences besides the professional training were observed between responders and non-responders.

After the two rounds of surveys, a consensus was achieved for thirty-three OUD concepts and factors as "very or extremely useful", three as "moderately or slightly useful", and one as "not useful" (Table 4.2).

Table 4.2 Delphi survey items and consensus post survey round 2

Domains	***Patient Information***	***Clinician Feedback***	***Literature***	***Guidelines(79)***	***Consensus Post – Delphi[a]***
Demographics	Age < 45 years		X(52, 106-115)	X	Yes (L)
	Male gender		X(52, 107, 110, 114, 116, 117)		No
Substance Use	Illicit drug use		X(107, 114, 118, 119)		Yes (H)
	Cannabis/Marijuana use		X(118, 120, 121)		No
	Kratom use	X			No
	Current substance use disorder		X(106, 108, 118, 122)	X	Yes (H)
	History of substance use disorder		X(75, 106, 118, 123-126)	X	Yes (H)

	Tobacco use		X(126)		No
	Heavy smoking		X(109)		No
	History of misuse of any sedative or stimulant		X		Yes (H)
	History of misuse of cold and cough medication		X		No
	History of non-fatal opioid overdose		X	X	Yes (H)
Psychiatric(52, 106, 115, 127)	Anxiety disorder		X(123)	X	Yes (L)
	Post-traumatic stress disorder		X		No
	Major depressive disorder		X(123)	X	Yes (L)
	Acute psychiatric instability		X		No
	History of suicide attempt/s		X		Yes (H)
	Suicidal ideation		X		Yes (H)
	Personality disorder		X		No
	Psychosomatic disorder		X		No
Psychiatric(52, 106, 115, 127)	Acute psychiatric instability		X		No
	History of suicide attempt/s		X		Yes (H)
	Suicidal ideation		X		Yes (H)
	Personality disorder		X		No
	Psychosomatic disorder		X		No
Socioeconomic	Housing instability		X		No
	Marital status separated or divorced		X		No
	History of DUI or drug conviction		X(114)		Yes (H)
	Family history of substance use disorder		X(106)	X	Yes (H)
	History of childhood physical, emotional or sexual abuse		X(106)		Yes (H)
Pain and Function	Pain diagnosis associated with no evidence of benefit.		X		No
	Longer pain duration		X		Yes (H)
	Involvement of multiple body locations(126)		X		No
	Lack of demonstrated functional improvement		X		Yes (H)
	High pain interference with daily activity		X		Yes (H)
	Pain catastrophizing		X(128)		Yes (H)
	On disability for pain-related condition		X		No
	Interference with vocation due to opioid use or pain		X		Yes (H)
Medication	Total opioid dose > 90 MME/day		X		Yes (H)
	Concurrent long-acting plus		X		Yes (H)

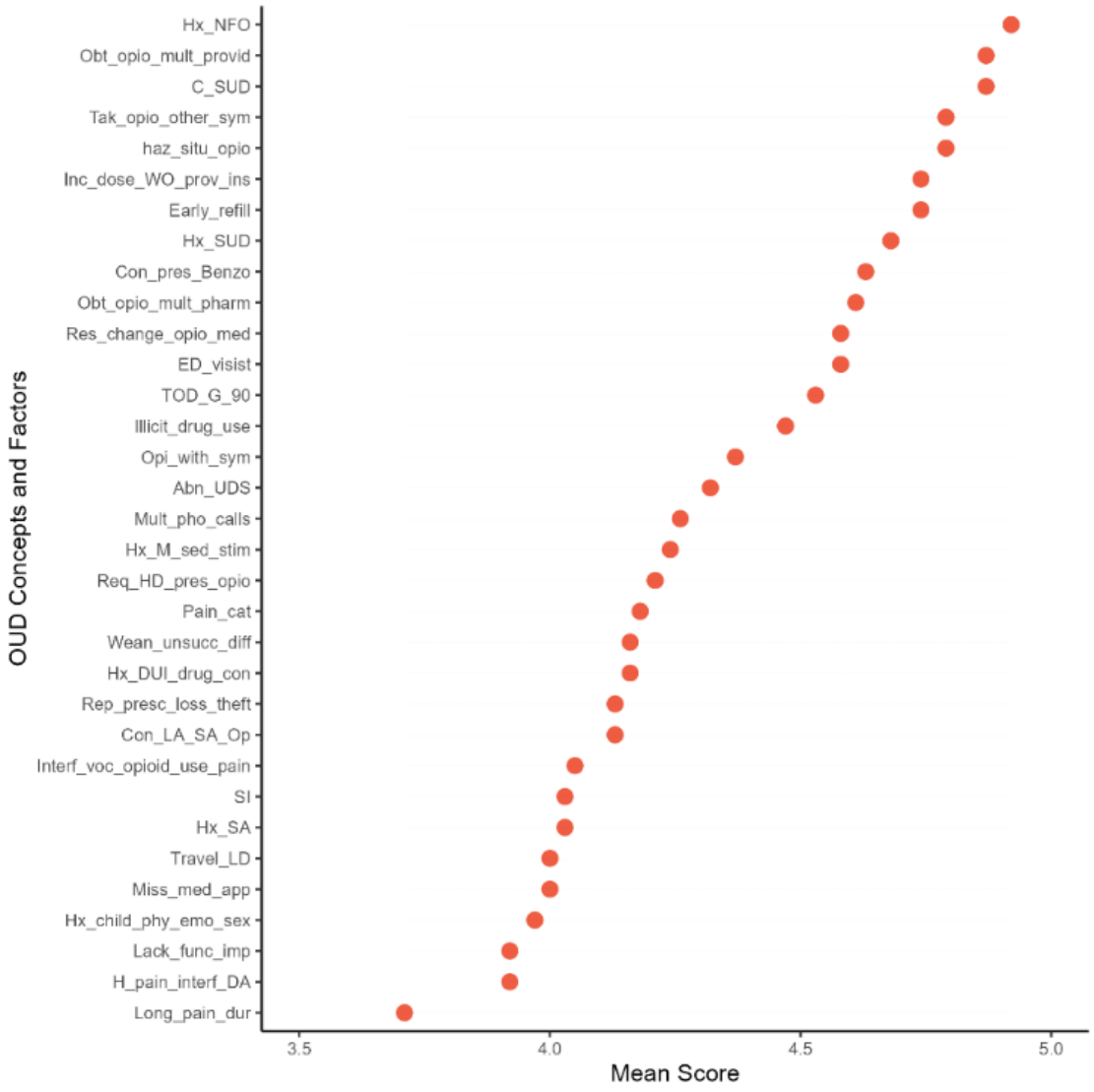
	short-acting opioids				
	Concurrent prescribed Benzodiazepines		X	X	Yes (H)
	Concurrent other psychiatric medication (SSRIs, SNRI, atypical antipsychotics)[b]	X		X	No
	Concurrent non-benzo sedative-hypnotics (e.g. zolpidem, zaleplon, butalbital)[b]	X		X	No
Aberrant Drug-Related Behaviors	Resistance to changing opioid medications despite a deterioration in function or significant negative effects		X(129)		Yes (H)
	Reporting prescription loss or theft		X(129)		Yes (H)
	Obtaining opioids from multiple providers in violation of the treatment agreement		X(110, 129)		Yes (H)
	Increasing dose without provider's instruction		X(129)		Yes (H)
	Running short with medication supply and requests for early refills		X(129)		Yes (H)
	Traveling long distances for pain care	X			Yes (H)
	Showing symptoms consistent with opioid withdrawal		X	X	Yes (H)
	Obtaining prescription opioids from multiple pharmacies		X(110)		Yes (H)
	Missing medical appointments		X(129, 130)		Yes (H)
	Being in a hazardous situation as a result of opioids		X		Yes (H)
Aberrant Drug-Related Behaviors	Weaning described as unsuccessful or difficult				Yes (H)
	Emergency department visits to obtain opioids		X(129)		Yes (H)
	Abnormal urine drug screening result		X(116)	X	Yes (H)
	Requesting higher doses of prescription opioids				
	Multiple phone calls to clinic requesting opioid medication		X(126)		Yes (H)
	Taking opioids for symptoms other than pain (e.g., anxiety, depression, sleep, or to produce		X(129)		Yes (H)

	euphoria)				
Medical Comorbidity	History of Hep C infection		X		No
	HIV infection		X		No
Genetic test	Genetic tests positive for gene polymorphism associated with OUD		X		Yes (N)

"X" means present for source
a Letters in brackets: (H) – Very and Extremely useful; (L) – Moderately and slightly useful; (N) – Not useful
b These categories were input from clinicians to substitute the use of psychotropic medication in the guidelines

Twenty items did not reach the cut-off percentage agreement of ≥ 75% for any three categories. All 16 survey items in the ADRBs domain reached an agreement as "very or extremely useful" and made up nearly half of the "very and extremely useful" OUD concepts and factors list. Substance use and pain and function domains contributed five items each, the medication domain contributed three items, and the socioeconomic and psychiatric domains each contributed two items to the list. None of the "very and extremely useful" OUD concepts and factors came from demographics, comorbidity, and genetics domains. The three items agreed as "slightly or moderately useful" comprised of age < 45 years from the demographic domain and anxiety disorder and major depressive disorder from the psychiatric domain. Genetic factors were the only item that reached consensus as not useful for OUD risk determination. The survey items were ranked based on their mean score in round two (Figure 4.3). Survey items in the ADBRs and substance use ranked highest, while those in the demographic, comorbidities, and genetic domains received the lowest mean score.

Figure 4.3. Ranked "Very" or "Extremely" Useful OUD Concepts and Factors



Hx_NFO = history of non-fatal overdose, Obt_opio_mult_provid = Obtaining opioids from multiple providers in violation of treatment agreement, C_SUD = Current substance use disorder, Tak_opio_other_sym = Taking opioids for symptoms other than pain (e.g., anxiety, depression, sleep, or to produce euphoria), haz_situ_opio = Being in hazardous situation as a result of opioids, Inc_dose_WO_prov_ins = Increasing dose without provider's instruction, Early_refill = Running short with medication supply and requests for early refills, Hx_SUD=History of substance use disorder, Con_pres_Benzo= Concurrent prescribed Benzodiazepines, Obt_opio_mult_pharm= Obtaining prescription opioids from multiple pharmacies, Res_change_opioi_med= Resistance to changing opioid medications despite deterioration in function or significant negative effects, ED_visist= Emergency department visits to obtain opioids, TOD_G_90= Total opioid dose > 90 MME/day, Illicit_drug_use= Illicit drug use, Opi_with_sym= Showing symptoms consistent with opioid withdrawal, Abn_UDS= Abnormal urine drug screening result, Mult_pho_calls= Multiple phone calls to clinic requesting opioid medication, Hx_M_sed_stim= History of misuse of any sedative or stimulant, Req_HD_pres_opi= Requesting higher dose of prescription opioids, Pain_cat= Pain catastrophizing, Wean_unsucc_diff= Weaning described as unsuccessful or difficult, Hx_DUI_drug_con= History of DUI or drug conviction, Rep_presc_loss_theft= Reporting prescription loss or theft, Con_LA_SA_op= Concurrent long-acting plus short-acting opioids, Interf_voc_opid_use_pain= Interference with vocation due to opioid use or pain, SI= Suicidal ideation, Hx_SA= History of suicide attempt/s, Travel_LD= Traveling long distance for pain care, Miss_med_app= Missing medical appointments, Hx_child_phy_emo_sex= History of childhood physical, emotional or sexual abuse, Lack_func_imp= Lack of demonstrated functional improvement, H_pain_interf_DA= High pain interference with daily activity, Long_pain_dur= Longer pain duration

Most OUD risk factors and concepts provided as open responses by the participants overlapped with risk concepts already included in the survey. They spanned substance use, aberrant drug-related behaviors, pain and function, and socioeconomic domains. (Table 4.3). History of diversion, current or history of alcohol use or disorder, and other forms of social instability besides housing were additional factors that PCPs identified as helpful.

Table 4.3. Qualitative response analysis

Qualitative response	**Items on the survey**	**Bio-psycho-social domain**
"etoh SUD – …current"	Current substance use disorder	Substance use
"patient's alcohol use history"; "etoh SUD – past..."	History of substance use disorder	
"multiple stated allergies or intolerances to non-opioid pain medications or treatments"; "refusal to participate in other pain treatment modalities (PT, massage, pain psychology, acupuncture, etc)"; "resistance to Buprenorphine"; "willingness to establish goals, with being pain-free as an unrealistic goal"; "willingness to take chronic pain education classes to learn to live with some degree of pain"; "willingness to accept that hyperalgesia can result from long-term opioid use"	Resistance to changing opioids	Aberrant drug-related behaviors
"history of diversion of controlled substance"	New Concept	
"PDMP"	Obtaining opioids from multiple providers in violation of treatment agreement; Total opioid dose > 90 MME/day; Concurrent prescribed Benzodiazepines; Obtaining prescription opioids from multiple pharmacies	Aberrant drug-related behaviors; Medication;
"contract" violation at other medical clinics"	Obtaining opioids from multiple providers in violation of treatment agreement;	Aberrant drug-related behaviors
"stable long term opioid use, without dose escalation"	Longer pain duration	Pain and function
"Meandering pain"	Involvement of multiple body locations	
"presence of individuals in patient's home with use disorder to any substance"; "family hx [of etoh]"; "some type of social instability / not just housing could also be helpful";	Family history of substance use; Marital status; Housing instability;	Socioeconomic

Discussion

Patient information spanning ADBRs, pain and function, substance use, and medication domains were most helpful to the PCPs in determining OUD risk for patients with LTOT seen in the primary care setting. The open-ended participant responses provided some complementary information and context, as well as some novel concepts that are worth further attention.

Comparison of literature concepts to Delphi results by domain

Most OUD factors specified in the CDC guidelines ranked high on the consensus list, but there were notable differences between the guidelines and the Delphi results.

Aberrant Drug-Related Behaviors: ADRBs are not explicitly mentioned in the CDC guidelines. However, the items in the ADBRs domain scoring high can be because most ADBRs serve as concepts to fulfill the 4 Cs criteria (loss of control, compulsive use, continued use despite the risk of harm, and craving) for OUD diagnosis.

Substance Use: As far as the OUD factors from the substance use domain were concerned, the five factors making the "very or extremely useful" list are well studied for their association with OUD. Four of the five (history of non-fatal overdose, current SUD, history of SUD, and illicit drug use) are listed as risk factors in the CDC guidelines. However, despite evidence of their strong association with OUD, certain risk factors like heavy smoking and tobacco use did not make the consensus list of "very or extremely useful". There is a need to explore the reason for this finding further. Kratom use was included as an OUD risk factor in the survey as input from a PCP specializing in pain and addiction care (J.R.). Kratom is a herbal substance that produces opioid- and stimulant-like effects. 66% of the participant agreed that Kratom use is a helpful factor for determining OUD risk. However, it failed to meet the cut-off of ≥ 75% for consensus. Failure to gain consensus on the importance of Kratom use could be due to

specialized knowledge of the PCP based on their exposure to specific patient populations. Current or history of alcohol use or disorder was lumped under the substance use disorder category on the survey. Personal and family history of alcohol use seem important to PCPs when determining the patient's OUD risk. Collecting patients' past and current alcohol use is a part of a standard clinical workflow at the primary care clinics at OHSU and emerged as a routine surveillance factor in the primary care setting. Considering the importance PCPs attach to this factor, it should be a stand-alone risk factor in any future decision support tool.

Psychiatric: It is well established in the literature and guidelines that patients with chronic pain on LTOT with co-occurring psychiatric conditions, such as major depressive disorder and anxiety disorder, are at increased risk for OUD. However, the two psychiatric conditions did not make the "very and extremely useful" list. Instead, these were "slightly or moderately useful" for OUD risk determination. Patients with mental health disorders receive about half of the total opioid prescriptions in America [8] and are more likely to suffer from chronic pain. The reason for specific psychiatric diagnoses (anxiety disorder, post-traumatic stress disorder, major depressive disorder, acute psychiatric instability, personality disorder, and psychosomatic disorder) not making the "very or extremely useful" list could be because of the unreliability of such data in the EHR and lack of guidance for alternative pain treatment for such patients. As one participant commented:

> *"While many of the items may be useful, I wouldn't trust our EHR to reliably provide me that information and things like "personality disorder" can be longstanding chart lore without any actual documentation."*

However, risk factors such as suicide ideation and history of suicide attempts are more actionable and appear high in the PCP information needs.

Medication: Medication-related factors such as concurrent Benzodiazepines and higher

doses of opioids, greater than 90 MME/day, are well-known risk factors that made the "very or extremely useful" list. The CDC guidelines mention that the risk of misuse of opioids increases with psychotropic medication use. Clinical input was used to collect all categories of psychotropic medications – including psychiatric medications and non-benzo sedative-hypnotics. However, these added factors did not reach a consensus for being useful for OUD risk determination. While there is evidence of their association with increased risk of overdose, there is not enough evidence to consider them for determining OUD risk. There needs to be increased effort to collect and document such information in a structured field in EHR to understand the contribution of such medication to OUD risk,

Pain and Function: Many pain and function domain factors made the "very or extremely useful" list. These factors are not explicitly stated in the CDC guidelines but have been associated with OUD in literature. However, these factors are also true for patients suffering from severe chronic pain. Making pain and function data accessible at the point of care is important to guide appropriate treatment and intervention. This data type may also be necessary to evaluate the quality of care and build the evidence base for alternative pain care. CDC guidelines discourage the prescription of opioids for pain diagnosis with no evidence of benefit. However, pain diagnoses with no evidence of benefit from prescription opioids did not receive consensus as a helpful factor when determining a patient's OUD risk. It is unclear if this factor, combined with other risk factors, would change how PCPs make decisions about a patient's OUD risk.

Socioeconomic: Social factors like history of childhood sexual abuse and history of DUI or drug conviction reached consensus, but factors like housing instability and marital status (as a proxy for social support) did not achieve a clear consensus. However, one of the participants alluded to "some type of social instability / not just housing…" for OUD risk decisions. Other

comments touched upon constructs like patient-provider trust, patient engagement, patient activation, and patient self-efficacy.

- *"Refusal to participate in other pain treatment modalities (PT, massage, pain psychology, acupuncture, etc)…."*
- *"What their goals are -- are they expecting to be pain-free? Are they willing to take chronic pain education classes to learn to live with some degree of pain? Are they willing to accept that hyperalgesia can result from long-term opioid use?"*
- *"patient's diet and exercise routine social support system"*
- *"length of my own relationship with this patient."*

Novel information needs

Some of the open-ended participant responses identified additional information needs and relevant concepts that were not specified in the CDC guidelines. These concepts included social support outside the healthcare setting and information on how the patient interacts with healthcare generally and their PCP specifically.

Many social support constructs align with the standard social determinants of health (SDoH) that are increasingly being collected in healthcare settings. Others, however, are not typically assessed or recorded. E.g., patient-provider trust, patient activation, and patient self-efficacy. Increasing the assessment and capture of such concepts may be valuable for OUD risk identification and any other clinical context where such constructs may influence care and adherence to medical recommendations.

It is important to note that PCPs consider the length of their relationship with the patient and the patient's social environment, like the "presence of individuals in patient's home with use disorder to any substance," as useful information for making risk determination. While risk

factors of OUD are essential considerations, protective factors such as social and family support are equally important.

Trustworthiness and generalizability

Our study was well designed to preserve generalizability. The Delphi process has been described as a method to harness the "wisdom of the crowd"[9]. Our Delphi process involved a diverse expert group, from those who occasionally managed patients on opioids for chronic pain to those who routinely collected patients and were involved in research and policy. The experts came from varied healthcare settings, specialties, years of practice, and expert levels. This diverse representation increases the generalizability and validity of our findings. Between rounds 1 and 2, we had a response rate of eighty percent, and we retained all level III experts. The quasi-anonymous study design reduced bias as participants, though known to the researcher and primary contacts at each site, were not peer-pressured to conform. The extensive a priori collection of concepts using peer-reviewed studies and input from stakeholders and the iterative study design to gain consensus from several experts makes our study findings more generalizable. Further, inviting participants from diverse settings increased the external validity of our study.

Limitations and Future Work

There are several limitations to our approach. Most survey participants belonged to a single academic health center, so findings may not be generalizable to other types of primary care settings. Due to project time limitations, we limited our Delphi process to two rounds and did not add new concepts that emerged from the qualitative response in the subsequent round. In addition, the survey was so structured that participants were asked to rank OUD risk factors and concepts in isolation. Each factor's importance may change when presented in combination with

other risk factors. Finally, the emergence of latent constructs from the open response from survey participants remains largely unexplored.

Many factors provided as feedback from the participants involve aspects of patient preference that need to be explored further. Unwillingness to try new pain treatment modalities may be due to underlying anxiety and fear of losing access to a treatment that has worked for the patient for many years.

Conclusion

Applying evidence to practice for complex patients with complex conditions is challenging. The task is even more problematic when it requires considerable time and specialized knowledge. Addressing the accessibility barriers to high-ranking OUD concepts and factors may improve OUD surveilling and improve care for patients on LTOT for chronic pain. This study is the first to identify and gain consensus on useful OUD concepts and factors in a real-world setting. The results from this work can be used to bridge the gap between evidence and practice for this patient population. Clinical decision-making involves many latent constructs that are not currently collected. The evidence-based practice encompasses clinical experience and patient preference; however current efforts in chronic pain management focus mainly on the evidence. This work is the first to uncover the reality of evidence-based decision-making in the primary care setting and lays the foundation for future informatics projects.

In the next phase, I will determine how accessible the data for the top thirty-three OUD risk factors and consents are. Since alcohol use was mentioned in the qualitative response of at least two PCPs, and the research evidence of its association with OUD is strong, I will add this risk factor to the list of high information needs items.

CHAPTER FIVE: AIM 3. ASSESSING INFORMATION READINESS - Step 1. Operationalization & Step 2. Data Quality Assessment

Abstract

Prescription opioids have a considerable impact on patient and population health. However, access to standard and computable data for decision-making and general surveillance is lacking. I developed a systematic approach to improve the data readiness for opioid use disorder (OUD) risk assessment in patients on long-term opioids for chronic non-cancer pain. I introduced "computability" as a data readiness dimension and applied it to previously identified 34 opioid use disorder risk factors and concepts (including alcohol use disorder). Out of the 34 risk factors and concepts, i) 10 are computable, ii) 14 are potentially computable, and iii) 10 are non-computable. Five potentially computable OUD factors and concepts require local and patient-level context, and ten can be derived from two or more structured fields. Two require establishing temporality between medications and lab tests to achieve computability. We determined the completeness and correctness of all ten computable OUD risk factors and concepts. Just one computable OUD risk factor, alcohol use disorder, has 100% completeness and correctness. The work highlights the data quality issues for high-need OUD risk factors and concepts that help PCPs make OUD risk decisions for their patients.

Introduction

Despite multiple guidelines, the current practice of OUD risk assessment in the chronic pain population is variable for many reasons, one of which is the challenge of timely access to patients' multi-dimensional data to determine their OUD risk at the point of care. Further, evaluating the OUD risk assessment practice is challenging, as it is unclear what patient factors influence providers' decision-making. For complex patients, it is critical to identify a minimal

data set required for clinical decision-making and enable its access at the right time for just-in-time care. I developed and used a generalized framework to assess the gaps between information needs and readiness for complex decision-making at the point of care. In earlier work, I determined a minimum set of high-need data that primary care providers find helpful in determining their patients' OUD risk. In this work, I present a methodology for operationalization and data quality assessment of high-need data on OUD risk factors and concepts to estimate EHR's data readiness to aid PCPs in OUD risk assessment.

Methods

Operationalization

Computable data is essential for integrating practice-based evidence with research-based evidence and a prerequisite for bridging the gap between evidence and practice. I propose "computability" as a data readiness construct. I used concepts of "definability," "structure," and "standards to determine computability for data on each high-ranked OUD risk factor and concept.

For all the 34 high-ranked OUD concepts and factors, I first determined if they could be defined clearly or needed additional context, if they were present in a structured field in the EHR and if standard codes could represent them. I used the standard codes developed by the Observational Medical Outcomes Partnership (OMOP). I used the Observational Health Data Sciences and Informatics (OHDSI) ATLAS tool to search for standard OMOP codes for each of 34 high-ranked OUD concepts and factors (Table 1–Supplementary Material). OMOP data standards were used because OMOP CDM is the most widely adopted common data model. The vocabulary is robust and provides mapping across multiple clinical data standards.

I defined computable, potentially computable, and non-computable data as follows

Definitions:

- Computable data - Presence of discrete structured field and representation by OMOP standard codes
- Potentially computable data – Either absence of a discrete structured field but with the potential to create one, as the data can be collected using a validated tool. This will also require developing standard OMOP code for the data collected using the validated tool, Or it can be derived from two or more structured fields by creating additional logic and establishing temporality.
- Non-computable data: has no standard tools to capture. In addition, there are no standard terminology and codes to record and represent. It is mainly recorded as unstructured narrative data.

Data quality assessment

Next, I assessed the data quality of all computable OUD concepts and factors. I determined the completeness (sensitivity) and correctness (positive predictive value or PPV) of all computable OUD risk factors and concepts. For this, I compared the presence and absence of each computable OUD concept/factor in the patient's chart to its presence and absence in the OMOP instance of the Research Data Warehouse (RDW) at Oregon Health & Science University (OHSU). I used Hogan and Wagner's method to calculate the sensitivity and PPV.(131)

		Concept in patient chart		
		Present	Absent	
Concept in the RDW	Present	a	b	a+b
	Absent	c	d	c+d
		a+c	b+d	

Completeness = Sensitivity = a/(a+c)

Correctness = Positive Predictive Value (PPV) = a/(a+b)

I received Institutional Review Board (IRB) approval for extracting data on all the computable concepts for 30 patients in the chronic prescription opioid management registry at Oregon Health & Science University (OHSU). The presence or absence of all computable OUD risk factors was determined in each patient chart. I common "search terms" for each OUD risk factor and concept to find them in the patient's chart. Dr. Mary Pickett, an internal medicine physician at OHSU, was consulted for developing and curating a list of search terms (Table 3 Supplementary Material)

I developed a data extraction strategy for all computable OUD concepts and factors. De-identified data were extracted for all computable OUD concepts and factors for adult patients on long-term prescription opioid treatment for chronic non-cancer pain between Jan 2018 to Dec 2019. To define the cohort of patients on chronic opioid therapy, I used the strategy proposed in the guidance document by CDC – "Quality Improvement and Care Coordination: Implementing the CDC Guideline for Prescribing Opioids for Chronic Pain (Appendix-Figure A). The search queries used for data extraction are also included in the supplementary material at the end of this chapter.

Results

Figure 5.1 is a decision tree flow chart for determining computability for each of the 34 OUD risk factors and concepts. Nearly 80% of OUD risk factors and concepts have clear definitions, with the remaining 20% needing additional patient and local practice context. 30% are computable because these have clear definitions, are documented in structured fields, and have standard codes. Approximately 41% of the OUD risk factors and concepts are potentially computable and can be derived from two or more structured data or captured using standard and

validated tools in the Epic flowsheet. Three of the 14 potentially computable data require establishing temporality to resolve concurrency issues. Just one-third of the high-ranked concepts can currently be represented using standard codes (Supplementary Material – Table 1) .

The prevalence, sensitivity (completeness), and positive predictive value (correctness) were determined for all ten computable OUD factors and concepts (Table 5.1). Percentage sensitivity (s) and positive predictive value (PPV) of all 10 computable concepts are: history of non-fatal overdose (s=0, PPV = undefined), current substance use disorder (s=50, PPV=100), alcohol use disorder (s=100, PPV=100), hazardous situation due to opioid use (s=77.8, PPV=100), history of substance use disorder (s=72.7, PPV=100), illicit drug use (s=66.7, PPV=100), showing symptoms consistent with withdrawal (s=8.3, PPV=100), suicide ideation (s=0, PPV=0), history of suicide attempt (s=0, PPV=undefined), history of childhood physical, emotional or sexual abuse (s=0, PPV=undefined).

Figure 5.1. Computability of high-ranked risk OUD risk concepts and factors

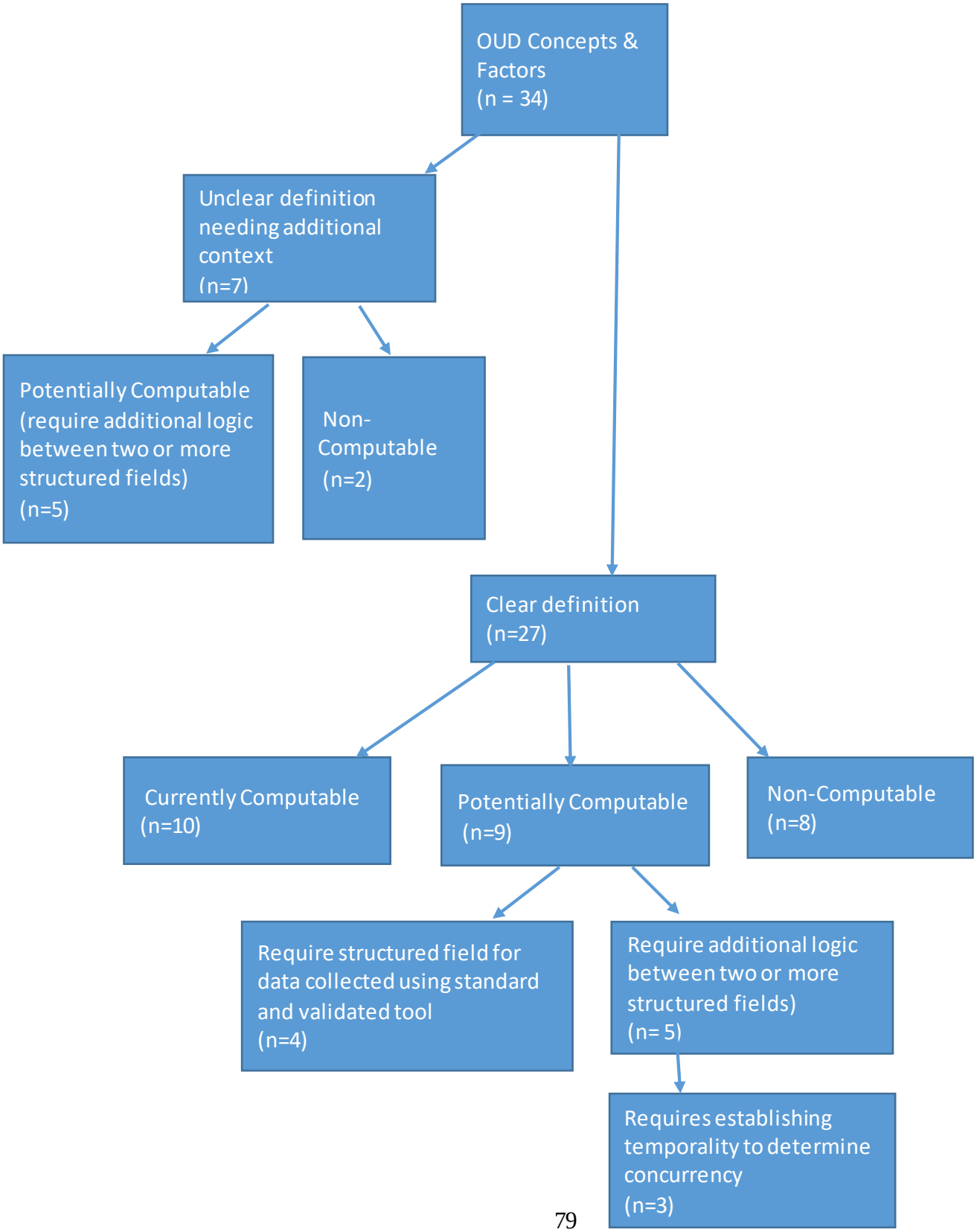


Table 5.1: Prevalence, Completeness, and Correctness of OUD risk factors and concepts in a sample of 30 patients on long-term opioid therapy.

Computable OUD Risk Factors and Concepts	Number of patients with OUD factors/concepts out of 30	Percentage of patients with OUD factors/concepts	True Positive	False Negative	True Negative	False Positive	Sensitivity	Specificity	PPV	NPV	Accuracy
			TP	FN	TN	FP	TP/(TP+FN)*100	TN/(TN+FP)*100	TP/(TP+FP)*100	TN/(TN+FN)*100	(TP+TN)/(TP+TN+FP+FN)*100
History of Non-Fatal Overdose	6	20.0	0	6	24	0	0.0	100.0	Undefined	80.0	80.0
Current Substance Use Disorder	7	23.3	2	2	26	0	50	100	100	92.9	93.3
Alcohol Use Disorder	5	16.7	5	0	25	0	100.0	100.0	100.0	100.0	100.0
Hazardous Situation due to Opioid Use	9	30.0	7	2	21	0	77.8	100.0	100.0	91.3	93.3
History of substance use disorder	11	36.7	8	3	19	0	72.7	100.0	100.0	86.4	90.0
Illicit drug use	6	20.0	4	2	24	0	66.7	100.0	100.0	92.3	93.3
Showing symptoms consistent with opioid withdrawal	12	40.0	1	11	18	0	8.3	100.0	100.0	62.1	63.3
Suicidal ideation	7	23.3	0	6	23	1	0.0	95.8	0.0	79.3	76.7
History of suicide attempt	7	23.3	0	7	23	0	0.0	100.0	Undefined	76.7	76.7
History of childhood physical, emotional or sexual abuse	6	20.0	0	6	24	0	0.0	100.0	Undefined	80.0	80.0

Discussion

In the sample of 30 patients on a long-term opioid for chronic pain, each OUD risk factor or concept was present in at least 20% of the patients. Patients with "current substance use

disorder" were more likely to have a "history of substance use disorder." "History of substance use disorder" and "showing symptoms consistent with opioid withdrawal" are present in almost 40% of the patients. But, there is a vast difference in their level of completeness. The "History of substance use disorder" has nearly 72% completeness, while "showing symptoms consistent with opioid withdrawal" has approximately 8% completeness. This is expected as providers are more likely to check and document "substance use" data in the problem list (structured field). Substance use (current or in history) is associated with a high risk of developing OUD. However, most patients on long-term prescription opioids develop dependence and are likely to exhibit withdrawals at some point during the taper. Primary care providers are less likely to capture the "withdrawal" as an encounter diagnosis or a problem in the problem list (structured data) and more likely to document it in unstructured notes, hence its low sensitivity/correctness.

Notably, correctness or PPV is high, 100%, for current substance use disorder, alcohol use disorder, hazardous situation due to opioid use, history of substance use disorder, illicit drug use, and showing symptoms consistent with opioid withdrawal. This is reassuring, as it will not incorrectly flag a patient for these risk factors. OUD risk factors and concepts having standard workflow for collection for all patients in the primary care setting, like alcohol use, have higher completeness and correctness.

There are several limitations to this study. There may have been some loss in granularity when using code sets to capture OUD risk factors and concepts using the OMOP standard codes. Incomplete code sets for OUD risk factors and concepts may have resulted in their lower completeness. My list of search terms for extracting OUD risk factors from patients' EHR may not have been exhaustive (even though informed by a subject matter expert) and have led to lower completeness and/or correctness for some of the OUD risk factors and concepts. This method was developed using the RDW data from an academic health center and is not

generalizable to other health care settings. Finally, I used manual chart review as the gold standard - but we know that not everything ends in the chart because of care fragmentation and limited interoperability

Conclusion

Triangulating patient-specific biopsychosocial risk factors from diverse information sources is ideal for making an informed OUD risk assessment. Identifying and improving access to patient-specific factors that drive OUD risk and prescription opioid treatment decisions in the real world are vital to improving the current practice of OUD risk assessment. Standard workflow for collecting OUD risk factors and concepts for all patients treated on opioids will improve their availability at the point of care for clinical decision-making. In addition, improving structured documentation of high-need risk factors, such as withdrawal, suicide ideation, and suicide attempts, will enhance their findability and accessibility for OUD risk assessment.

History of childhood sexual, physical, or mental abuse is sensitive information that needs extra compassion and time for a PCP to determine. It will require specialized workflow and training to collect and document this risk factor and additional resources to address the long-term psychological and health effects of the past abuse. For OUD risk concepts with considerable stigma and the potential to affect patient-provider trust, it is crucial to adopt appropriate information gathering and retrieval techniques to have better data for triangulation and decision-making. It is worth noting that all ten theoretically computable OUD risk factors and concepts have a high degree of specificity and positive predictive value and are less likely to flag a patient falsely for the OUD risk factor. We will need to employ data retrieval techniques using natural language processing (NLP) for high-need data that are not easy to structure.

Standards and codes for OUD and aberrant drug-related behaviors are lacking. As a result,

not all aberrant behaviors and OUD risk factors and concepts can be represented using OMOP standard codes. Considering opioid use disorder has a role in the current opioid crisis, and there are efforts to improve prevention and treatment, risk factors and concepts for OUD must be findable and computable. These efforts will help bridge the gap between evidence and practice of OUD risk assessment.

Chapter Five - Supplementary Material

Table 1 - Determining the computability of 34 OUD factors & concepts useful for determining patient's risk

Table 2 - Computability of high-ranked OUD concepts and factors

Table 3 - Chart search strategy for the 10 computable OUD concepts and factors

Query for extracting data from OMOP version of RDW

- Query for defining study cohort
- Query for all computable OUD factor/concepts, except current substance use disorder
- Query for current substance use disorder

Table 1 - Determining the computability of 34 OUD factors & concepts useful for determining patient's risk

Rank*	OUD factors and concepts from Delphi Study	Clear definition (Y/N)	Has Discrete Structured Field (Y/N)	Can be structured (Y\N)	Can be derived (Y/N)	Recorded for all patients (Y/N)	Equivalent OMOP Standard Vocabulary*				
							Name	Domain ID	Concept Class ID	Concept ID	Vocabulary ID
1	History of Non-Fatal Overdose	Y	Y	-	-	N	Illegal drug overdose	Condition	Clinical Finding	45769428	SNOMED
							Drug overdose	Condition	Clinical Finding	4208104	SNOMED
							Overdose of opiates	Condition	Clinical Finding	4053782	SNOMED
2	Current Substance Use Disorder	Y	Y	-	-	N	Anxiolytic dependence with current use	Condition	Clinical Finding	37110412	SNOMED
							Volatile inhalant dependence with current use	Condition	Clinical Finding	37110446	SNOMED
							Cannabis dependence with current use	Condition	Clinical Finding	37109953	SNOMED
							Cocaine dependence with current use	Condition	Clinical Finding	37110436	SNOMED
							Hallucinogen dependence with current use	Condition	Clinical Finding	37110442	SNOMED
							Hypnotic dependence with current use	Condition	Clinical Finding	37110411	SNOMED
							Sedative dependence with current use	Condition	Clinical Finding	37110410	SNOMED
							Tobacco dependence with current use	Condition	Clinical Finding	3655996	SNOMED

Table 1 - Determining the computability of 34 OUD factors & concepts useful for determining patient's risk

Rank *	OUD factors and concepts from Delphi	Clear definition (Y/N)	Structured Field (Y/N)	Can be structured (Y\N)	Can be derived (Y/N)	Recorded for all patients (Y/N)	Equivalent OMOP Standard Vocabulary*				
							Name	Domain ID	Concept Class ID	Concept ID	Vocabulary ID
							Nicotine dependence with current use	Condition	Clinical Finding	37110445	SNOMED
							Opioid dependence with current use	Condition	Clinical Finding	37110407	SNOMED
							Psychoactive substance abuse	Condition	Clinical Finding	4239381	SNOMED
							Psychoactive substance use disorder	Condition	Clinical Finding	4004672	SNOMED
							Psychoactive substance dependence with current use	Condition	Clinical Finding	37110467	SNOMED
							Substance abuse	Condition	Clinical Finding	4279309	SNOMED
3	Alcohol Use Disorder	Y	Y	-	-	N	Alcohol abuse	Condition	Clinical Finding	433753	SNOMED
							Alcohol Use Disorder	Observation	Clinical observation	44786700	SNOMED
							Alcohol Use Disorder Identification Test [AUDIT]	Observation	Survey	46234681	SNOMED
							Alcohol Use Disorder Identification Test Consumption [AUDIT-C]	Observation	Survey	46234680	SNOMED
							Alcohol use disorder identification test consumption questionnaire	Measurement	Staging / Scale	44792141	SNOMED

Rank*	OUD factors and concepts from Delphi Study	Clear definition (Y/N)	Structured Field (Y/N)	Can be structured (Y\N)	Can be derived (Y/N)	Recorded for all patients (Y/N)	Equivalent OMOP Standard Vocabulary*				
							Name	Domain ID	Concept Class ID	Concept ID	Vocabulary ID
4	Obtaining opioids from multiple providers in violation of treatment agreements	N	N	N	N	N	-	-	-	-	-
5	Being in Hazardous Situation due to Opioid Use	N	Y	-	-	N	Falls	Condition	Clinical Finding	4059015	SNOMED
							Motor vehicle accident	Observation	Event	435134	SNOMED
							Motor vehicle accident, driver	Condition	Clinical Finding	435988	SNOMED
6	Taking opioids for symptoms other than pain (e.g., anxiety, depression, sleep, or to produce euphoria)	Y	N	N	N	N	-	-	-	-	-
7	Increasing Dose Without Provider Instruction	Y	N	N	N	N	-	-	-	-	-
8	Running short with medication supply and requests for early refills	N	N	N	Y	N	-	-	-	-	-
9	History of substance use disorder	Y	Y	-	-	N	History of drug abuse**	Observation	Context-dependent	4155607	SNOMED
10	Concurrent prescribed Benzodiazepines	Y	N	N	Y	N	Benzodiazepine therapy	Procedure	Procedure	36674742	SNOMED
							Benzodiazepine derivatives	Drug	ATC 4th	21604565	ATC 4th
11	Obtaining prescription opioids from multiple pharmacies	Y	N	N	N	N	-	-	-	-	-

Rank*	OUD factors and concepts from Delphi Study	Clear definition (Y/N)	Structured Field (Y/N)	Can be structured (Y\N)	Can be derived (Y/N)	Recorded for all patients (Y/N)	Equivalent OMOP Standard Vocabulary*				
							Name	Domain ID	Concept Class ID	Concept ID	Vocabulary ID
12	Resistance to changing opioid medications despite deterioration in function or significant negative effects	N	N	N	N	N	-	-	-	-	-
13	Emergency department visits to obtain opioids	N	Y	-	-	N	Pain medicine Emergency department Note	Observation	Clinical Observation	42527289	LOINC
							Emergency department patient visit	Observation	Procedure	4163685	SNOMED
14	Total opioid dose > 90 MME/day	Y	N	N	Y	Y		Drug	ATC 4th	1123896	ATC
15	Illicit drug use	Y	N	Y	-	N	Drug, Abuse Screening Test [DAST]	Observation	Survey	42528829	LOINC
							Illicit medication use	Condition	Clinical Finding	4143732	SNOMED
16	Showing symptoms consistent with opioid withdrawal	Y	N	Y	-	N	Opioid Withdrawal	Condition	Clinical Finding	4336384	SNOMED
17	Abnormal urine drug screening result	Y	Y	-	-	Y	Urine screening abnormal	Condition	Clinical Finding	4064386	SNOMED
							Urine opiates screening test	Measurement	Procedure	4195515	SNOMED
							Urine cannabinoids screening	Measurement	Observable Entity	37394356	SNOMED

Table 1 - Determining the computability of 34 OUD factors & concepts useful for determining patient's risk

Rank*	OUD factors and concepts from Delphi Study	Clear definition for operationalization (Y/N)	Has Discrete Structured Field (Y/N)	Can be structured (Y\N)	Can be derived (Y/N)	Recorded for all patients (Y/N)	Equivalent OMOP Standard Vocabulary*				
							Name	Domain ID	Concept Class ID	Concept ID	Vocabulary ID
18	Multiple phone calls to clinic requesting opioid medication	N	N	N	Y	Y	-	-	-	-	-
19	History of misuse of any sedative or stimulant	Y	Y	-	-	N		Condition	Clinical Finding		
20	Requesting higher dose of	Y	N	N	N	N	-	-	-	-	-
21	Pain catastrophizing	Y	N	Y	-	N	-	-	-	-	-
22	Weaning described as unsuccessful or difficult	N	N	N	N	N	-	-	-	-	-
23	History of DUI or drug conviction	Y	N	N	N	N	-	-	-	-	-
24	Concurrent long-acting plus short-acting	Y	N	N	N	N	-	-	-	-	-
25	Reporting prescription loss or theft	Y	N	N	N	N	-	-	-	-	-
26	Interference with vocation due to	Y	N	Y	-	N	-	-	-	-	-
27	Suicidal ideation	Y	N	Y	-	N	Suicidal thoughts	Condition	Clinical Finding	4273391	SNOMED
28	History of suicide attempt	Y	Y	-	-	N	njury due to suicide attempt	Condition	Clinical Finding	4257906	SNOMED
							Suicide attempt	Observation	Clinical Finding	4219484	SNOMED

Table 1 - Determining the computability of 34 OUD factors & concepts useful for determining patient's risk

Rank*	OUD factors and concepts from Delphi	Clear definition for operationalization (Y/N)	Has Discrete Structured Field (Y/N)	Can be structured (Y\N)	Can be derived (Y/N)	Recorded for all patients (Y/N)	Equivalent OMOP Standard Vocabulary*				
							Name	Domain ID	Concept Class ID	Concept ID	Vocabulary ID
29	Travelling long distance for pain	N	N	N	Y	N	-	-	-	-	SNOMED
30	Missing medical appointm ents	N	N	Y	-	Y	Number of appointments missed	Observation	Observable Entity	4183104	SNOMED
31	History of childhoo d physical, emotiona l or sexual abuse	Y	N	Y	-	N	History of childhood psychological abuse	Observation	context-dependent	762058	SNOMED
							History of victim of child sexual abuse	Observation	context-dependent	36713088	SNOMED
							Opioid risk tool panel	Measurement	clinical observation	37019864	LOINC
32	High pain interfere nce with	Y	N	Y	-	N	-	-	-	-	-
33	Lack of demonstr ated functiona	Y	N	Y	-	N	-	-	-	-	-
34	Longer pain duration	N	N	N	Y	N	-	-	-	-	-

Table 2 - Computability of high-ranked OUD concepts and factors

OUD Factor/Concept	Clear Definition (Y/N)	Computable (Y/N)	Potentially Computable (Y/N)		Non – Computable (Y/N)
		Structured field and standard OMOP codes	Discrete Structured Field Absent but can be Created	Can be Computed by Additional Logic between Two or More Structured Fields	
History of Non-Fatal Overdose	Y	Y	-	-	-
Current Substance Use Disorder	Y	Y	-	-	-
Alcohol Use Disorder	Y	Y	-	-	-
Obtaining opioids from multiple providers in violation of treatment agreements	Y	N	N	N	Y
Being in Hazardous Situation due to Opioid Use	Y	Y	-	-	-
Taking opioids for symptoms other than pain (e.g., anxiety, depression, sleep, or to produce euphoria)	Y	N	N	N	Y
Increasing Dose Without Provider Instruction	Y	N	N	N	Y
Running short with medication supply and requests for early refills	Y	N	N	Y	-
History of substance use disorder	Y	Y	-	-	-
Concurrent prescribed Benzodiazepines	Y	N	N	Y	-
Obtaining prescription opioids from multiple pharmacies	Y	N	N	N	Y
Resistance to changing opioid medications despite deterioration in function or significant negative effects	N	N	N	N	Y
Emergency department visits to obtain opioids	N	N	N	Y	-
Total opioid dose > 90 MME/day	Y	N	N	Y	-
Illicit drug use	Y	Y	-	-	-
Showing symptoms consistent with opioid withdrawal	Y	Y	-	-	-
Abnormal urine drug screening result	Y	N	N	Y	-
Multiple phone calls to clinic requesting opioid medication	N	N	N	Y	-

History of misuse of any sedative or stimulant	Y	N	N	N	Y
Requesting higher dose of prescription opioids	Y	N	N	N	Y
Pain catastrophizing	Y	N	Y	-	-
Weaning described as unsuccessful or difficult	N	N	N	N	Y
History of DUI or drug conviction	Y	N	N	N	Y
Concurrent long-acting plus short-acting opioids	Y	N	N	Y	-
Reporting prescription loss or theft	Y	N	N	N	Y
Interference with vocation due to opioid use or pain	Y	N	Y	-	-
Suicidal ideation	Y	Y	-	-	-
History of suicide attempt	Y	Y	-	-	-
Travelling long distance for pain care	N	N	N	Y	-
Missing medical appointments	N	N	N	Y	-
History of childhood physical, emotional or sexual abuse	Y	Y	-	-	-
High pain interference with daily activity	Y	N	Y	-	-
Lack of demonstrated functional improvement	Y	N	Y	-	-
Longer pain duration	N	N	N	Y	-

Table 3 - Chart search strategy for the 10 computable OUD concepts and factors

Concept	Chart Search Strategy
History of Non-Fatal Overdose	Dx code or Documentation ANYTIME before 12/2019 Search term/s - "overdose"
Current Substance Use Disorder	Dx code or Documentation in the current period (1/2018 - 12/2019). Search term/s - "substance use", "SBIRT", tobacco use disorder
Alcohol Use Disorder	Dx code or Documentation ANYTIME before 12/2019 Search term/s - "alcohol"
Being in Hazardous Situation due to Opioid Use	Documentation of fall & MVA only ANYTIME before 12/2019 Search terms "fall", "accident", "DUI", "motor vehicle accident", "MVA"
History of substance use disorder	SUD Dx or documentation ANYTIME before 12/2019 Search term - "SBIRT", "substance use"
Illicit drug use	Documentation of illicit drug use ANYTIME before 12/2019 Search term/s - "illicit", "drug"; check DAST answer
Showing symptoms consistent with opioid withdrawal	Documentation of withdrawal symptoms ANYTIME before 12/2019 Search term/s - " c/o withdrawal", "withdrawal", "sweat"
Suicidal ideation	Dx or Documentation ANYTIME before 12/2019 Search term/s - "Denies anxiety, depression, thoughts of suicide or hallucinations", “ideation”, “suicide”, “suicidal”
History of suicide attempt	Dx or documentation ANYTIME before 12/2019 Search term/s of "overdose," “suicide.”
History of childhood physical, emotional or sexual abuse	Dx or documentation ANYTIME before 12/2019 Search term/s of "childhood abuse," “childhood sexual abuse,” “childhood emotional abuse,” childhood physical abuse.”

Query for defining study cohort

```
SELECT *
FROM RDW_OMOP.person p
WHERE
   DATE'2019-12-31' - TRUNC(p.birth_datetime) >= 6570
   AND DATE'2018-01-01' - TRUNC(p.birth_datetime) <= 32485

   AND p.person_id IN (
                        --CHRONIC PAIN
                  SELECT co.person_id
                  FROM RDW_OMOP.CONDITION_OCCURRENCE co
                        INNER JOIN RDW_OMOP.CONCEPT_ANCESTOR ca ON co.condition_concept_id =
ca.descendant_concept_id
                  WHERE ca.ancestor_concept_id = 436096)

         AND p.person_id IN (
                  --OPIOIDS >60 DAYS
                  SELECT de.person_id
                  FROM RDW_OMOP.DRUG_EXPOSURE de
                        INNER JOIN RDW_OMOP.CONCEPT_ANCESTOR ca ON de.drug_concept_id =
ca.descendant_concept_id
                  WHERE ca.ancestor_concept_id = 21604254 --opioids
                        --AND to_date(de.drug_exposure_end_date,'yyyy-MM-dd') -
to_date(de.drug_exposure_start_date,'yyyy-MM-dd') > 60
                        AND TRUNC(de.drug_exposure_end_date) - TRUNC(de.drug_exposure_start_date) > 60
                        AND (de.route_source_value <> 'intravenous' OR de.route_source_value IS NULL))

         AND p.person_id NOT IN (
                  --NEOPLASTIC DISEASE
                  SELECT co.person_id
                  FROM RDW_OMOP.CONDITION_OCCURRENCE co
                        INNER JOIN RDW_OMOP.CONCEPT_ANCESTOR ca ON co.condition_concept_id =
ca.descendant_concept_id
                  WHERE ca.ancestor_concept_id = 438112)

   AND p.person_id IN (
      SELECT vo.person_id
      FROM RDW_OMOP.visit_occurrence vo
      WHERE vo.visit_concept_id = 9202
         AND vo.care_site_id IN (1546, 819, 1275, 2279, 2286, 2486, 2236, 2280, 1403, 2287, 1447, 2235, 824, 848, 2456,
1442)
         AND TRUNC(vo.visit_start_datetime) BETWEEN DATE'2018-01-01' AND DATE'2019-12-31'
                        AND vo.visit_source_value like '%101%')
         -- GROUP BY vo.care_site_id, cs.care_site_name
         -- ORDER BY many DESC
         --1546     FM FACULTY CHH1
         --819      FM FACULTY GPC
         --1275     IMC FACULTY PPV
         --2279     FM FQHC RICHMOND OHSU
         --2286     FM RHC SCAPPOOSE OHSU
         --2486     MCMC INTERNAL MED WE
         --2236     FM FACULTY BVTN
         --2280     FM FQHC OFFSITE
         --1403     FM RICHMOND
         --2287     FM RHC OFFSITE
         --1447     CWH FAMILY PLAN KPV
```

```
    --2235    IMC FACULTY BVTN
    --824     FM SPORTS MED GPC
    --848     IMC CIM PAIN OPC
    --2456    MCMC BH FM CH
    --1442    CWH GENERALISTS  KPV


AND p.person_id NOT IN (
                    -- Palliative care
   SELECT  po.person_id
   FROM RDW_OMOP.procedure_occurrence po
      INNER JOIN RDW_OMOP.concept_ancestor ca ON ca.descendant_concept_id = po.procedure_concept_id
   WHERE ca.ancestor_concept_id = 4176643)
```

Query for all computable OUD factor/concepts, except current substance use disorder

```
SELECT DISTINCT co.person_id, p.pat_mrn_id, co.condition_concept_id, co.condition_start_date, co.condition_end_date,
co.condition_source_value, c.concept_name
FROM RDW_OMOP.condition_occurrence co
    INNER JOIN RDW_OMOP.concept_ancestor a ON a.descendant_concept_id = co.condition_concept_id
    INNER JOIN RDW_OMOP.concept c ON c.concept_id = co.condition_concept_id
    INNER JOIN RDW_OMOP_EXT.ohsu_person p ON co.person_id = p.person_id
WHERE a.ancestor_concept_id IN (
    4336384 -- Condition - Opioid withdrawal
    ,4273391 -- Condition - Suicidal thoughts
    ,45769428, 4208104, 4053782 -- Condition - Non-fatal overdose
    ,4218106 -- Condition - AUD
    ,4059015 -- Condition - Falls
    ,435988 -- Condition - Motor vehicle accident, driver
    ,37110412, 37110446, 37109953, 37110436, 37110442, 37110411, 37110410, 3655996, 37110445,  37110407, 4239381,
4004672, 37110467, 4279309 -- Condition - SUD
    ,4219484 -- Condition - Suicide attempt
    ,4143732 -- Condition - Illicit medication use (Illicit drug use)
    ,762058 -- Condition - History of childhood psychological abuse
    ,36713088 -- Condition - History of child sexual abuse
    ,36717284 -- Condition - History of victim of child abuse
    ,4169278 -- Condition - Child abuse
)
AND p.pat_mrn_id IN ()
```

Query for current substance use disorder

```
SELECT DISTINCT co.person_id, p.pat_mrn_id, co.condition_concept_id, co.condition_start_date, co.condition_end_date,
co.condition_source_value, c.concept_name
FROM RDW_OMOP.condition_occurrence co
   INNER JOIN RDW_OMOP.concept_ancestor a ON a.descendant_concept_id = co.condition_concept_id
   INNER JOIN RDW_OMOP.concept c ON c.concept_id = co.condition_concept_id
   INNER JOIN RDW_OMOP_EXT.ohsu_person p ON co.person_id = p.person_id
WHERE a.ancestor_concept_id IN
                (37110412,37110446,37109953,37110436,37110442,37110411,37110410,
                3655996,37110445,37110407,4239381,4004672,37110467,4279309)
   AND ((co.condition_type_concept_id = 38000245) -- limit to problem list dx
                AND (co.condition_end_date > TO_DATE(current_date - 30) OR co.condition_end_date IS NULL)
        OR co.condition_start_date > TO_DATE(current_date - 365))

         AND p.pat_mrn_id IN (
```

MAJOR TAKEAWAYS AND FUTURE STEPS

The primary goal of this effort was to highlight the data needs and readiness gaps for evidence-based care for complex and stigmatized conditions. Such conditions require careful consideration of patient and practice context and real-world challenges. The EHR data readiness must account for the real-world challenges of caring for complex and stigmatized conditions.

My original research question in aim 1 was why there is a gap between guidelines and practice. I found that part of this gap is due to insufficient documentation. So then I asked, in aim 2, if the problem is that providers disagree with the guidelines in determining OUD risk. I found that they do not, for the most part, though they did identify additional psycho-social factors. So then, knowing that providers agree with guidelines on high-priority concepts, I asked if the data available for those concepts are sufficient for the task. I found that often they are not. Either they're not computable, or they're computable but incomplete.

Many system-level factors affect the guideline-concordant risk assessment in patients with chronic non-cancer pain. External and internal policies and guidelines may not be sufficient to improve the practice. Increasing time and resources for PCPs to support them in caring for patients with complex healthcare needs is critical. Interoperable information systems and improved data standards are needed in this space. We can improve access to high-need data at the point of care to inform OUD risk assessment practices. The computability of some of the high-need data can be enhanced by establishing better workflows to collect and document them in structured fields. We will need to employ data retrieval techniques using natural language processing (NLP) for high-need data that are not easy to structure. We will need to collaborate with patient stakeholders to develop patient engagement and self-efficacy tools.

Developing better documentation templates that prompt PCPs to fill in the high-need data are also an option. But overall, this isn't just a problem of needing improved documentation and balancing that with the provider burden. This is a clinical space with significant stigma, where patient-provider trust is crucial. The latter is a key consideration in documentation practices and not one that is present in many common medical conditions. Methods to address documentation insufficiency and improve risk prediction, data availability at the point of care, and other data uses must be informed by these challenges. We need de-stigmatizing vocabulary to document aberrant drug-related behaviors. Shared decision-making tools can be built for patients and providers to reach a mutually acceptable pain treatment, and opioid taper plans are needed. But overall, policies, tools, and workflows that enable patient-provider trust are crucial in this space.

If we learned anything from the efforts to address the recent Covid epidemic, it is the need for highly contextual data to determine a patient's risk from the SARS-CoV-2 virus. Understanding which patient is at greater risk for OUD is equally complex with multiple socio-technical factors. This work is a novel attempt to incorporate provider knowledge and experience from the real-world practice of OUD risk assessment. It provides a framework for defining the gaps between information needs and readiness for complex conditions with considerable stigma. The methodology employed in this research project is generalizable. It can help prioritize informatics efforts for standard and computable data needed for surveillance of problems that contribute to a national crisis. Computable data are necessary for learning health systems and evidence-based care. The proposed computability construct in this work extends the current data readiness frameworks for Learning Health Systems, which enables the triple aim of improving practice, helping research, and informing policy.

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APPENDIX

Exhibit A

"OUD chart footprint is hard.

The reason it is hard is that it is such a sensitive topic for patients, and many have a hard time accepting their diagnosis, so until it is severe it is common for doctors to go light on the charting footprint—sometimes it is left off of the problem list, sometimes it is charted in obtuse ways ("features concerning for…") or not named.

It can really break trust between a patient and provider if this is added to problem list or used as a visit diagnosis. It is commonly left out of diagnosis codes (problem list or diagnoses for visit) even when it is the main concern of a visit.

There are some tools in the chart including the Opioid Risk Tool (ORT) flowsheet to screen for Use disorder and the DSM V flowsheet to screen for use disorder, but I do not believe we have an effective way to discern who and how many patients truly have use disorder by scouring charts electronically (or even by doing a manual review of charts)"

Dr. Mary Pickett

Data for Graph A - 2015-2019 NSDUH survey

Table 6.53B Source Where Pain Relievers Were Obtained for Most Recent Misuse among Past Year Misusers Aged 12 or Older, by Age Group: Percentages, 2015 and 2016

Source for Most Recent Misuse among Past Year Misusers of Pain Reliever	Aged 12+ (2015)	Aged 12+ (2016)	Aged 12-17 (2015)	Aged 12-17 (2016)	Aged 18+ (2015)	Aged 18+ (2016)	Aged 18-25 (2015)	Aged 18-25 (2016)	Aged 26+ (2015)	Aged 26+ (2016)
GOT THROUGH PRESCRIPTION(S) OR STOLE FROM A HEALTH CARE PROVIDER	36.4	37.5	27.3	26.3	37.1	38.4	26.5	28.4	40.8	41.3
Prescription from One Doctor	34.0	35.4	23.1	21.2	34.9	36.5	24.9	25.9	38.3	39.7
Prescriptions from More Than One Doctor	1.7	1.4	1.7	3.6	1.7	1.3	0.9	1.4	2.0	1.2
Stole from Doctor's Office, Clinic, Hospital, or Pharmacy	0.7	0.7	2.5	1.5	0.5	0.6	0.7	1.1	0.5	0.4
GIVEN BY, BOUGHT FROM, OR TOOK FROM A FRIEND OR RELATIVE	53.7	53.0	56.2	57.4	53.6	52.7	59.5	61.2	51.5	50.2
From Friend or Relative for Free	40.5	40.4	37.4	38.8	40.8	40.6	42.5	43.1	40.2	39.8
Bought from Friend or Relative	9.4	8.9	9.7	9.1	9.4	8.9	13.6	11.7	8.0	8.1
Took from Friend or Relative without Asking	3.8	3.7	9.2	9.5	3.4	3.2	3.5[a]	6.4	3.3	2.3
BOUGHT FROM DRUG DEALER OR OTHER STRANGER	4.9	6.0	5.1[a]	9.4	4.9	5.8	8.3	7.3	3.7[a]	5.4
SOME OTHER WAY[1]	4.9[a]	3.4	11.5[a]	6.9	4.4	3.1	5.6[a]	3.2	4.0	3.1

* = low precision; -- = not available; da = does not apply; nc = not comparable due to methodological changes; nr = not reported due to measurement issues.

NOTE: Respondents were asked to choose one of eight sources as their best answer. Respondents with unknown data on Source for Most Recent Misuse and respondents with unknown or invalid responses to the corresponding other-specify questions were excluded from the analysis.

NOTE: Misuse of prescription psychotherapeutics is defined as use in any way not directed by a doctor, including use without a prescription of one's own; use in greater amounts, more often, or longer than told; or use in any other way not directed by a doctor. Prescription psychotherapeutics do not include over-the-counter drugs.

NOTE: Prescription psychotherapeutic subtypes were revised in 2016; one effect was the comparability of codeine products between 2015 and 2016.

[a] The difference between this estimate and the 2016 estimate is statistically significant at the .05 level. Rounding may make the estimates appear identical.

[b] The difference between this estimate and the 2016 estimate is statistically significant at the .01 level. Rounding may make the estimates appear identical.

[1] Some Other Way includes write-in responses not already listed in this table or responses with insufficient information that could allow them to be placed in another category.

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2015 and 2016.

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Table 6.5B Source Where Pain Relievers Were Obtained for Most Recent Misuse among Past Year Misusers Aged 12 or Older, by Age Group: Percentages, 2017 and 2018

Source for Most Recent Misuse among Past Year Misusers of Pain Relievers	Aged 12+ (2017)	Aged 12+ (2018)	Aged 12-17 (2017)	Aged 12-17 (2018)	Aged 18+ (2017)	Aged 18+ (2018)	Aged 18-25 (2017)	Aged 18-25 (2018)	Aged 26+ (2017)	Aged 26+ (2018)
GOT THROUGH PRESCRIPTION(S) OR STOLE FROM A HEALTH CARE PROVIDER	36.6	37.6	31.6	35.3	36.9	37.8	27.4	24.3	39.8	41.1
Prescription from One Doctor	34.6	34.7	28.1	31.7	35.0	34.9	24.9	22.9	38.2	37.9
Prescriptions from More Than One Doctor	1.5	2.0	1.9	2.4	1.4	2.0	1.5	0.9	1.4	2.3
Stole from Doctor's Office, Clinic, Hospital, or Pharmacy	0.5	0.9	1.6	1.2	0.5	0.9	1.0	0.6	0.3	1.0
GIVEN BY, BOUGHT FROM, OR TOOK FROM A FRIEND OR RELATIVE	53.1	51.3	57.0	49.5	52.8	51.4	57.4	61.6	51.4	48.8
From Friend or Relative for Free	38.5	38.6	38.0	34.2	38.5	38.9	37.6	42.2	38.8	38.1
Bought from Friend or Relative	10.6	9.5	12.3[a]	6.7	10.5	9.7	12.3	12.2	10.0	9.0
Took from Friend or Relative without Asking	4.0	3.2	6.8	8.6	3.8	2.8	7.5	7.2	2.7	1.7
BOUGHT FROM DRUG DEALER OR OTHER STRANGER	5.7	6.5	5.5	7.3	5.7	6.5	9.4	9.2	4.5	5.8
SOME OTHER WAY[1]	4.6	4.6	5.8	7.9	4.5	4.3	5.8	4.8	4.2	4.2

* = low precision; -- = not available; da = does not apply; nc = not comparable due to methodological changes; nr = not reported due to measurement issues.

NOTE: Respondents were asked to choose only one source. Respondents with unknown data on Source for Most Recent Misuse and respondents with unknown or invalid responses to the corresponding other-specify questions were excluded from the analysis.

[a] The difference between this estimate and the 2018 estimate is statistically significant at the .05 level. Rounding may make the estimates appear identical.

[1] Some Other Way includes write-in responses not already listed in this table or responses with insufficient information that could allow them to be placed in another category.

Definitions: Measures and terms are defined in Appendix A.

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2017 and 2018.

Table 6.5B Source Where Pain Relievers Were Obtained for Most Recent Misuse among Past Year Misusers Aged 12 or Older, by Age Group: Percentages, 2018 and 2019

Source for Most Recent Misuse among Past Year Misusers of Pain Relievers	Aged 12+ (2018)	Aged 12+ (2019)	Aged 12-17 (2018)	Aged 12-17 (2019)	Aged 18+ (2018)	Aged 18+ (2019)	Aged 18-25 (2018)	Aged 18-25 (2019)	Aged 26+ (2018)	Aged 26+ (2019)
GOT THROUGH PRESCRIPTION(S) OR STOLE FROM A HEALTH CARE PROVIDER	37.6	37.5	35.3	36.7	37.8	37.6	24.3[a]	29.9	41.1	39.3
Prescription from One Doctor	34.7	35.7	31.7	31.5	34.9	35.9	22.9	26.9	37.9	37.9
Prescriptions from More Than One Doctor	2.0	1.1	2.4	3.8	2.0[a]	0.9	0.9	1.7	2.3[a]	0.7
Stole from Doctor's Office, Clinic, Hospital, or Pharmacy	0.9	0.8	1.2	1.4	0.9	0.8	0.6	1.2	1.0	0.7
GIVEN BY, BOUGHT FROM, OR TOOK FROM A FRIEND OR RELATIVE	51.3	50.8	49.5	51.3	51.4	50.8	61.6[a]	55.0	48.8	49.8
From Friend or Relative for Free	38.6	37.0	34.2	31.1	38.9	37.3	42.2	37.8	38.1	37.2
Bought from Friend or Relative	9.5	9.2	6.7	9.4	9.7	9.2	12.2	10.7	9.0	8.8
Took from Friend or Relative without Asking	3.2	4.6	8.6	10.7	2.8	4.2	7.2	6.5	1.7[a]	3.7
BOUGHT FROM DRUG DEALER OR OTHER STRANGER	6.5	6.2	7.3	5.4	6.5	6.2	9.2	8.5	5.8	5.7
SOME OTHER WAY[1]	4.6	5.5	7.9	6.6	4.3	5.4	4.8	6.5	4.2	5.2

* = low precision; -- = not available; da = does not apply; nc = not comparable due to methodological changes; nr = not reported due to measurement issues.

NOTE: Respondents were asked to choose only one source. Respondents with unknown data on Source for Most Recent Misuse and respondents with unknown or invalid responses to the corresponding other-specify questions were excluded from the analysis.

[a] The difference between this estimate and the 2019 estimate is statistically significant at the .05 level. Rounding may make the estimates appear identical.

[1] Some Other Way includes write-in responses not already listed in this table or responses with insufficient information that could allow them to be placed in another category.

Interpretation of Recommendation Categories and Evidence Type in the CDC Guidelines by Dowell et al. (2016)

Recommendation Categories

Recommendation categories are based on evidence type, balance between desirable and undesirable effects, values and preferences, and resource allocation (cost).

Category A recommendation: Applies to all persons; most patients should receive the recommended course of action.

Category B recommendation: Individual decision-making needed; different choices will be appropriate for different patients.

Clinicians help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.

Evidence Type

Evidence type is based on study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects.

Type 1 evidence: Randomized clinical trials or overwhelming evidence from observational studies.

Type 2 evidence: Randomized clinical trials with important limitations or exceptionally strong evidence from observational studies.

Type 3 evidence: Observational studies or randomized clinical trials with notable limitations.

Type 4 evidence: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations..

Figure A – Strategy for dataset extraction from the Research Data Warehouse (RDW)

Inclusion and exclusion criteria for the dataset is based on the guidance from CDC document - Quality Improvement and Care Coordination:
Implementing the CDC Guideline for Prescribing Opioids for Chronic Pain

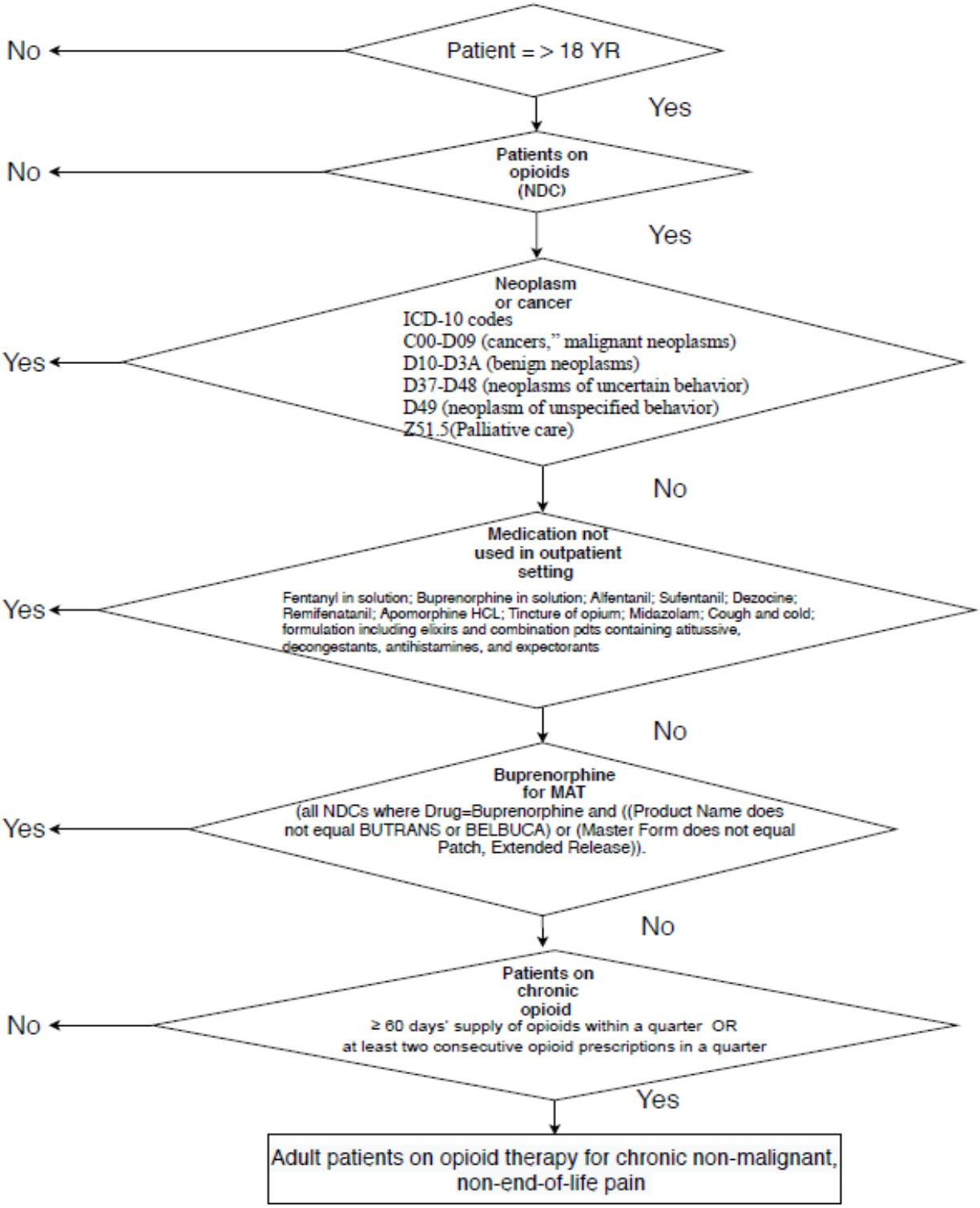

TABLE 1– Literature Review for Risk Factors for Opioid Misuse, Abuse, Addiction and Opioid Use Disorder

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Reid	2002	Abuse (aberrant behaviors)	None	Abuse behavior - (1) one or more reports of lost or stolen opioid medications (or prescription); (2) documened use of other sources (eg other physician practices, street purchases, etc.) to obtain opioid medications; and (3) requests for 2 or more early refills.	Psychiatric comorbidities (depressive disorder), anxiety disorder,) alcohol abuse, narcotic abuse/dependense, lifetime history of substance use disorder (adjusted odds ratio 3.8; 95% confidence interval 1.4 to 10.8) and age (adjusted odds ratio 0.94; CI 0.89 to 0.99) ndependent predictors of opioid abuse behavior	Retrospective (April 1, 1997 through March 31, 1998)	50 VA patients and 48 primary care center patients with chronic pain who received 6 months of opioid prescription during the study period.	Yes
Ives	2006	Misuse (Aberrant behaviors)	None	Aberrant behaviors Opioid misuse was defined as: 1. Negative urine toxicological screen (UTS) for prescribed opioids; 2. UTS positive for opioids or controlled substances not prescribed by our practice; 3. Evidence of procurement of opioids from multiple providers; 4. Diversion of opioids; 5. Prescription forgery; or 6. Stimulants (cocaine or amphetamines) on UTS.	younger, male, past alcohol abuse (OR-2.6), past cocain abuse (OR 4.3), previous drug or DUI conviction (OR 2.6)	Prospective cohort study	Patients were eligible if they had non-cancer pain of greater than three months duration, and we encouraged referral of patients whose pain was considered difficult to manage and in whom opioid misuse was suspected. Patients were managed by a multidisciplinary team in consultation with the patient's primary care physician. The team was composed of a clinical pharmacist practitioner, an internist, a psychiatrist with sub specialization in pain medicine, a nurse, and a program assistant.	Yes

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Kahan	2006	Misuse (Aberrant behaviors)	None	Aberrant behaviors	younger age; current, past, or family history of substance abuse; concurrent psychiatric disorders; and childhood sexual abuse.	Review article	NA	Yes
Edlund	2007	Abuse (ICD-9)	NR	ICD-9	non-opioid substance abuse (OR=2.34), mental health disorders (OR = 1.46), Metal health more prevalent than substance abuse (45.3% vs 7.6%), males, younger adults, greater days supply of prescription opioids	Retrospective	VA longitudinal administrative data - years 2000–2005 - n = 15,160	No
Wasan	2007	Misuse - SOAPP, COMM, POTQ, and urine screens,	For misuse abuse scores - SOAPP (V.1), COMM, PDUQ, POTQ To collect other factors- Marlowe-Crowne Social Desirability Scale-Short Form (M-C), BPI (Brief pain inventory) - pain history, intensity, and location, degree to which the pain interferes with daily activities, mood, and the	Based on screenin tools and UDS - SOAPP (V.1), COMM, PDUQ, POTQ, SOAPP - risk potential for potential future aberrant drug-realted behavior. COMM - Current Misue Measure - score >= 9 PDUQ - A positive response to 2 or more items was classified as High Psych (history of psychopathology or at a greatly elevated risk for it) and to less than 2 was classified as low psychiatric morbidity POTQ - A positive rating of prescription opioid abuse on the basis of the POTQ was given to anyone with 2 or more physician-rated aberrant behaviors.	Psychiatric Disorder - High Psych patients on COT at significantly greater odds for prescription opioid misuse	Prospective cohort study of oral opioid therapy (5-month)	228 patients prescribed opioids for chronic pain	No

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Fleming	2008	Abuse	12 aberrant drug behavior list - based on literature; Addiction Severity Scale (ASI) - This measure assesses seven areas, including alcohol, drugs, employment, legal problems, family and social problems, medical issues, and psychiatric problems.	DSM-IV	>= 4 aberrant behavior were at increased odds for substance use disorder, (OR - 10.14; CI 3.72-27.64), a positive test for cocain (OR - 3.01; CI 1.74, 15.4), Addiction Severity Index (ASI) psychiatric composite score >0.5 (OR 2.38; 1.65, 3.44), male gender (OR 2.08: 1.48, 2.92), and older age (OR 0.69; 0.59, 0.81) compared with subjects with three or fewer behaviors.	Cross-sectional	904 patients taking daily or intermittent opioids in the previous 6 months	Yes
Morasco	2008	Misuse	PMQ - Misuse; pain related disability - Roland–Morris disability questionnaire; Chronic Pain Grade (CPG) - pain intensity, AUDIT-C - alcohol abuse; DAST-10 - drug abuse screening; PHQ (Patient health Questionnaire) - assess depression diagnosis and severity; DSM-IV - diagnose major depression; PTSD checklist - diagnose PTSD; EQ-5D - current health status.	Prescription medication misuse was assessed using six questions from the Pain Medication Questionnaire (PMQ)	history of substance use disorder. After adjusting for age and clinical factors (pain severity, depression severity, current alcohol or substance use disorder), participants with SUD history were significantly more likely than participants without SUD history to report borrowing pain medications from others (OR=6.62, 95% CI=1.4–30.7) and requesting an early refill of pain medication (OR=3.86, 95% CI=1.5–9.6).	Cross-sectional	127 primary care patients who receive opioid medications for treatment of chronic pain	Yes

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Turk	2008	misuse/ abuse	NA	NA	The strongest predictor reported in the literature was a personal history of alcohol and illicit drug abuse, 2 variables were not found to be significant predictors—pain severity and female sex; moderately positive predictors - younger age, history of legal problems, and positive urine toxicology screen. Using the same criterion, there were several variables identified as ''mixed predictors''; meaning they were found to be significant in some studies but not others. These included male sex, a history of an anxiety disorder, a history of prescription drug abuse, and race (nonwhite). Finally, there were several variables that were largely not examined but, when they were evaluated, they were positive predictors, namely, a family history of drug and illicit drug abuse, a history of childhood sexual abuse, a history of DUIs or drug convictions, lost or stolen prescriptions, and using supplemental sources to obtain opioids. Several variables that, although only examined in some studies, when included were found not to be significant predictors (socioeconomic status and disability level). A set of variables that were infrequently examined but, when they were, the results indicated that they were ''mixed predictors''; these included education level, a history of schizophrenia, and a history of motor vehicle collisions.	Systematic Review	NA	NA
Dunn	2010	Overdose	NA	NA	Higher dose - Compared to patients receiving 1-20mg of opioids per day (0.2% annual overdose rate), patients receiving 50-99 mg had a 3.7 fold increase in overdose risk (95% C.I. 1.5, 9.5) and a 0.7% annual overdose rate. Patients receiving 100mg or more per day had an 8.9 fold increase in overdose risk (95% C.I. 4.0, 19.7) and a 1.8% annual overdose rate	Retrospective	9940 patients who received 3+ opioid prescriptions within 90-days for CNCP between 1997 and 2005	NA

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Edlund	2010	abuse/dependence	NA	ICD-9-CM codes	HIGHER RISK younger age, mental health disorder (more common), substance use disorders (more strong) , opioid exposure (dose); higher days supply, higher average doses, and LOWER RISK when using Schedule III-IV opioids only,	Retrospective	claims data from two disparate populations, one national, commercially insured population (HealthCore) and one state-based, publicly insured (Arkansas Medicaid).There were 36,605 enrollees in HealthCore and 9,651 enrollees in Arkansas Medicaid in the study samples	Yes
Liebschutz	2010	abuse (PDUD) based on DSM-IV criteria	Composite International Diagnostic Interview (PDUD, other substance use disorders (SUD), Post-traumatic Stress Disorder (PTSD)); Graded Chronic Pain Scale,	Prescription Drug Use Disorder (PDUD) was defined as meeting DSM-IV criteria for lifetime sedative and/or opioid analgesic prescription drug abuse or dependence as measured by the Composite International Diagnostic Interview (CIDI) v.2.1 module on Drug Disorders. 4; 58 Sedative was explicitly described, and included benzodiazepines and barbituates.	jail time, family history of SUD , greater pain-related limitations, cigarette smoking, be white, male, have PTSD . Those with PDUD were more likely than those without any current or past SUD to report jail time (OR 5.1, 95% CI 2.8–9.3), family history of SUD (OR 3.4, 1.9–6.0), greater pain-related limitations (OR 3.8,1.2–11.7), cigarette smoking (OR 3.6, 2.0–6.2), or to be white (OR 3.2, 1.7–6.0), male (OR 1.9, 1.1–3.5) or have PTSD (OR 1.9, 1.1–3.4).	Cross-sectional	597 patients- 18 to 60 years old, had pain for ≥ 3 months, took prescription or nonprescription analgesics, and spoke English	Yes
Kahan	2011	misuse/addiction/overdose	NA	NA	Patients with mood and anxiety disorders, type of pain, age, health status, Psychiatric status, age (elderly), concurrent sedative drug (Benzodiazepines), Pregnancy, Adolescents,	Guidelines	NA	NA

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Manchikanti	2012	Misuse/ Addiction/ Overdose	NA	NA	comprehensive history, general medical condition, psychosocial history, psychiatric status, and substance use history (evidence good), PDMP review for doctor shopping, urine drug tests, ----------Physical and psychological diagnosis ----------pain treatment history (long acting vs short acting opioids) - type of pain--------espiratory instability, acute psychiatric instability, uncontrolled suicide risk, active or history of alcohol or substance abuse, confirmed allergy to opioid agents, coadministration of drugs capable of inducing life-limiting drug interaction, concomitant use of benzodiazepines, active diversion of controlled substances, and concomitant use of heavy doses of central nervous system depressants.(fair to limited evidence)----------	Guidelines	NA	NA
Miotto	2012	Abuse	NA	NA	younger age, benzodiazepine use, and comorbid conditions such as depression, anxiety, and heavy smoking. BIOPSYCHOSOCIAL	Review article	co-occurring chronic pain and substance abuse	NA
Pergolizzi	2012	Misuse/Abuse	NA	Misuse: The inappropriate use of the prescription opioid agent, whether intentional or unintentional, and regardless of motivation (Passik, 2009) Abuse: A maladaptive pattern of prescription opioid use leading to considerable impairment and/or distress (Passik, 2009)	taking single or multiple opioids, pain intensity, mental health disorders, including a history of preadolescent sexual abuse, personal and familial history of substance abuse, a history of legal problems, being a crime victim, drug-seeking behaviors, drug craving, and age.	Narrative review - examined the literature for a variety of dynamic risk factors associated with opioid misuse among the chronic pain population	Variable	NA

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Sehgal	2012	Abuse/ Misuse	NA	Variable definitions. Crieteria set forth in the DSM-IV is hard to apply on chronic pin population, who often meet the 2 crieteria of tolerance and physical dependence. "A consensus document by the American Pain and Addiction Societies identifies 4 criteria for addiction: impaired control over drug use, compulsive use, continued use despite harm, and craving (15). These criteria have not been validated or tested in large studies according to the principles of evidence-based medicine (EBM)."	**sociodemographic factor**s: abuse - young, white men, Women: misuse - emotional issues and affective distress, first using illicit drugs at 24 years or older, serious mental illness, and cigarette smoking; Men: misuse - legal and problematic behavioral issues, pastyear inhalant use; women and men: misuse - illicit drug **pain related factor**s: more subjective pain, multiple pain complaints, and a greater degree of pain-related limitations, Low pain tolerance **Psychosocial:** young age, depression, back pain, multiple pain complaints, and substance abuse disorders, psychotropic medications, and pain impairment **Comorbid Psychopathology:** history of mood disorder, psychological problems, and psychosocial stressors, Panic, social phobia and agoraphobia, low self-rated health status, and other substance misuse, depression and anxiety disorders **SUD:** ABUSE **- p**ersonal history of illicit drug and alcohol abuse (143) and cannabis use (144), hepatitis A, B, or C, and poisonings **Drug-Related Factors:** Self-reported craving, high daily dose opioids (especially > 120 mg morphine equivalent per day) and short-acting Schedule II opioids, high daily dose opioids (especially > 120 mg morphine equivalent per day) and short-acting Schedule II opioids, receiving excess suppy, requesting higher opioids. **Genetic: 118A>G and the 17C>T SNP in the coding region of OPRM1. Variants of the -opioid receptor gene (OPRK1) and δ-opioid receptor (OPRD1) - include 36G>T SNP of OPRK1 and 80G>T and 921C>T SNPs of OPRD1, polymorphism of the PENK gene, melanocortin receptor type 2 (MC2R)**	Review article	Variable	NA

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Cheatle	2013	Misuse	Observing and identifying aberrant behaviors suggestive of addiction - an inability to adhere to the prescription schedule; resistance to other nonopioid treatments; and insistence on certain forms of medication (American Pain Society, 2001). Other aberrant behaviors identified as possible surrogates for addiction include use of multiple prescription providers or doctor shopping; patterns of early prescription refills; emergency room visits for analgesics; increasing analgesic dose/frequency without proper authorization; hoarding unused medications; and using alcohol or psychoactive drugs in combination with prescription opioids (Compton, 1998). Another source suggest patterns of lost/stolen prescriptions; missing appointments unless opioid renewal is scheduled, inability or resistance to use nonopioid medication formulations; and urgent calls or unscheduled visits to the clinic (Savage, 2008)	Aberrant drug related behaviors	positive history of substance abuse (p=0.001), tobacco use (p=0.011), taking multiple doses of prescribed opioids together (0.024), multiple complaints of pain requiring opioid treatment (p=0.006), and multiple phone calls to the clinic requesting opioid medications (p=0.027). Logistic regression on continuous variables revealed that only the number of phone calls to the clinic regarding opioids in the last 12 months achieved significance (p=0.028).	Retrospective chart review	33 Patients with chronic noncancer pain (CNCP) identified by their treating physician as misusing opioid analgesics, and 33 patients with similar characteristics who had not been identified as misusing opioids	Yes

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Marino	2013	Misuse	COMM	Items on COMM	Impulsivity - Bratt Impulsiveness Scale (BIS)	Cross sectional	42 chronic, low-back pain patients enrolled in a larger study examining problematic opioid analgesic use	NA
Martel	2013	Misuse	SOAPP-R	Based on cut off scores on SOAPP-R	pain catastrophizing (association between catastrophizing and risk for opioid misuse was partially mediated by patients' levels of anxiety.)	Cross-sectional.	Patients with chronic musculoskeletal pain (n=115)	NA
Morasco	2013	Misuse Abuse	PMQ - Misuse SUD - Structured Clinical Interview for DSM-IV	Based on the scores from validated instruments	pain catastrophizing	Cross-sectional	Inclusion criteria were a history of being tested for hepatitis C (both positive and negative hepatitis C patients were included), at least 18 years of age, and English-speaking. Patients with hepatitis C have high lifetime rates of chronic pain (Morasco et al., 2010; Whitehead et al., 2008) and SUDs (Huckans et al., 2005; el-Serag et al., 2002) making this sample ideal for examining factors associated with risk for prescription opioid misuse among patients with a history of SUD. Exclusion criteria were age over 70 years, pending litigation or disability compensation for pain, advanced liver disease, current suicidal ideation, or other serious psychiatric condition such as untreated bipolar disorder or schizophrenia.	Yes
Garland	2014	Misuse	COMM	based on COMM score (cut-point of 13)	attentional bias (AB) towards drug-related cues & cue-elicited craving	Prospective (3 months)	Participants reported recurrent pain on more days than not stemming from chronic non-cancer-related pain conditions, and had taken opioid analgesics daily or nearly every day for at least the past 90 days	Yes

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Martel	2014	Misuse	COMM	based on COMM score (cut-point of 13)	Negative Affect (NA). Opioid craving (not pain intensity) is the mediator between NA and opioid misuse	Cross-sectional	82 patients with chronic musculoskeletal pain being prescribed opioid medication	No
Huffman	2015	Addictio n	DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revised, criteria,3 supplemented by the consensus definitions developed by the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine,2 were used to diagnose TOA. Per consensus definitions, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revised, diagnostic criteria of tolerance and withdrawal3 were not used as diagnostic criteria, as physical dependence is a normal response to appropriate long-term use. Diagnosis instead utilized the remaining criteria, which focus on such characteristics of addiction as loss of control, compulsive use, and continued use despite consequences. A positive diagnosis required the presence of 3 of these remaining criteria.	nonopioid substance use disorders history, absence of improvemnent in pain and function, opioid dose	Retrospective study	199 patients undergoing long-term opioid therapy at the time of admission to a pain rehabilitation program - High risk population	No

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Setnik	2015	misuse, abuse, and diversion	COMM, UDS, Self-Reported Misuse, Abuse, and Diversion [SR-MAD],	Based on cut off scores on COMM and UDS results	Aberrant behaviors and unexpected UDS results - 60% indicated having taken more opioids than prescribed and 10.9% reported chewing or crushing their opioids in the past.One-third of patients (33.8%) had at least one abnormal urine drug test result	Cross-sectional	Enrolled patients were men or women aged >=21 years with chronic (>=3 months) moderate-to-severe pain who required an around-the-clock opioid for optimal analgesia. The patients had to be opioid-experienced, defined by taking a daily opioid dose for >=30 days prior to screening, excluding tramadol and/or ER morphine products. The patients had to be safely converted to a morphine dose of <=20 mg/day. To assess the ability to convert patients from various opioids, patients using the following opioids were recruited: transdermal fentanyl; immediate-release (IR) hydrocodone (including combinations with acetaminophen and ibuprofen); IR hydromorphone; IR oxycodone (including combinations with aspirin, acetaminophen, and ibuprofen); IR morphine; methadone; ER oxycodone; or ER oxymorphone. Female patients could not be pregnant or lactating. If of childbearing age, females had to have a confirmed negative serum pregnancy test at baseline and practice appropriate methods of contraception throughout the study period. Those excluded from the study were patients with current evidence of opioid and/or alcohol abuse; those participating in and/or seeking treatment for opioid and/or alcohol abuse; and those with respiratory or gastrointestinal contraindications to opioid therapy (eg, significant respiratory depression, acute or severe bronchial asthma, or severe chronic obstructive pulmonary disease, suspected of having paralytic ileus).	Yes

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Wasan	2015	Misuse - SOAPP	Hospital Anxiety and Depression Scale (HADS); Brief Pain Inventory (BPI; for 24-h pain and pain interference levels), Oswestry Disability Index (for self-reported function), Neuropathic Pain Questionnaire Short Form (for symptoms of burning, shooting, and sensitivity to touch) Neuroticism Subscale of the NEO personality inventory, Pain Catastrophizing Scale Screener and Opioid Assessment for Patients with Pain, revised (SOAPP, for estimating the risk of opioid misuse)	Based on cut off score on SOAPP	Negative affect (high levels of depression and anxiety symptoms, pain catastrophizing)	Prospective cohort study (6½-month - conducted from 2009 to 2012)	81 CLBP (chronic low back pain) patients with low, moderate, and high levels of Negative Affect (ClinicalTrials.gov Identifier: NCT01502644)	No
Arteta	2016	Misuse	Beck Anxiety Inventory, Beck Depression Inventory, Coping Skill Questionnaire-catastrophizing subscale (CSQ-CAT), COMM, pain intensity was measured through the use of four items that ask for reports about average, least, and worst pain in the past 24 h, as well as pain right now, through the use of a Likert-scale which ranges from 0 to 10 .	Based on cut off score on COMM	Catastrophizing, anxiety, and depression. (anxiety and depression acted as mediators while controlling for the effects of gender and age.)	Retrospective	215 patients with chronic occupational musculoskeletal disorders completed self-report measures upon admission to a functional restorational program	No

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Dowell	2016	Misuse, OUD & overdose	NA	NA	Factors associated with increased risk of misuse included -history of substance use disorder, younger age, major depression, and use of psychotropic medications. moderate or severe sleep-disordered breathing , pregnancy (neonatal opioid withdrawal syndrome), renal or hepatic insufficiency, 65 years and older, anxiety, depression, drug or alcohol use disorders , prior nonfatal overdose.	Guidelines	Variable	Yes
Ciesielski	2016	de novo dependence and abuse	Claims data	ICD-9 codes (opioid abuse (ICD9 code 304.0×) or dependence (305.5).)	younger age [per decade (older) odds ratio (OR) 0.68], being a chronic opioid user [OR 4.39], history of mental illness [OR 3.45], non-opioid substance abuse [OR 2.82], alcohol abuse [OR 2.37], high morphine equivalent dose per day user [OR 1.98], tobacco use [OR 1.80], obtaining opioids from multiple prescribers [OR 1.71], residing in the South [OR 1.65], West [OR 1.49], or Midwest [OR 1.24], using multiple pharmacies [OR 1.59], male gender [OR 1.43], and increased 30-day adjusted opioid prescriptions [OR 1.05].	Retrospective	694,851 patients >= 18 years of age	No
Grey	2016	Misuse, OUD & overdose	NA	NA	personal or family history of alcohol or drug abuse, younger age (16-45), a history of preadolescent sexual abuse, and comorbid psychiatric disease (Depression)	Review article	Older adults	NA
Page	2016	Abuse	ORT Numeric Rating Scale (NRS) for Pain Intensity Pain Interference Items of the Brief Pain Inventory (BPI-10) Chronic Pain Sleep Index (CPSI)42 Beck Depression Inventory-I (BDI-I)-is Short-Form-12 Health Survey version 2 (SF-12v2) Sociodemographic	pain intensity, pain interference, and QOL, taking into account opioid treatment.	Civil status, pain duration, mental health-related quality of life, and cigarette smoking were significantly associated with risk of opioid abuse.	Prospective cohort study	3040 patients adult patients (mean age=53.3±14.7 y; female=56%) enrolled in the Quebec Pain Registry between July 2012 and May 2014. Patients answered self-report and nurse-administered questionnaires (pain and psychosocial constructs, Opioid Risk Tool, pain medication, etc.)	No

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Peacock	2016	Misuse	BPI	10 aberrant behaviors - requested an increased opioid dose, early script renewal, diversion, using opioids from non-medical sources, stock-piling, doctor shopping, frequently losing opioid medication, unsanctioned dose alteration, tampering, and nonpain related opioid use.	Multiple comorbodities (including mental), history of substance abuse (higher odds of being younger)	Prospective cohort study	1,514 people in Australia (adult) prescribed pharmaceutical opioids for CNCP interviewed 3 months apart.	No
Vest	2016	Misuse/OUD	POMI, SOAPP, items from the National Survey on Drug Use and Health (for OUD symptoms)	Based on scores on validated instruements used	impulsivity - urgency	Cross-sectional	143 patients receiving treatment for chronic pain at a regional pain clinic completed a series of questionnaires including the UPPS and measures of opioid risk and misuse.	No
Feingold	2017	Misuse (COMM)	GAD - 7, COMM	Based on cut off score on COMM	Anxiety	Cross-sectional	Chronic pain patients receiving prescription opioids (N=554)	No
Webster	2017	Opioid Use Disorder	NA	Definition of misuse, abuse, addiction, tolerance and dependence taken from Katx et al. 2007 Opiod Use Disorder defoned per DSM V criteria	past or current substance abuse, untreated psychiatric disorders, younger age, and social or family environments that encourage misuse. Nonfunctional status due to pain Exaggeration of pain Unclear etiology for pain Young age Smoking Poor social support Personal history of substance abuse Family history of substance abuse Psychological stress Psychological trauma Psychological disease Psychotropic substance use Focus on opioids Preadolescent sexual abuse History of legal problems History of substance-abuse treatment Craving for prescription drugs Mood swings Childhood adversity	Review article	Variable	NA

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Kaye	2017	Abuse	NA	Definitions of misuse, abuse, and related events as specified by ACTTION - Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks	Demographic factors abuse - male gender, young adults aged 18-25, misuse - , nonmedical use of prescription opioids among men but not women, was associated with past-year inhalant use in one survey; in the case of women who first used illicit drugs at 24 years or older, serious mental illness, and cigarette smoking were associated with the nonmedical use of prescription opioids Pain severity and Interference misuse - more subjective pain, multiple pain complaints, and a greater degree of pain-related limitations Psychsocial factors abuse/dependence/misue - younger; unmarried; unemployed; have a lower education level; have poor/fair health; and use tobacco, alcohol, and illicit drugs misuse - young age, back pain, multiple pain complaints, and substance abuse disorders Co-morbid psychopathology Abuse/dependence - mental disorder(depression, anxiety), PTSD, Panic, social phobia and agoraphobia, low self-rated health status, and other substance misuse misuse - A history of mood disorder, psychological problems, and psychosocial stressors Current substance use disorder	Review article	variable	NA

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Lutz	2017	Misuse	SOAPP-R	Based on cutoff score on SOAPP-R	pain-related catastrophizing	cross-sectional	119 chronic pain patients referred by physicians for an assessment of their qualifications and risk factors for long-term opioid treatment. The mean age of participants was 52.0 years (SD 11.4), and the sample was 54.6% male.	Yes
Bakhai	2018	Misuse	UDS	Unexpected UDS results	history of smoking, substance use , missed medical appointments for other chronic conditions, and nonadherence to other medications (non-opiates) correlated with misuse group	cross-sectional	UDT performed in 206 patients on COT for at least 3 months duration within a one-year period. included male and female patients, between the ages of 19-90 years that were prescribed COT for more than 3 months by IMC physicians for CNCP from April 2011-April 2012. UDT was performed on every patient who was on COT for more than 3 months.	Yes
Chang	2018	Misuse	None	In this study, prescription opioid misuse was defined as on any day in the calendar, participants took more of their opioids than the prescribed dose without communicating with their providers.	age (younger), level of education (higher), level of depression (moderate level), alcohol use problem, illicit drug use, and a higher level of pain interference on walking ability and normal work	cross-sectional	130 patients with chronic pain aged 50 or above, taking prescription opioids	Yes
Coutinho	2018	Abuse	Classification and regression tree (CART)	ICD-9	younger age, higher average daily opioid dose, and total days' opioid supply/year	Retrospective cohort	21,072 patients aged ≥18 years diagnosed with ≥1 of 5 types of CNCP and a prescription for Schedule II or III/IV opioid medication used long-term (≥90 days).	No

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
DiBenedetto	2018	Misuse	COMM, UDS, SOAPP, Oswestry Disability Index (ODI), Roland Morris Disability Questionnaire (RMDQ), Pain severity rating	Unexpeted urine toxicology result An inconsistent UDT result was defined as • the presence of an opioid medication not currently prescribed by the pain management center; • the absence of a prescribed opioid medication; or • the presence of an illicit substance (including cannabis) or alcohol, cocain, nonprescribed medication.	cannabis use	Retrospective chart review	209 patients who were evaluated for a medication management program between October 1, 2011, and January 1, 2014, and met inclusion criteria	No
Feingold	2018	Misuse	Patient Health Questionnaire (PHQ-9) COMM	Based on cut off score on COMM	severity of depression	cross sectional	All participants were recruited during a 6-month period (November 2014–April 2015), were 18 years old or older, currently diagnosed with chronic pain by a pain physician and currently prescribed POs. Patients were excluded from the study if they were not prescribed POs or if they had a cognitive impairment or language difficulties that did not allow for an independent completion of the study assignments. Among 1561 patients who were approached, a total of 890 agreed to participate in the study, representing a 57% response rate, of whom 540 (men: N = 274) met all inclusion/exclusion criteria and were thereafter included in the final sample.	No

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Garland	2018	Misuse	COMM Emotion Regulation Questionnaire (ERQ) Emotional distress was assessed with the 21-item Depression, Anxiety and Stress Scale Opioid craving in the past week was assessed with a single item, "In the past week, how much have you craved opioid medication," measured on a visual analogue scale (VAS) from 0–100 mm. BPI (Brief Pain Inventory)	Based on cut off score on COMM	reduced use of reappraisal	cross-sectional	127 pain patients receiving chronic opioid analgesic pharmacotherapy were classified as at risk for opioid misuse (n = 62) or taking opioids as prescribed (n = 65) using the Current Opioid Misuse Measure (COMM).	Yes
Just	2018	Misuse	COMM	Based on cut off score on COMM	Depression	cross-sectional	recruited 15 GPs practices and asked all patients on long-term opioid therapy (> 6 months) to fill out a questionnaire including the "Current Opioid Misuse Measure" (COMM®), a self-report questionnaire. Patients with a malignant disease were excluded. RESULTS: N = 91 patients	Yes
Lutz	2018	Misuse	COMM, SOAPP-R	Based on cut off score on COMM & SOAPP-R	emotion regulation and disability	Cross-sectional	149 patients (age 25-80, 59% female) - 18 years and over	No
Garland	2019	OUD	COMM	Based on cut off score on COMM	ACE (Adverse Childhood Experience)	cross-sectional	A sample of women (N = 36, mean age = 51.2 ± 9.5) with chronic pain receiving long-term opioid analgesic pharmacotherapy (mean morphine equivalent daily dose = 87.1 ± 106.9 mg)	Yes
Oberleitner	2019	Misuse/Abuse	PDUQ The Toronto Alexithymia Scale-20 The ambivalence over emotional expression questionnaire 8-item emotional approach coping scale Structured Clinical Interview for the DSM-IV-TR	Score on PDUQ and DSM-IV interview	ambivalence over emotional expression (AEQ), personal history of substance abuse disorder	cross-sectional	100 patients with chronic pain (mean age = 47.57 years, SD = 11.57; 53% female; 81% African American) who were receiving a self-administered opioid medication through a local pain clinic.	No

Author	year	Opioid risk	Tool used	Definition of outcome used for the study	Risk Factors	Type of study	Population	Primary Care
Rogers	2019	Misuse/abuse	COMM	Based on cut off score on COMM	cannabis use	crosss-sectionsl	cannabis co-use was associated with elevated anxiety and depression symptoms, as well as tobacco, alcohol, cocaine, and sedative use problems, but not pain experience	No
Rogers	2019	Misuse/abuse	COMM	Based on cut off score on COMM	anxiety sensitivity	cross-sectional	Participants were 429 adults (73.9% female, Mage = 38.32 years, SD = 11.07) recruited via an online survey that reported current chronic pain and opioid use. Eligible participants were between the ages of 18–64, reported current moderate to severe chronic pain that persisted at least 3 months, and current use of opioid pain medication. Participants were excluded if they were younger than 18 years, a non-English speaker (to ensure comprehension of the study questions), and were unable to provide informed, voluntary, written consent to participate.	No
Reps	2020	OUD	ICD	Diagnosis of opioid abuse, dependency or unspecified drug abuse as a proxy for opioid use disorder from 1 day until 365 days after the first opioid is dispensed	8 baseline variables were age 15-29, medical history of substance abuse, mood disorder, anxiety disorder, low back pain, renal impairment, painful neuropathy and recent ER visit.	Retrospective	Population level claims data	No
Cheatle	2020	OUD	ICD	Diagnosis of OUD	tobacco use, age, marital status, financial status, education and pain severity.	cross sectional		No

Table 2. Risk factors for opioid -related harm – misuse, abuse, addiction, opioid use disorder and overdose

S.No.	Risk factors	Reference	Risk
1	Mood disorder	(132)	overdose, misuse, abuse
2	Anxiety Disorder	(132),(109),(133),(79),(134)	overdose, misuse, abuse
3	Psychiatric status(mental health disorder)	(132),(125),(135),(136),(112),(137),(52),(138)	overdose, misuse, abuse
4	Age (younger), (65 years and older - 18), (younger age 16-45 , 19), (younger age <45 years, 22), (younger age <65, 29)	(132), (109),(75), (79), (139),(119),(113),(51),(114),(140),(138)	misuse, abuse, overdose, non-adherent (aberrant) use
5	Concurrent sedative drug (Benzo); concomitant use of heavy doses of central nervous system depressants.	(132), (125),(109),(136)	overdose
6	Comorbidity	(132)	overdose, misuse, abuse
7	Psychosocial history	(132)	overdose, misuse, abuse
8	PDMP Review (doctor shopping)	(132)	overdose, misuse, abuse
9	UDS (higher odds of aberrant UDS associated with male gender, history of SUD, current smoker, under the age of 45, short acting opioids)	(132), (141)	overdose, misuse, abuse
10	Pain treatment history(long acting vs short acting opioids)	(132)	overdose, misuse, abuse
11	Type of pain	(132)	overdose, misuse, abuse
12	Respiratory instability	(125)	overdose, misuse, abuse
13	Acute psychiatric instability	(125)	overdose, misuse, abuse
14	Uncontrolled suicide risk	(125)	overdose, misuse, abuse
15	Current/active Substance abuse (including alcohol)	(125),(142),(136),(79)	overdose, misuse, abuse
16	History of alcohol or substance abuse	(132),(126),(75),(79),(112),(51),(114)	misuse/abuse/overdose
17	Confirmed allergy to opioid agents	(125)	overdose, misuse, abuse
18	Co-administration of drugs capable of inducing life-limiting drug interaction	(125)	overdose, misuse, abuse

19	Concomitant use of benzodiazepines	(125)	overdose, misuse, abuse
20	Active diversion of controlled substances---	(125)	overdose, misuse, abuse
21	Depression	(109),(142),(133),(79)(major depression),(112),(143)	misuse/abuse/overdose
22	Heavy smoking.	(109)	abuse
23	Taking single or multiple opioids	(75)	misuse
24	Pain Intensity	(75)	misuse
25	History of preadolescent sexual abuse	(75),(112)	misuse/abuse/overdose
26	Familial history of substance abuse(drug or alcohol)	(75),(112)	misuse/abuse/overdose
27	History of legal problems	(75),(51)	misuse
28	Being a crime victim	(75)	misuse
29	Drug-seeking behaviors	(75)	misuse
30	Drug craving (correlates with urge to take more medication, fluctuations in mood, and preoccupation with the next dose)	(75),(144),(145)(mediator between negative affect and misuse)	misuse
31	Tobacco use	(126)	misuse
32	Taking multiple doses of prescribed opioids together	(126)	misuse
33	Multiple complaints of pain requiring opioid treatment	(126)	misuse
34	Multiple phone calls to the clinic requesting opioid medications	(126)	misuse
35	Impulsivity	(146)	misuse
36	Pain catastrophizing	(147),(142),(133) - (anxiety & depression as mediators between pain catastrophizing and misuse), (148)	misuse
37	Higher score on Pain Medication Questionnaire (PMQ)	(142)	misuse
36	Attentional bias (AB) towards drug-related cues & cue-elicited craving	(149)	misuse
39	Negative Affect	(145),(127)	misuse

40	Non-opioid substance use disorder	(122),(140)	addiction
41	Absence of improvement in pain and function	(122)	addiction
42	Higher dose (>100 MEM)	(150)	overdose
43	Mean morphine dose > 50 mg/d	(136)	overdose
44	Methadone use	(136)	overdose
45	Number of pharmacies used by the beneficiary (≥4 pharmacies vs. 1 pharmacy;	(136)	overdose
46	Use of psychotropic medications	(79)	misuse/abuse/overdose
47	Sleep-disordered breathing (moderate or severe - 18)	(79)	misuse/abuse/overdose
48	Renal or hepatic insufficiency,	(79)	misuse/abuse/overdose
49	Prior nonfatal overdose.	(79)	misuse/abuse/overdose
50	Distress intolerance (controlling for pain severity and negative affect-20)	(151)	misuse
51	Civil status	(152)	abuse
52	Pain duration	(152)	abuse
53	Mental health-related quality of life	(152)	abuse
54	Cigarette smoking	(152),(117)	abuse
55	Personal history of drug and/or alcohol misuse	(139)	non-adherent (aberrant) use
56	Family history of drug and/or alcohol misuse,	(139)	non-adherent (aberrant) use/misuse, (abuse, 44)
57	Affective disorder	(139)	non-adherent (aberrant) use
58	Childhood abuse	(139)	non-adherent (aberrant) use
59	Post-traumatic stress disorder	(139)	non-adherent (aberrant) use
60	Significant personality disorder	(139)	non-adherent (aberrant) use
61	Problematic physical condition	(139)	non-adherent (aberrant) use
62	Involvement of multiple body regions	(139)	non-adherent (aberrant) use

63	Functioning below normal expectation	(139)	non-adherent (aberrant) use
64	Poor coping strategies	(139)	non-adherent (aberrant) use
65	Lack of social support	(139)	non-adherent (aberrant) use
66	Impulsivity - Urgency	(153)	Misuse
67	Higher dose	(154),(138)	Overdose
68	long-acting plus short-acting Schedule II opioids	(154)	Overdose
69	Sedative-hypnotic use	(154)	Overdose
70	Opioids combined with benzodiazepines and skeletal muscle relaxants	(154)	Overdose
71	Alcohol Abuse or Dependence	(155)	Overdose
72	History of smoking	(156)	Misuse
74	Substance use	(156),(140)	Misuse
75	Missed medical appointments	(156)	Misuse
76	Non-adherence to other medications	(156)	Misuse
77	Level of education (higher)	(119)	Misuse
78	level of depression (moderate level)	(119)	Misuse
79	Alcohol use problem	(119)	Misuse
80	Illicit drug use	(119)	Misuse
81	Higher level of pain interference on walking ability and normal walk	(119)	Misuse/Abuse
82	Average daily opioid dose	(113)	Abuse
83	Total days' opioid supply/year	(113),(140),(138)	Abuse
84	Cannabis use	(120), (121)	Misuse - (SOAPP-R, 31); (COMM, 38)
85	Severity of depression	(157)	Misuse - COMM
86	Reduced use of reappraisal	(158)	Misuse - COMM

87	Emotion regulation and disability	(159)	Misuse - COMM, SOAPP-R
88	Adverse Childhood Experience	(160)	OUD
89	Ambivalence over emotional expression (AEQ)	(161)	Misuse - COMM
90	Anxiety sensitivity	(162, 163)	Misuse - COMM
91	Positive Urine Drug Test	(51)	Misuse
92	Male gender	(51),(117),	Misuse, abuse,
93	History of anxiety disorder	(51)	Misuse
94	History of prescription drug use	(51)	Misuse
95	Race - Nonwhite	(51)	Misuse
96	History of childhood sexual abuse	(51)	Misuse
97	History of DUIs or drug convictions	(51)	Misuse
98	Lost or stolen prescriptions	(51)	Misuse
99	Using supplemental sources to obtain opioids.	(51)	Misuse
100	Jail time	(117)	Misuse
101	Race - white	(117)	Abuse
102	PTSD	(117)	Abuse

Table 3. Risk factors selected for the Delphi style survey

Bio-Psychosocial Domains	Opioid Misuse, Abuse, Addiction and OUD Risk Factors
Demographics	Age < 45 years
Demographics	Male gender
Substance Use	Illicit drug use
Substance Use	Cannabis/Marijuana use
Substance Use	Kratom use
Substance Use	Current substance use disorder
Substance Use	History of substance use disorder
Substance Use	Tobacco use
Substance Use	Heavy smoking
Substance Use	History of misuse of any sedative or stimulant
Substance Use	History of misuse of cold and cough medication
Substance Use	History of non-fatal opioid overdose
Psychiatric	Anxiety disorder
Psychiatric	Post-traumatic stress disorder
Psychiatric	Major depressive disorder
Psychiatric	Acute psychiatric instability
Psychiatric	History of suicide attempt
Psychiatric	Suicidal ideation
Psychiatric	Personality disorder
Psychiatric	Psychosomatic disorder
Socioeconomic	Housing instability
Socioeconomic	Marital status separated or divorced
Socioeconomic	History of DUI or drug conviction
Socioeconomic	Family history of substance use disorder
Socioeconomic	History of childhood physical, emotional or sexual abuse
Pain and Function	Pain diagnosis associated with no evidence of benefit.
Pain and Function	Longer pain duration
Pain and Function	Involvement of multiple body locations
Pain and Function	Lack of demonstrated functional improvement
Pain and Function	High pain interference with daily activity
Pain and Function	Pain catastrophizing
Pain and Function	On disability for pain related condition
Pain and Function	Interference with vocation due to opioid use or pain
Medication	Total opioid dose > 90 MME/day
Medication	Concurrent long-acting plus short-acting opioids
Medication	Concurrent prescribed Benzodiazepines
Medication	Concurrent other psychiatric medication (SSRI's, SNRI, atypical antipsychotics)
Medication	Concurrent non-benzo sedative hypnotics (e.g. zolpidem, zaleplon, butalbital)

Aberrant Drug-Related Behaviors	Resistance to changing opioid medications despite deterioration in function or significant negative effects
Aberrant Drug-Related Behaviors	Reporting prescription loss or theft
Aberrant Drug-Related Behaviors	Obtaining opioids from multiple providers in violation of treatment agreement
Aberrant Drug-Related Behaviors	Increasing dose without provider's instruction
Aberrant Drug-Related Behaviors	Running short with medication supply and requests for early refills
Aberrant Drug-Related Behaviors	Travelling long distance for pain care
Aberrant Drug-Related Behaviors	Showing symptoms consistent with opioid withdrawal
Aberrant Drug-Related Behaviors	Obtaining prescription opioids from multiple pharmacies
Aberrant Drug-Related Behaviors	Missing medical appointments
Aberrant Drug-Related Behaviors	Being in hazardous situation as a result of opioids
Aberrant Drug-Related Behaviors	Weaning described as unsuccessful or difficult
Aberrant Drug-Related Behaviors	Emergency department visits to obtain opioids
Aberrant Drug-Related Behaviors	Abnormal urine drug screening result
Aberrant Drug-Related Behaviors	Requesting higher dose of prescription opioids
Aberrant Drug-Related Behaviors	Multiple phone calls to clinic requesting opioid medication
Aberrant Drug-Related Behaviors	Taking opioids for symptoms other than pain (e.g., anxiety, depression, sleep, or to produce euphoria)
Medical Comorbidity	History of Hep C infection
Medical Comorbidity	HIV infection
Genetic test	Genetic tests positive for gene polymorphism associated with OUD