UC Irvine UC Irvine Electronic Theses and Dissertations

Title

An Analysis of Opioid-Risk Screening Instruments for Use in the Emergency Department: A Qualitative Systematic Review

Permalink https://escholarship.org/uc/item/1wx595nb

Author Sahota, Preet Kaur

Publication Date 2017

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at https://creativecommons.org/licenses/by/4.0/

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA, IRVINE

An Analysis of Opioid-Risk Screening Instruments for Use in the Emergency Department: A Qualitative Systematic Review

THESIS

submitted in partial satisfaction of the requirements for the degree of

MASTER OF SCIENCE

in Biomedical and Translational Science

by

Preet Kaur Sahota

Thesis Committee: Associate Professor Dr. Bharath Chakravarthy, Chair Professor Dr. Dana B. Mukamel Professor Dr. Shahram Lotfipour

© 2017 Preet Kaur Sahota

TABLE OF CONTENTS

Page

LIST OF FIGURES	iii
LIST OF TABLES	iv
ACKNOWLEDGMENTS	v
ABSTRACT OF THE THESIS	vi
CHAPTER 1: INTRODUCTION	1
CHAPTER 2: BACKGROUND	8
CHAPTER 3: METHODS	16
CHAPTER 4: RESULTS	28
CHAPTER 5: DISCUSSION	42
REFERENCES/BIBLIOGRAPHY	52

LIST OF FIGURES

		Page
Figure 1	Systematic Literature Review Methodology Flow Diagram	26
Figure 2	PubMed/MEDLINE Literature Search Strategy	27

LIST OF TABLES

		Page
Table 1	List of Articles Chosen for Qualitative Review: Study Title, Author and Year of Publication	28-29
Table 2	Part 1 – Screening Instrument Characteristics	29-30
Table 3	Part 2 – Screening Instrument Characteristics	31-32
Table 4	Part 1 – Study Characteristics	34-35
Table 5	Part 2 – Study Characteristics	36-37
Table 6	Patient Demographics	37
Table 7	Validity and Reliability Data	38-39
Table 8	Specificity, Sensitivity and Predictive Value Data	40
Table 9	Effect on Morbidity/Mortality, Clinical Utility/Feasibility and Accuracy Data	40-41

ACKNOWLEDGMENTS

This thesis would not have been possible without the support, generosity and mentorship of my committee chair, Dr. Bharath Chakravarthy. I would like to highlight my deepest appreciation to Dr. Chakravarthy, who provided endless advice and direction as I worked on this project throughout this past year. I would not have successfully completed this thesis without his altruistic guidance and willingness to help however possible. Dr. Chakravarthy truly cares for his students and helps us prepare for our future careers, in addition to providing continuous reassurance as we pursue our aspirations. I could not have asked for a more dedicated and thoughtful faculty mentor and advisor. I hope that I can follow in his footsteps and continue conducting research to improve the quality of medical care for all patients.

I thank my committee members, Dr. Dana B. Mukamel and Dr. Shahram Lotfipour, whose expertise guided me throughout the process of conducting a systematic review for the very first time. Both advisors answered all my questions and helped alleviate my concerns regarding how systematic reviews are formulated and the necessary components to keep in mind throughout the literature search process.

Additionally, I sincerely thank Linda Murphy, who provided me with information regarding the framework of systematic reviews, and assisted with finalizing the search strategy steps and terms. Linda has always helped the Biomedical and Translational Science students with their work, and I am thankful for her selflessness and willingness to answer all questions, and how she directs students towards the appropriate resources for further assistance.

I thank the University of California, Irvine for the opportunity to pursue a Master of Science degree in Biomedical and Translational Science as well as the Biomedical and Translational Science Faculty and Staff for an unforgettable graduate school experience. Thank you, Dr. Sherrie Kaplan; Dr. Sheldon Greenfield; Dr. John Billimek; Dr. Richard Kelly; Dr. Joel Adelson; Marissa Saplala; Thuy Pham and Daniel Nguyen for teaching us how to conduct ethical and sound clinical research, and for your boundless dedication towards the accomplishments of your students.

Finally, I thank my family and friends for their love and support throughout the process and for the encouraging words and endless inspiration to pursue all my goals. No one has been more important to me throughout the completion of this project than the members of my family and my close friends. Thank you.

ABSTRACT OF THE THESIS

An Analysis of Opioid-Risk Screening Instruments for Use in the Emergency Department: A Qualitative Systematic Review

By

Preet Kaur Sahota

Master of Science in Biomedical and Translational Science University of California, Irvine, 2017 Dr. Bharath Chakravarthy, Chair

Opioid use, misuse, abuse and addiction is a growing epidemic in the United States. The purpose of this systematic review is to identify screening instruments used in emergency medicine (EM) settings to detect opioid drug use and to assess the psychometric data for each screening instrument. The review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. PubMed/MEDLINE, PsychINFO, Cochrane Database of Systematic Reviews, Web of Science, CENTRAL, CINAHL, CRD and ClinicalTrials.gov were searched for articles published up to June 2017. We extracted 172 articles for initial screening and 66 articles were assessed for eligibility. Ten articles were extracted from the full-text assessment. Eight instruments were identified from the finalized article list: SOAPP-R; ASSIST; two, single-item screening questions; oneitem binge-drinking screener question; patient medical charts; medical history and physical/patient self-reporting in medical charts; Drug Abuse Screening Test; and HERA/SBIRT. Screening instrument characteristics, study characteristics, and reliability and validity data were extracted from the 10 studies. A meta-analysis was not conducted

vi

due to heterogeneity between the studies. There is a lack of validity and reliability evidence in all 10 articles; and sensitivity, specificity and predictive values varied between the different instruments. These instruments are not validated for use in EM settings. There is no clear evidence to state which screening instruments are appropriate for use in detecting opioid drug abuse in EM patients. There is a need for brief, reliable, valid and feasible screening instruments and more psychometric data.

INTRODUCTION

At the beginning of 1999, the opioid drug epidemic began to extend across the United States and continues to persist in American society despite efforts to end this epidemic from spreading further. The Centers for Disease Control and Prevention (CDC) report that drug overdose deaths tripled in volume between 1999 to 2014.¹ During 2014, 47,055 drug-related overdoses deaths were reported across the U.S. Of these overdoses deaths, about 61% (28,647) involved the use of opioids.² Also in 2014, the number of deaths reported in the U.S. due to alcoholic liver disease was 19,388 deaths and the number of alcohol-induced deaths (excluding accidents and homicides) was 30,722.³ In that same year, the number of deaths reported in the U.S. due to motor vehicle traffic collisions was 33,736. The rate of motor vehicle traffic deaths is 10.6 per 100,000 in the U.S. population.⁴ The number of drug overdose deaths exceeds alcohol use and motor vehicle traffic deaths, illustrating the severity and concern of drug overdose and abuse in the U.S.^{3,4}

The CDC analyzed opioid-related overdose deaths from 2014 to 2015, dividing them into the following drug categories: natural/semisynthetic opioids, methadone, heroin and synthetic opioids. In 2015, drug-related overdoses comprised of 52,404 deaths, where 63.1% (33,091) involved the use of opioids.¹ The death rates involving methadone have decreased by 9.1% in 2015; however, heroin and synthetic opioid-related overdose deaths have increased dramatically across the U.S.^{1,5,6}

As defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, the terms substance abuse and dependence have been replaced with the expression "substance use disorders," categorized on a scale from mild to severe. The Substance Abuse and Mental Health Services Administration describes concrete symptoms of opioid use disorder, such as

"strong desire[s] for opioids, inability to control or reduce use, continued use despite interference with major obligations or social functions, use of larger amounts over time, development of tolerance, spending a great deal of time to obtain and use opioids"⁷... as well as adverse health outcomes. During periods of attempted withdrawals, individuals may experience changes in mood or behavior, nausea, vomiting, fatigue, fever and insomnia, to name a few.⁷ The rise in opioid use disorders reinforces the severity of the opioid drug epidemic, as well as the undue burdens placed on individuals as well as the American healthcare system.

A retrospective study reported on the economic burden of prescription opioid use and misuse in 2013. The study concluded that about \$78.5 billion of total U.S. economic burden was accredited to prescription opioid misuse. About one-third (\$28.9 billion) was spent on healthcare and substance abuse treatments. About one-quarter was used in the public sector for healthcare, substance abuse treatment and criminal justice costs.⁸ The opioid epidemic is an ongoing public health concern and affects multiple patient populations, including all age groups, genders and racial/ethnic groups.

As of July 2015, the U.S. Preventative Services Task Force (USPSTF) determined that a deficit exists in the evidence available to comment on the use of illicit drug screening in primary care settings for adolescents, adults and pregnant women.^{9,10} There is an urgent need to identify possible screening tools for illicit drug use, specifically opioid use disorders, in various patient populations. Screening tools provide healthcare providers with information concerning substance use disorders and help providers disseminate resources to patients who may be suffering from a drug-related addiction. Screening tools are available to almost all patient populations, in several clinical settings, and there are different forms of screening tools available, including questionnaires/instruments and toxicology (blood/urine/saliva) tests.¹¹

In particular, EM settings require time-sensitive screening tools due to the fast-paced nature of the clinical environment and patient volume. A retrospective, cross-sectional study, using data from an urban-teaching EM setting in Indianapolis, concluded from 1,665 patient medical charts that pain was the chief complaint of 52.2% of EM visits.¹² The prevalence of chronic pain and pain-related health conditions in EM is well known across the nation. Due to previously studied correlations between chronic pain and opioid use, it is imperative to screen for opioid use disorders in EM settings and provide resources for patients who may be susceptible to addiction or already suffer from an opioid use disorder.¹³

Screening instruments have been validated for other health concerns, conditions and disorders, including alcohol use disorders (AUDs) and intimate partner violence, in EM settings.^{14,15} Alcohol screening instruments have been widely studied due to the high prevalence of AUDs. A systematic review conducted in 2011 evaluated which alcohol screening instruments provide the most accurate information for alcohol abuse in ED patients. The study found that the fast alcohol screening tool (FAST) was the most sensitive screening tool, with high specificity and high positive predictive values. The study also found that the Paddington alcohol test (PAT) can be used to screen specific ED populations, and there is evidence of its cost-effectiveness.¹⁴

An alcohol screening report states that "in the case of AUDs…various diagnostic interviews…lead to different diagnoses…[L]ack of an at least near-perfect gold standard introduces some uncertainty into estimating the validity of screening tests for AUDs."¹⁶ This report claims that although screening instruments are used as "gold standards" for comparisons with other screening instruments, it is important to use screening instruments that have specificities and sensitivities close to 1 to truly serve as clinical standards.¹⁶ As mentioned previously, the FAST screening tool was found to have high sensitivity and specificity in EM

settings.¹⁴ A survey-based study conducted in two London accident and emergency (A&E) departments used the Alcohol Use Disorders Identification Test (AUDIT) as the reference standard to test the utility of FAST. The study found that FAST had good sensitivity and specificity in multiple clinical settings when compared to the AUDIT standard. The study also concluded that the FAST is time efficient and can be used in fast-paced clinical settings for alcohol abuse detection.¹⁷

Intimate partner violence screening instruments have also been validated for EM settings. Specifically, the Partner Violence Screen (PVS) was created to detect partner violence in female ED patients. The PVS is a three-item questionnaire and focuses on past physical violence and perceived personal safety. The PVS validation study assessed the sensitivity, specificity and predictive values of the instrument and included the Index of Spouse Abuse (ISA) and the Conflict Tactics Scale (CTS) as reference standards.¹⁵ These previous studies show that it is possible to screen for multiple health conditions in EM settings. These findings support the feasibility of using opioid drug screening tools to screen EM patients for possible abuse patterns.

Taking this previous data into consideration, we propose to address the validation and utility of screening tools used to screen for patients who are using, abusing and misusing opioids. For the scope of this research, we plan to focus on three key questions to address the issue of effective opioid use disorder screening in EM. Our research questions include the following: (1) What screening tool(s) can detect opioid use disorders, addiction and misuse? (2) What screening tool(s) are best suited for fast-paced EM settings? (3) Which reliability and validity tests and data provide existing information concerning clinical utility of screening tools in EM settings? We

commentary on the use of screening tools to effectively screen EM patients for opioid use disorders.

To best present research on opioid use screening in EM settings, we will conduct a systematic review of existing literature in this field. There are several benefits to conducting a systematic review. Systematic reviews locate and integrate pre-existing research data to answer an explicit research question. The key to a successful systematic review is careful methodology and consistency when searching for literature in the specific field of study.¹⁸To capture wide-spread data on the efficacy of various screening tools, we plan to conduct an extensive systematic review on opioid use screening tools used within emergency departments (ED) across the nation. In order to conduct a systematic review, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) provides a checklist to ensure all necessary components of a systematic review are accounted for. We did not include Participants, Interventions, Comparisons and Outcomes (PICO) in our review, because this review does not analyze clinical or comparison trials, for which PICO is more appropriate.¹⁹

The focus of the research will be the extraction of data from the finalized list of articles chosen for review. We will extract the following data points from all articles, if the data are available: study design, study population, sample size, study aims/objectives, study setting (location), patient demographics, year of study, descriptive statistics, study conclusions and whether the tool was self-administered or clinician-administered. Descriptive statistics will include reliability, validity, specificity, sensitivity, predictive value, effect on morbidity/mortality and clinical utility/feasibility data. Analyses of these quantitative and qualitative data points will provide information concerning the usefulness of various screening tools and which screening tool(s) are best suited for EM settings and detection of opioid dependency in patients.

We hypothesize that shorter, highly reliable and validated questionnaires will serve as the best option for screening tools to implement in EM settings for opioid use disorders. Due to contamination, mislabeling and lost sampling of toxicology tests, blood, urine and saliva sampling may not provide the most time-efficient or accurate screening assessments for active departments such as EM.¹⁰ For this research study, we do not comment on the usefulness of toxicology tests due to inconsistencies in reported data, difficulties in comparing toxicology tests with questionnaire/survey instrument data, and to maintain the brevity of this systematic review. Questionnaires are easy to use and can be administered by a clinician or completed by the patients themselves; however, reliability and validity data must be available to comment on the usefulness of the instrument(s).

After analyzing the data for this review, we hope to contribute to the existing literature on screening for opioid use disorders and general substance abuse screening in EM settings. By referring to the data we will obtain from the review, we will construct a screening instrument to implement within our academic ED. We will conduct pilot tests to determine reliability and validity of the model instrument. Once we finalize the screening instrument for use, we will conduct a prospective study to determine the usefulness of the instrument in providing evidence of opioid use disorders within our EM patient population.

The opioid drug epidemic is an economic burden and public health concern in U.S. society. To address this widespread occurrence and provide resources to individuals who suffer from substance use disorders, patients must be screened for drug addictions in clinical settings. Because most pain-related cases filter through the ED, screening in EM settings is of utmost importance and the probability of capturing substance use disorders increases within this healthcare environment. Screening instruments can provide useful evidence to inform clinicians

of possible substance use disorders within a timely manner. We hope to summarize the existing literature in this field and provide EM researchers and physicians with evidence for implementing screening instruments in EDs to capture patients who are dependent upon opioids.

BACKGROUND

An opioid is any drug that interacts with opioid receptors on neurons in the brain and peripheral areas of the body.²⁰ Opioids exist as natural or synthetic compounds; the body can secrete endorphins, which are peptide hormones that bind to opioid receptors. Opioids can decrease pain signaling to the brain and influence areas that regulate emotion and pain reception.²¹ There are different classifications of opioid drugs, including heroin, fentanyl (a synthetic opioid) and various prescription opioids such as oxycodone, hydrocodone, codeine and morphine. For most opioid-classified drugs, metabolism occurs within the liver. Although metabolism aids the body in dispelling the drug, opioid metabolism can lead to the formation of inactive and active metabolites, which can continue to harm the body.²⁰

Because opioids can readily cross target cell membranes due to their lipid-favorable properties, it is the goal of metabolism to oxidize opioids into water-favorable compounds. This conversion allows the body to dispel the drug in urine. The liver contains enzymes to facilitate the multi-phase metabolic process.²² Different opioids remain in the body for different time periods. Heroin remains in saliva for five hours, in blood for six hours and between two to seven days in urine; however, the drug may remain in hair follicles up to 90 days, on average. Codeine leaves the body faster than most opioid drugs. Codeine remains in blood for 24 hours and in urine for 24 to 48 hours; however, codeine can be found in saliva from one to four days and remains in hair follicles up to 90 days, on average. Individuals who misuse and/or abuse opioids over an extended period may have excess buildup of the drug in fatty tissues and the probability of positive toxicology screening increases.²³

Opioid drugs are used in various medical specialties for chronic pain management and relief.^{20,24} For example, morphine relieves pain from surgeries and in patients with advanced

stages of cancer. When used for short periods of time and as directed, opioids can safely assist in pain relief. However, if the drug is used for long periods of time, the probability of developing a substance use disorder increases.²⁴ Recently, policymakers and the public have started to focus on effective pain management regulations and methods to reduce addiction and abuse. Yet there is no agreed upon treatment for chronic pain, notably for cancer patients.²⁵

There are three main classifications of drug misuse and abuse: physical dependence, addiction, and substance use disorders. Physical dependence occurs when the body needs a continuous source of the drug to avoid withdrawal effects. Addiction is considered as an abnormal disease and includes "uncontrollable cravings, inability to control drug use, compulsive drug use, and use despite doing harm to oneself or others"²⁶ due to chemical changes in the brain. Addiction is more severe when compared to physical dependence, which is typically expected to occur when a drug is consumed for extended periods of time.²⁶ Substance use disorders manifest when the use of the drug results in health concerns and issues with functioning in daily life. Substance use disorders are also classified as substance abuse.²⁷ Specifically, opioid use disorders focus on the need for opioids and the individual's loss of control to the drug. Drug tolerance is established and withdrawal from the drug results in adverse effects such as mood changes, nausea, vomiting, fatigue, diarrhea, fever, insomnia, restlessness, cold flashes, involuntary movements, respiratory depression and euphoria.^{21,24,28}

Despite the adverse health effects caused by opioid misuse and abuse, there are methods available to counteract these drugs. Naloxone is an "opioid antagonist" that is used to reverse the effects of morphine and heroin overdose. Due to opioid overdose, the central nervous and respiratory systems begin to shut down; naloxone assists with respiratory failures and helps the overdose victim with breathing normally. Naloxone can be given to overdose victims by anyone

who is trained to administer the drug. Fortunately, naloxone cannot be abused and the drug is administered via injection or spray.²⁹ In most cases, naloxone can save the lives of opioid overdose victims, if administered in time.³⁰

Despite the presence of naloxone, prevention techniques precede all other possible treatments. The CDC states that "the best way to prevent opioid overdose deaths is to improve opioid prescribing to reduce exposure to opioids, prevent abuse and stop addiction."³⁰ The CDC claims that the following can assist in preventing opioid abuse and misuse: prescription drug monitoring programs (PDMPs), state drug laws, quality improvement programs, substance abuse prevention in adolescents via family and school-based programs, and education on how to use prescription opioids. However, if addiction treatment is needed, medication-assisted therapies (MATs) can assist patients via behavioral counseling and with methadone, buprenorphine and naltrexone. These medications counteract the effects of opioid abuse, similar to naloxone.³⁰

Several studies report on adverse outcomes associated with opioid drug abuse and overdose. Self-medication, use for reward, compulsive use due to addiction and diversion for profit can lead to drug misuse and abuse.³¹ The CDC reports that from 2000 to 2015, close to half a million individuals died from drug overdose and about 91 individuals die every day due to opioid overdose in the U.S.³² Additionally, from 1999 to 2010, prescription opioid-related death rates quadrupled, while heroin overdose rates rose less than 50%. Since 2010, various states and cities throughout the U.S. have reported growth in heroin-related death rates. As examined by a CDC *Morbidity and Mortality Weekly Report*, the death rate from heroin overdose rose from 1.0 to 2.1 per 100,000 from 2010 to 2012, while the death rate from opioid pain relievers decreased from 6.0 per 100,000 in 2010 to 5.6 per 100,000 in 2012. This analysis represents drug overdose

rates for 28 states. Heroin overdose rates rose in both genders, all geographic regions studied and all racial/ethnic groups, with the exception of American Indians/Alaska Natives.³³

A retrospective study, which focused on San Diego and Imperial County Medical Examiner data in 2013, compares the number of unintended prescription-related deaths with California PDMP data. The study found 254 unintended prescription-related deaths, where 186 patients had PDMP data 12 months before their death. An interesting statistic to note from this study is that opioids composed the majority of single medication deaths (70.6% of the study population). The average number of prescriptions per patient was 23.5; the average number of pharmacies and healthcare providers per patient were 3 pharmacies and 4.5 providers. Another remarkable finding shows that chronic prescription use was discovered in 68.8% of patients who had PDMP data.³⁴

A retrospective analysis of the National Hospital Ambulatory Medical Care Survey (NHAMCS) found that 42% of U.S. ED visits consisted of pain-related symptoms. The study found that prescriptions for opioids increased by 14% (from 23% to 37%) from 1993 to 2005 and patients who identified as White had higher probabilities of receiving opioid prescriptions than Black or Hispanic patients (31% v. 23% v. 24%, respectively). These trends did not change throughout the duration of the study.³⁵

The effects of opioid drug overdose and misuse are not limited to adult populations. It is important to understand the reasons behind the misuse of prescription opioids and other recreational drug use in the pediatric population due to growing concerns of substance abuse in children and teenagers across the U.S. One cross-sectional, survey-based study found that among high school senior-level students, who reported nonmedical use of prescription opioids, 56.4% stated that they used opioids "to relax or relieve tension," 53.5% "to feel good or get high,"

52.4% "to experiment," and 44.8% stated "to relieve physical pain."³⁶ The study also found that one in every ten students used prescription opioids for nonmedical purposes.³⁶

Demographical trends, focusing on the use of prescription opioids among adolescents, have also been studied. A retrospective study, analyzing data in pain-related ED visits from 2001 to 2010, found that opioids are often prescribed to female, non-Black patients with private insurance. Additionally, this study found a statistically significant rise in opioid use by White patients.³⁷In contrast, another retrospective study from 2004 to 2013 found a decrease in the use of nonmedical prescription opioids in non-Hispanic White adolescents. This study also found a decrease in the use of nonmedical prescription opioids in female adolescents between the ages of 15 and 17 years. By 2013 the rates for females were similar to the rates for males within the 15-17 age range. Negative confounding variables associated with nonmedical prescription use included lower household income, poor grades in school, comorbid substance abuse, externalizing and delinquent behavior, and fighting at school and/or work. The study mentions two positive variables associated with the decrease of nonmedical prescription opioid use: religiosity in non-Hispanic Whites and parental involvement among non-Hispanic Whites and Hispanic adolescents.³⁸

In the *Journal of Pediatrics*, a national, cross-sectional survey study conducted from 2004 to 2011 found that prior nonmedical use of prescription opioids was significantly associated with the start of heroin abuse (hazard ratio: 13.12, with 95% confidence interval: 10.73, 16.04). The study found that children starting nonmedical prescription opioid use between the ages of 10 to 12 years had the greatest risk of future heroin use. This finding did not differ between racial/ethnic groups or by income. The study also found that heroin use was 13 times greater among children who responded with prior nonmedical use of prescription opioids than

those who did not previously use prescription opioids. The average risk of heroin use was lower in Black and Hispanic children when compared to White children. The study concludes that prior nonmedical prescription opioid use is associated with future heroin use in adolescents.³⁹

Moreover, there is a steady increase in heroin use throughout the U.S. A review article published in *The New England Journal of Medicine* comments on the connection between nonmedical prescription opioid use and heroin use. The article states that nonmedical use of prescription opioids can change; some individuals may use the drug once or twice annually while others misuse the drug daily to the point of addiction. The article asserts that there is a correlation between the rise in the number of opioid prescriptions and opioid-related death rates, and lower quality of life.⁴⁰ Additionally, pain is not well-addressed in healthcare settings; as stated before, if used appropriately, prescription opioids can successfully treat pain caused by an assortment of health problems.²⁴ The use of interventions and educational programs are vital in this case. It may be possible that interventions and other programs used to educate or prevent prescription opioid abuse have slowed the progression of opioid drug abuse.⁴⁰

According to the review article, the rate of opioid prescribing in the U.S. plateaued between 2010 and 2012.⁴⁰ Despite the decline in prescription opioid abuse, there are surges of heroin use and overdose deaths. Heroin use has increased since 2007 in the U.S. About 914,000 people reported use of heroin in 2014, which is a 145% increase since 2007.⁴¹Additionally, death rates due to heroin overdose quintupled from 2000 to 2014.⁴² Nonmedical prescription opioid use is associated as a risk factor for future heroin use, although the transition from nonmedical prescription opioids to heroin is rare and occurs at a steady rate.⁴⁰ However, as demonstrated in the *Journal of Pediatrics* article, there appears to be a different trend in pediatric population groups.³⁹ Trends observed in adult populations may not necessarily extrapolate to pediatric

populations; however, to halt the increases in heroin use in the pediatric population, early detection of opioid use disorders is necessary.

At this time, the USPSTF states that there is a deficit in evidence to determine the benefits and harms of screening tools for illicit drug use in primary care settings. After conducting a systematic review of articles up to August 2006 to discuss validated screening instruments for illicit drug use in the ambulatory and general healthcare environments, the USPSTF found that the studies analyzed for the review were of fair ranking due to small sample sizes and lack of patients from general healthcare environments. Only some studies commented on the accuracy of the instruments or used other standards for comparison. The review found evidence that shorter, standardized questionnaires can be useful if they have accurate validity and reliability data for illicit drug-use screening. The Car, Relax, Alone, Forget, Friends, Trouble (CRAFFT) instrument was validated for adolescent screening and the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST), Cut down, Annoyed, Guilty, Eye-opener -Adapted to Include Drugs (CAGE-AID) and Drug Abuse Screening Test (DAST-20) instruments were validated for adult screening. However, because there is a lack of evidence and studies on screening instruments, it is not yet possible to verify that an instrument can be used in any healthcare environment when determining illicit drug use and abuse in differing patient populations.^{9,10}

Screening instruments, specifically questionnaires and surveys, provide further information concerning the patient's health condition, depending on what condition the screening instrument focuses on. Instruments can help clinicians and other healthcare providers assess whether a patient has a disorder or condition and elucidate the next steps in the healthcare process, including interventions or further assessments. Instruments do not provide all the

information possible for one condition; however, instruments can assist healthcare providers to learn more about the patient's condition and provide necessary evidence in relation to the patient's health.

Screening instruments include questions that are carefully chosen to help the healthcare providers and patients determine if the patient has the condition or disorder of interest. Screening predictably results in one of two possible answers: either the patient has the condition/disorder or they do not. Most screening instruments do not require training and can be administered by the healthcare provider (verbally) or completed by the patient (on-paper/electronically). Due to the usability and efficiency of screening instruments, numerous medical specialties employ the use of screening instruments to determine various conditions and disorders patients may experience.⁴³

The objective of this systematic review is to analyze existing literature and provide comprehensive evidence concerning the use of opioid use disorder and abuse screening instruments in EM settings. We hypothesize that shorter, highly-reliable and validated screening instruments will provide accurate data regarding opioid use disorders and abuse, and serve as the best options for screening instruments to use in EM settings. Due to contamination, mislabeling and lost sampling of toxicology screening tests, we will not analyze invasive screening tests such as blood, urine and saliva sampling.¹⁰ We aim to provide reliability and validity evidence for screening instruments that can detect opioid use disorders, addiction, abuse and misuse in fast-paced EM settings to contribute to the existing literature in this field. We hope to provide EM physicians and clinicians with information concerning which screening instruments they can utilize to screen their patients for possible opioid use disorders and provide immediate interventions and educational programs for these patients.

METHODS

Research Study Design

We conducted a comprehensive systematic literature review to locate screening instruments used in EM settings for opioid use disorders, opioid addiction, opioid misuse and opioid abuse. This is a qualitative, systematic literature review. Systematic reviews employ impartial methods to summarize the quality of existing literature. Systematic reviews aim to answer a specific research question by identifying articles relevant to the research topic and comment on the quality of the study outcomes and combined quantitative and qualitative data presented within the literature.⁴⁴ For this research, we present the article data as a qualitative research synthesis. Qualitative analyses are used for variety of reasons. Meta-analysis of data may be difficult to achieve due to quantitative heterogeneity between the articles. Approaches to research may have changed throughout time and to review all articles within the scope of the research topic, qualitative analyses may provide more accurate comparisons than quantitative syntheses. Additionally, qualitative analyses are typically used when reviewing measurement approaches, such as the assessment of screening instruments.⁴⁵ In reference to the PRISMA guidelines, there is no review protocol or registration number associated with this study.¹⁹

The focus of this review is to analyze the usefulness of screening instruments to determine opioid dependency in EM patients. Our three main focal points are the use of screening instruments, EM environments, and differing degrees of opioid drug dependency. We carefully constructed the search terms used in our search strategy to capture these three objectives successfully within the literature.

Search for Comprehensive Lists of Drug Abuse Screening Instruments

We reviewed one governmental database, the USPSTF report and the National Institute on Drug Abuse Chart of Evidence-Based Screening Tools for Adults and Adolescents to search for comprehensive lists of drug abuse screening instruments to use within our literature review search strategy. We first searched for drug abuse screening instruments already in use within different medical fields to further our understanding of which screening instruments are available in circulation and what type of instruments exist within this field.

The Alcohol and Drug Abuse Institute (ADAI) Library at the University of Washington contains research and literature that focus on alcohol and other drug use from the following medical disciplines: medicine, nursing, social work, criminal justice, sociology and psychology. We used the following search terms in the "ADAI Library Catalog Multi-Search" field to locate a list of drug screening instruments: "opioid & instrument" and "opioid & screening."⁴⁶ The ADAI Library governmental database located the following drug screening instruments: the ALERRT®, the Clinical Opiate Withdrawal Scale (COWS), the Clinical Institute Narcotic Assessment (CINA), the Pain Medication Questionnaire (PMQ), the Brief Treatment Outcome Measure (BTOM), the Addiction Brief Risk Scale Assessment (BRSA-A), the Screener and Opioid Assessment for Patients with Pain (SOAPP-R), the Prescription Opioid Misuse Index (POMI), and the Screening, Brief Intervention, and Referral to Treatment (SBIRT).⁴⁶

We referenced the USPSTF supplemental evidence update report to locate the following drug screening tools used in primary care settings: ASSIST; CAGE-AID; CRAFFT; DAST; the Drug Use Disorders Identification Test (DUDIT); the Relax, Alone, Forget, Friends, Trouble (RAFFT); the Reduce, Annoyed, Guilty, Start (RAGS); the Rapid Drug Problems Screen (RDPS) and the Simple Screening Instrument for Substance Abuse (SSI-SA).¹⁰

The National Institute on Drug Abuse Chart of Evidence-Based Screening Tools for Adults and Adolescents was used to locate the following drug screening instruments: the National Institute on Drug Abuse (NIDA) Drug Use Screening Tool; CRAFFT; the Alcohol Use Disorders Identification Test-C (AUDIT-C); the Opioid Risk Tool; AUDIT, CAGE-AID; the Cut down, Annoyed, Guilty, Eye-opener (CAGE); DAST-10; DAST-20; the Clinical Opiate Withdrawal Scale; the McCaffrey Initial Pain Assessment Tool; the Pain Assessment and Documentation Tool and the Patient Health Questionnaire-9.⁴⁷

Main Database Search

In June 2017, we systematically searched for literature in the PubMed/MEDLINE, PsycINFO, Cochrane Database of Systematic Reviews, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Centre for Reviews and Dissemination (CRD) and ClinicalTrials.gov databases. We accessed the Cochrane Library, Web of Science, Cochrane Central Register and ClincialTrials.gov databases via a simple Google search. We accessed the PsycINFO database via the ProQuest online search engine. We accessed the CRD database via the University of York online search engine. We accessed the PubMed/MEDLINE and CINAHL databases via the University of California, Irvine library online search engine.

PubMed/MEDLINE contains over 27 million citations for biomedical literature from MEDLINE, life science journals and online books.⁴⁸ PsycINFO is the largest peer-reviewed literature database in the behavioral science and mental health disciplines; the database was created by the American Psychological Association.⁴⁹ The Cochrane Database of Systematic Reviews provides systematic reviews across the healthcare spectrum.⁵⁰ Web of Science contains citation search for 256 disciplines including science, social science, arts and humanities.⁵¹ The

CENTRAL contains reports of randomized and quasi-randomized controlled trials; the records are taken from MEDLINE and Embase and contain published and unpublished records.⁵² CINAHL contains nursing and allied health literature including nursing, biomedicine, health sciences librarianship, alternative/complementary medicine, consumer health and 17 additional health-related disciplines. CINAHL contains healthcare books, nursing dissertations, selected conference proceedings, standards of practice, audiovisuals, book chapters, full-text journals, legal cases, clinical innovations, critical paths, research instruments and clinical trials.⁵³ The Centre for Reviews and Dissemination (CRD) contains policy-related research and methods to improve population health.⁵⁴ ClinicalTrials.gov is a registry of public and private clinical studies and trials conducted worldwide.⁵⁵ All eight databases are available to the public and/or researchers for academic use within the university library system, and contain relevant literature within the scope of this review.

Main Search Strategy

After locating the drug abuse screening instruments from the comprehensive screening instrument search, we extracted articles from the eight chosen databases regarding the use of opioid-drug screening instruments in EM settings. We did not contact authors of the extracted studies to obtain additional studies or extra data due to time constraints. Additionally, we did not use funding for this study to purchase access to additional databases for review. There were no restrictions placed on article publication dates; we included all articles available in the databases up to June 2017.

Search Strategy Steps

Eight steps were involved in the literature search. We followed all eight steps, in chronological order, in all eight databases with minor revisions of the search terms for databases

that would not accept titles and/or dashes, commas and brackets. The "OR" operator allowed us to search for articles that contain variations of the topic we wished to focus upon for the single step. The "AND" operator allowed us to combine the steps together to account for all topics we chose to include in our final step and obtain articles that cover multiple topics.¹⁸ We did not change the search terms between databases. To appropriately capture opioid screening instruments used in EM settings, we received assistance from a research librarian for the Health Sciences at UC Irvine. The librarian provided an exhaustive list of terms and synonyms to construct the search terms for each step in the strategy. The principal investigator (PI), a board-certified EM and trauma physician, finalized the search terms used for each step. Although we could not include all terms and synonyms for each step, we agreed upon the chosen search terms for each step to ensure that we captured as many relevant articles for the review as possible and maintain the rigor of the research. We used the following search term syntax in each of the eight databases, step-by-step:

Step #1: Emergency Medicine OR EM[ti] OR Emergency Department OR ED[ti] OR Emergency Room OR ER[ti] OR Emergency Service OR Emergency Services OR ES[ti] OR Emergency Medical Service OR Emergency Medical Services OR EMS[ti] OR Accident and Emergency OR Accident and Emergency Department OR Trauma Center OR Emergency Care OR Emergency Unit OR Emergency Units OR Emergency Ward OR Emergency Wards OR Hospital Emergency Service OR Hospital Emergency Services OR Emergency service, Hospital

<u>Step #2</u>: Screening OR screen OR screener OR screeners OR assessment OR assessments OR Assess OR evaluate OR evaluation

<u>Step #3</u>: Opioid-related disorders OR opioid dependence OR opioid dependency OR opioid dependent OR opioid misuse

<u>Step #4</u>: (Prescription OR prescriptions OR OTC OR over the counter OR OTC OR analgesics opioid OR illicit drug OR illicit drugs OR illegal drug OR illegal drugs OR street drug OR street drugs OR recreational drug OR recreational drugs) AND (Misuse OR Abuse OR Misused OR Dependence OR Addiction OR addict drug abuse OR abuse drugs)

<u>Step #5</u>: Step #3 OR Step #4

Step #6: NIDA OR CRAFFT OR Opioid Risk Tool OR ORT OR CAGE OR CAGE-AID OR drug abuse screen test OR DAST-20 OR Clinical Opiate Withdrawal Scale OR McCaffrey Initial Pain Assessment Tool OR Pain assessment and documentation tool OR NIDAMED OR DAST-10 OR current opioid misuse measure OR COMM OR mass screening OR screen[ti] OR screening[ti] OR surveys and questionnaires OR risk assessment OR rapid opioid dependence screen OR RODS OR opioid risk tool OR ALERRT OR ASSIST OR DAST OR DUDIT OR RAFFT OR RAGS OR RDPS OR SSI-SA OR COWS OR CINA OR Clinical Opiate Withdrawal Scale OR Clinical Institute Narcotic Assessment OR Pain Medication Questionnaire or PMQ OR Brief Treatment Outcome Measure OR BTOM OR BRSA-A OR Screener and Opioid Assessment for Patients with Pain OR SOAPP-R OR Prescription Opioid Misuse Index OR POMI OR Screening, brief intervention, and referral to treatment OR SBIRT

<u>Step #7</u>: Reliability OR reliable OR Validity OR validation OR valid OR validated OR Feasibility OR feasible OR Sensitivity OR Specificity OR sensitivity and specificity OR Effect on morbidity OR effect on mortality OR predictive value OR negative predictive value OR positive predictive value OR positive and negative predictive value OR clinical utility

Step #8: Step #1 AND Step #2 AND Step #5 AND Step #6 AND Step #7

The eighth and final step produced a list of articles that captured the following topics within the article titles, abstracts and/or keywords: EM settings, screening, opioid use, drug

abuse screening tools, and reliability and validity data. We followed each step, in each of the eight databases, to finalize our preliminary list of articles for the review. After combining the lists of articles from each database, we obtained a preliminary list of 239 articles. The breakdown of the number of articles per database is illustrated in Figure 1.

Inclusion/Exclusion Criteria

After retrieving our preliminary list of articles, we deleted all repeating articles and articles without results (primarily from ClinicalTrials.gov). We deleted a total of 67 articles and obtained 172 articles for screening. To obtain the finalized list of articles for full-text, extensive review and qualitative data analysis, we established inclusion/exclusion criteria to screen all article titles, abstracts and keywords. The inclusion/exclusion criteria were determined by the research team and finalized by the PI. The inclusion/exclusion criteria determine which articles to include for the full-text review from initial screening. The inclusion/exclusion criteria must be relevant to the research question and contain a breadth of information to ensure that as many articles as possible are captured for the full-text review.¹⁸

The article titles, abstracts and keywords were screened by the research student who is conducting the systematic review for her Master's thesis. The studies were cross-checked by the UC Irvine research librarian, who has extensive knowledge concerning research in the Health Sciences and how to conduct systematic reviews. Additionally, a former medical student began the review in 2016 and assisted with finalizing the search strategy and search terms.

Our inclusion criteria contain the following requirements: must be history and/or questionnaire-based screening tools; must take less than 10 minutes to perform and score⁵⁶; no formal training required to use or interpret the screening tool (as determined by a previous systematic review conducted on illicit drug screening instruments used in general hospital ward

settings)⁵⁶; include screening tools for opioid drugs, misuse of opioid prescription drugs, and misuse of opioid drugs; only English-language articles (there is no funding for translational services); all age groups; all study types including peer-reviewed articles and all study designs; all locations (within and out of the U.S.); no restriction on publication dates (all articles up to June 2017); only in EM settings; and studies that assess at least reliability and/or validity of the instrument and may include sensitivity, specificity, feasibility, and effects on morbidity and mortality data.

The exclusion criteria contain the following requirements: invasive screening (urine, plasma, saliva testing), non-English instruments; non-English studies; and studies on alcohol screening only. After screening the preliminary article list using the inclusion/exclusion criteria, we deleted 106 articles and obtained 66 articles for full-text assessment. Next, we assessed the full-text of the 66 remaining articles using the inclusion/exclusion criteria. We deleted 56 articles for full-text of the 66 remaining articles using the inclusion/exclusion criteria. We deleted 56 articles for full-text of the inclusion/exclusion criteria for the review.

Figure 1 illustrates the number of articles excluded after initial screening of the 172 article titles, abstracts and keywords, and after full-text assessment of the 66 remaining articles. Additionally, the figure includes information on how many articles were excluded by each exclusion criterion. There were a few articles screened that were borderline or did not completely match the inclusion criteria of the review. We excluded these studies because they contained reliability and/or validity data established in medical settings outside of EM and/or were determined in a previous study that was cited by the article. We obtained a final list of 10 articles for qualitative data analysis.

Figure 2 illustrates the search strategy steps for the PubMed/MEDLINE database. All eight databases follow the step-by-step search strategy outlined in Figure 2.

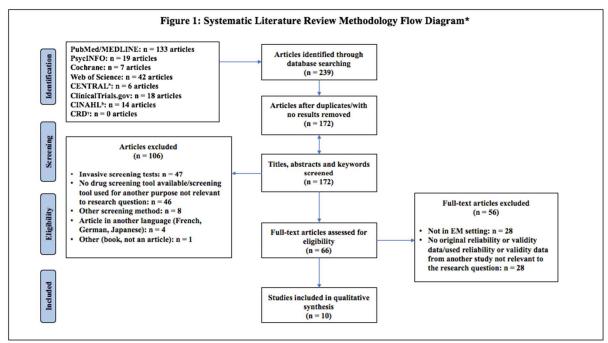
Data Extraction and Analysis

Our primary outcome variables (principal summary measures) of interest were any reliability and validity data presented in the 10 articles chosen for data analysis and final review. This included test-retest reliability, inter-rater reliability (kappa), internal consistency reliability testing (Cronbach's alpha) and other statistics and tests that commented on the reliability and validity of the screening instruments.

We extracted the following secondary outcome variables if the data was available in the literature: study design; study population; sample size; study aims/objectives; study setting (location); patient demographics (i.e., age, race/ethnicity, gender); year of study; information concerning the screening instrument (i.e., number of items/questions, time to complete the questionnaire, self-administered/clinician-administered); the reference standard in relation to the screening instrument; secondary descriptive statistics (specificity, sensitivity, predictive value, effect on morbidity/mortality, accuracy rate and clinical utility/feasibility data); quality of the study; and study conclusions. We separated each variable into a table for clarity. We also separated the variables and data points by article within the tables, and compared all available screening instrument data qualitatively between the 10 studies. All statistics were analyzed descriptively and presented qualitatively due to the complexities of the data points and statistics involved. We chose these primary and secondary outcome variables by referencing the USPSTF review, a systematic review which commented on illicit drug screening instruments used in general hospital ward settings, and a systematic review which commented on illicit drug screening instruments used in general adult psychiatric populations.^{10,56,57} We aimed to present a thorough analysis of the 10 finalized articles for review and provide relevant information to reach meaningful conclusions and answer our research questions and hypothesis.

This systematic review contains lawfully obtained data, accurate reporting of information to the best of the research team's knowledge and meets all ethical considerations and guidelines. *Prevalence of Bias*

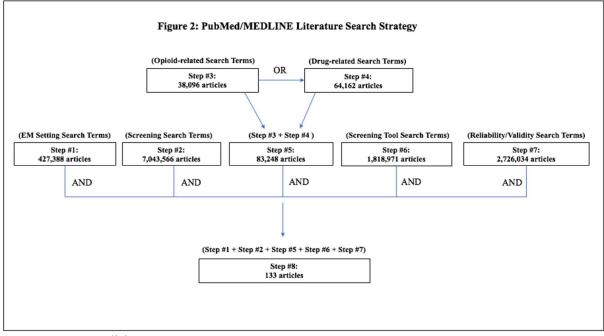
Due to the research design of a systematic review, biases are present. Systematic reviews can only comment on and analyze data presented in the chosen articles. The articles may include a subset of data or emphasize certain outcomes to increase chances of publication in a journal. This is publication bias. Publication bias can result in over- or under-estimations of the results presented in the review.⁵⁸ For our review, the articles contain the following limitations: missing or unavailable data due to selective reporting and the use of reliability and validity data from previous studies without confirming use of the screening instrument in EM settings (which we excluded from the final article list to the best of our abilities). We will assess bias at the study level and report biases from the chosen articles in our Discussion. Another bias that exists within our systematic review is the use of a previous study protocol, specifically the USPSTF protocol, which commented on the use of screening instruments in primary care settings, not EM settings. We incorporated elements of the USPSTF review to design our systematic review.¹⁰ Because we could not locate a systematic review of opioid use screening instruments used in EM settings, we used review protocols of other systematic reviews performed in different medical settings to conduct our research.^{10,56,57} Overall, this risk of bias exists and may affect the cumulative qualitative evidence presented in our review, and we cannot prevent this bias from occurring.



*Adapted from the PRISMA 2009 Flow Diagram¹⁹; ^aCENTRAL: Cochrane Central Register of Controlled Trials;

^bCINAHL: Cumulative Index to Nursing and Allied Health Literature; ^γCRD: Centre for Reviews and

Dissemination; EM: Emergency Medicine



EM: Emergency Medicine

RESULTS

Screening Instrument Characteristics

Table 1 contains information of all 10 studies reviewed for data analysis. The studies will be referred to by their "Study Number" to maintain consistency throughout the analysis. The study number, title, author and year of publication are included in this table. The following eight screening instruments were identified for data analysis: SOAPP-R; ASSIST; two, single-item screening questions; one-item binge-drinking screener question; patient medical charts; medical history and physical/patient self-reporting in medical charts; the Drug Abuse Screening Test; and HERA/SBIRT. All screening tools were used in EM settings and administered to adult and/or adolescent patients.

Table 1: List of Articles Chosen for Qualitative Review: Study Title, Author and Year of
Publication

Study Number	Study Title	Author	Year of Publication
1	An investigation of completion times on the Screener and Opioid Assessment for Patients with Pain - revised (SOAPP-R). ⁵⁹	Finkelman MD	2016 December
2	Validation of the Alcohol, Smoking and Substance Involvement Screening Test in a low- and middle- income country cross-sectional emergency centre study. ⁶⁰ C		2016 November
3	Risk for opioid misuse among emergency department cancer patients. ⁶¹ Reyes-Gibby CC		2016 February
4	A comparison of an opioid abuse screening tool and prescription drug monitoring data in the emergency department. ⁶² Weiner SG		2016 February
5	Pilot validation of a brief screen tool for substance use detection in emergency care. ⁶³	Broderick K B	
6	Alcohol abuse and illegal drug use among Los Angeles County trauma patients: prevalence and evaluation of single item screener. ⁶⁴	Ramchand R	2009 May
7	Accuracy of information on substance use recorded in medical charts of patients with intentional drug overdose. ⁶⁵	orded in medical charts of patients with Tournier M	
8	Medical clearance and screening of psychiatric patients in the emergency department. ⁶⁶	Olshaker JS	1997 February

9	Identifying patients with problematic drug use in the emergency department: results of a multisite study. ⁶⁷	Macias Konstantopoulos WL	2014 November
10	A randomized clinical trial of the health evaluation and referral assistant (HERA): research methods. ⁶⁸	Boudreaux ED	2013 July

Table 2 illustrates that the longest screening instrument, for which data is available, is the SOAPP-R. The SOAPP-R instrument contains 24 questions. However, Study 1 reports that patients completed the SOAPP-R assessment within one to eight minutes, as shown in Table 3.⁵⁹ The other studies do not report the time frame for completion of the instruments; however, information presented in the articles implicitly report that all assessments take at most 10-12 minutes to complete. (They are all brief screening instruments.) Only the SOAPP-R and HERA/SBIRT instruments are self-administered, as reported in the studies.^{59,62,68} The remaining six instruments were conducted, to some degree, by the clinicians involved in the studies.

Only the SOAPP-R instrument reports that it is composed of subtle questions. Direct questions ask directly about substance use whereas indirect and subtle questions implicitly ask about substance use patterns and/or focus on behaviors associated with substance use.⁵⁹

All reported instruments screen for opioid drug use in addition to other illicit drug use. The ASSIST, the single-item binge-drinking screener question, the medical history and physical/patient self-reporting in medical charts, and HERA/SBIRT also screen for alcohol use.^{60,64,66,68} The drug types that each instrument screens for are included in Table 2.

Study Number	Screening Instrument	Number of Items/Questions	Direct, Indirect or Subtle Questions	Screen for Opioids, Drugs or Other Substances
1	Screener and Opioid Assessment for Patients with Pain - Revised (SOAPP-R)	24-item	Subtle	Aberrant drug- related behavior (include opioids)
2	Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)	8-item	N/A	Alcohol or other drugs (include

Tab	le 2:	Part	1 - 5	Screening	Instrument	Characteristics
-----	-------	------	-------	-----------	------------	-----------------

				opioids)
3	Screener and Opioid Assessment for Patients with Pain - Revised (SOAPP-R)	24-item	N/A	Opioid misuse
4	Screener and Opioid Assessment for Patients with Pain - Revised (SOAPP-R)	24-item	N/A	Opioid and other illicit/abuse drugs
5	Two, single-item screening questions	2, 1-item	N/A	Illicit drugs (include opioids) and marijuana
6	Single-item binge-drinking screener question	1-item	N/A	Alcohol abuse and illegal drug use (opium, other drugs and prescription drugs)
7	Medical Charts	N/A	N/A	Psychotropic drugs; intentional drug overdose (include opiates)
8	Medical History and Physical/Patient Self-Reporting in Medical Charts	N/A	N/A	Drug (include opioids) and ethanol use
9	Drug Abuse Screening Test	N/A	N/A	Problematic drug use (include opioids)
10	Health Evaluation and Referral Assistant (HERA)/Screening, Brief Intervention, and Referral to Treatment (SBIRT)	N/A	N/A	Tobacco, alcohol, and illicit drugs (include opioids)

N/A: Data Not Available

All eight screening instruments screen for recent drug use; however, the time frames for recent use differ substantially. THE SOAPP-R screens for drug use within seven days prior to screening, whereas the single-item binge-drinking screener question and HERA/SBIRT instruments can screen for drug use within 12 months prior to the administration of the instrument.^{59,62,64,68} The ASSIST and SOAPP-R instruments can also detect lifetime drug use.^{60,61,62}

Each study in this review uses a different reference standard for comparison. A reference standard serves as the "gold standard" for instrument-based studies. A reference standard is a "highly characterized, standardized and validated reference material"⁶⁹ and assists with

sensitivity and specificity calculations of the study instruments in validation analyses. A reference standard is considered the most accurate test possible for what the standard aims to test and expected to have specificity/sensitivity of 100%.⁷⁰ Studies 3, 6 and 9 do not report on the use of reference standards. Reference standards can include previously validated instruments, such as the Mini International Neuropsychiatric Interview version 6.0 (MINI), ASSIST, AUDIT and DAST-10, as shown in Table 3.^{60,63,68} Although we excluded studies that focused on toxicological screening tests from our initial literature search, we included two studies that use toxicological tests as reference standards.^{65,66} We did not analyze the data presented for the toxicological tests in these studies; we did analyze the data presented for the screening instruments in relation to their respective reference standards.

Study Number	Screening Instrument	Time Required	Recent and/or Lifetime Use?	Reference Standard	Self- administered or Clinician- Administered
1	SOAPP-R	57-463 seconds (1-8 minutes)	Recent (prior 7-days)	PDMP data showing both ≥4 opioid prescriptions and ≥4 providers (prior 12- months)	Self- administered
2	ASSIST	N/A	Recent (prior 3- months) & Lifetime	Mini International Neuropsychiatric Interview version 6.0 (MINI)	Clinician- administered
3	SOAPP-R	N/A	Recent & Lifetime	N/A	N/A
4	SOAPP-R	N/A	Recent (prior 7-days) & Lifetime	PDMP data showing both ≥4 opioid prescriptions and ≥4 providers (prior 12- months)	Self- administered
5	Two, single-item screening questions	N/A	Recent (prior 3- months)	ASSIST	Clinician- administered
6	Single-item binge-drinking screener question	N/A	Recent (prior 12- months)	N/A	Clinician- administered

Table 3: Part 2 – Screening Instrument Characteristics

7	Medical Charts	N/A	Recent	Toxicological assays	Clinician- administered
8	Medical History and Physical/Patient Self-Reporting in Medical Charts	N/A	Recent	Positive toxicology screen	Clinician- administered
9	Drug Abuse Screening Test	N/A	Recent (prior 30- days)	N/A	Clinician- administered
10	HERA/SBIRT	N/A	Recent (prior 12- months)	AUDIT & DAST-10	Self- administered

PDMP: prescription drug monitoring program; N/A: Data Not Available

Study Characteristics

Table 4 contains the aims/objectives, conclusions and study quality of the 10 studies. We assessed the quality of the 10 articles using the evaluation method outlined by the established USPSTF grading scales. Good quality articles "used a credible reference standard, interpreted the reference standard independently of the questionnaire, and included more than 100 patients with and without a drug use problem."¹⁰ Fair quality articles "used a reasonable, although not the best possible, reference standard, interpreted the reference standard independently of the questionnaire, and included a sample size of 50-100"¹⁰ patients. Poor quality studies were classified if an "inappropriate reference standard was used, there was a potentially biased ascertainment of the reference standard, or the study included a small (<50) sample size."¹⁰ The studies that assessed ASSIST, the two, single-item screening questions, the medical history and physical/patient self-reporting in medical charts, and HERA/SBIRT were rated as "Good" due to the strength of their reference standards and sample sizes.^{60,63,66,68}

We included the study aims/objectives and conclusions to compare and contrast the types of studies analyzed for this review. Study 1 aims to determine whether SOAPP-R completion times predict aberrant drug-behavior and found no statistically significant evidence to affirm this correlation.⁵⁹ Study 2 validates the ASSIST for use in low socioeconomic areas in South

Africa.⁶⁰ The goal of Study 3 was to determine opioid misuse in cancer patients and what caused high-risk opioid misuse in this patient population. The study concludes that opioid misuse risk exists in this patient population and screening for opioid misuse in EM settings is feasible.⁶¹ Study 4 reviews the number of patients who received prescription opioids for pain and whether these patients were at risk for abuse. This study compares SOAPP-R data with PDMP data to determine opioid abuse risk. The study concluded that SOAPP-R is feasible to use in the ED.⁶² Although Studies 1 and 4 use the same patient data, we included both studies in our review to highlight the differences in study design and aims/objectives between these two studies.^{59,62}

The aims of Study 5 include the validation of two, single-item screening questions used to screen for illicit drug use and to ascertain whether time-efficient screening questions can be used in fast-paced medical specialties. Study 5 found that the two, single-item screening questions do not meet sensitivity criteria for use in clinical environments.⁶³

Study 6 comments on alcohol and substance use, and the usefulness of a single-item binge-drinking screener question to determine substance abuse problems in patients who have consumed drugs within the past year. The study concludes that further assessments of one-item screening questions can determine whether these tools provide useful information in fast-paced environments.⁶⁴ Study 7 reviews the accuracy of recorded substance use information in medical charts. This study found that only half of substance use patients had this information recorded in their medical charts.⁶⁵ The goal of Study 8 was to review the amount of medical complaints and toxicological screening clearance in psychiatric patients. This study found that screening all patients is not cost or time-efficient and impedes on clinical care for this patient population.⁶⁶

The aims of Study 9 focus on the identification of ED patients who need substance use treatment interventions. Study 9 found that clinical correlations with substance abuse can help

with identifying patients who would benefit from screening, intervention and treatment. The involvement of the ED setting in determining substance use treatment for patients can ultimately lower healthcare spending.⁶⁷ Study 10 reviewed the HERA's usefulness in decreasing substance use and starting treatment in patients suffering from drug dependency. The program provided counseling and treatment resources to at-risk patients and can serve as an asset in healthcare settings to target larger patient populations, and increase the efficiency of the healthcare environment.⁶⁸ All 10 studies focus on different aims/objectives; however, all studies assess the importance of screening instruments in EM settings to determine possible opioid and other drug abuse.

Study Number	Aims/Objectives	Conclusions	Quality of the Studies*
1	Determine if SOAPP-R completion time predicts ADB	No evidence that SOAPP-R completion times can predict ADB; greater SOAPP-R completion times tended to exhibit more ADB: this association was not statistically significant	Fair
2	Validate ASSIST for South African communities	ASSIST was found to be useful for South African healthcare and may lead to cost- effective task-shifting approaches in lower- resourced environments	Good
3	Assess the risk for misuse and factors that may be associated with high-risk for opioid misuse in cancer patients	The risk of opioid misuse among cancer patients is substantial and screening for opioid misuse in the ED is feasible	Poor
4	Determine percentage of ED patients receiving prescriptions for opioid pain medications that meet the criteria for "high-risk for abuse potential"; determine the percentage of patients with high- risk behavior using PDMP data; compare SOAPP-R with PDMP data and determine psychometric properties of SOAPP-R	About one-third of patients being considered for discharge with an opioid prescription scored "at-risk" on SOAPP-R and 15.9% met the PDMP high-risk criteria; high negative predictive value of SOAPP-R indicates that it may be a useful screening tool for the ED	Fair
5	Assess pilot validation of two, single-item screening questions to detect illicit substance use; identify	This tool does not exhibit sufficient sensitivity to be used as a screening tool in clinical settings; it is important to use	Good

Table 4: Part 1 – Study Characteristics

	sensitive, time-efficient screening questions that can be easily integrated into busy healthcare settings	validated questions to identify substance misuse so that individuals are not missed in the screening process	
6	Determine alcohol abuse and illegal substance use patterns; identify correlates of alcohol abuse and assess the utility of a single- item binge-drinking screener to identify patients with substance use problems	In the busy trauma care setting, a one-item screener could be helpful in identifying patients who would benefit from more thorough assessment and possible brief intervention	Poor
7	Assess accuracy of information concerning substance use recorded in medical charts in subjects admitted for IDO	Compared with toxicological assays, medical records identified only half of the subjects with current substance use; usefulness of systematic toxicological assays during hospitalization for IDO should be assessed	Fair
8	To study the frequency of medical complaints and need for routine ED medical, laboratory and toxicological clearance for patients presenting with psychiatric complaints	Toxicological screening is costly and of extremely low-yield; screening all patients is an unnecessary investment of time, money, and manpower; counterproductive delays in psychiatric care of patients	Fair
9	Identify clinical factors of problematic drug use to determine ED patients in need of substance use treatment	Clinical correlates of drug use problems may assist in the identification of ED patients who would benefit from comprehensive screening, intervention, and referral to treatment; correlation between problematic drug use and resource-intense ED triage levels suggests that ED-based efforts to reduce the unmet need for substance use treatment may help decrease overall healthcare costs	Poor
10	Evaluate HERA's efficacy in leading increased treatment initiation and reduced substance use	HERA is an innovative program designed to assist in the identification, counseling, and connection of risky substance using individuals to appropriate treatment resources; HERA has the potential, if implemented as part of routine care, to reach patients in a manner that reduces provider burden	Good

*Determined by previously published United States Preventive Services Task Force (USPSTF) grading scales.¹⁰ ADB: Aberrant drug-related behavior; ED: Emergency Department; PDMP: prescription drug monitoring program; IDO: illicit drug overdose

Additional study characteristics are presented in Table 5. The majority of the studies are

prospective, cross-sectional studies. Also, most of the studies survey patients within a two- to

three-month time period, with the exception of studies that assess other outcomes aside from the psychometrics of the screening instruments.

All 10 studies were conducted within trauma and/or EM settings, with few exceptions. Study 5 includes patients from the Adult Urgent Care Clinic and the ED.⁶³ Eight studies were conducted within the U.S. Study 2 was conducted in South Africa and Study 7 was conducted in France.^{60,65} The study populations composed of adult and/or adolescent ED patients, the majority of whom were adults with pain symptomatology. There is a wide range of sample sizes reported between the 10 studies. The sample sizes range from as low as 82 patients (Studies 1 and 4) to 2,084 patients (Study 9).^{59,62,67}

Study Number	Design	Population	Setting (Location)/Country	Sample Size	Time Frame
1	Retrospective	ED patients with diagnosis of a painful condition & considered for opioid treatment	Level 1 trauma center in an inner-city teaching hospital/USA	n = 82	May - August 2013
2	Cross- sectional	EC patients with treatment of an assault injury or an unintentional injury (falls, burns, etc.)	24-hour ECs in two urban, low socioeconomic areas/South Africa	n = 200	January - March 2013
3	Cross- sectional, single-center	Cancer ED patients	Comprehensive cancer center ED/USA	n = 209	February 2012 - March 2014
4	Cross- sectional, prospective, convenience sample	ED patients considered for discharge with a prescription for an opioid pain medication	Urban, academic Level 1 trauma center ED/USA	n = 82	May - August 2013
5	Prospective convenience sample	Adult ED/AUCC patients	Urban safety-net hospital ED and AUCC/USA	n = 1,692	August - October 2010
6	Prospective, survey-based	All adult, admitted patients with injuries	Four large trauma centers/USA	n = 677	February 2004 - August 2006
7	Prospective	ED patients consecutively admitted	Hospital setting ED/France	n = 302	July 2001 - December

Table 5: Part 2 – Study Characteristics

		for IDO			2002
8	Retrospective, observational analysis	All ED patients with psychiatric complaints/brought in for psychiatric evaluation	High-acuity urban university teaching hospital-adult ED/USA	n = 345	2-month period
9	Multicenter randomized prospective trial	Adult ED patients presented for medical treatment	Six academic hospital EDs/USA	n = 2,084	October 2010 - February 2012
10	Randomized controlled trial	Adult ED patients	Four EDs/USA	n = 1,006	N/A

ED: Emergency Department; EC: Emergency Center; AUCC: Adult Urgent Care Clinic; IDO: illicit drug overdose; USA: United States of America; N/A: Data Not Available

Patient Demographics

Table 6 contains demographic information of the subjects sampled in all 10 studies. The variables we included in this analysis were gender, age and race/ethnicity, which are typically reported by most studies. Across the 10 studies, the majority of patients identified as male and White, with exceptions from study to study due to differences in study location and patient population composition. The majority of subjects were about 35 years old; the average age ranges expand from 25 to 55 years across all 10 studies.

Study Number Gender Age* **Race/Ethnicity*** 52% Male 28% 46-55 years old 62% White 1 2 43% 25-40 years old 67% Male 53 % Black 3 78.9% White 50.7% Male Mean: 54.2 years 4 52.4% Male 28% 46-55 years old N/A 5 57% Male Mean: 43 years 41% White 48.7% Latino 6 77.5% Male 36.3% 25-37 years old 7 30.5% Male** Mean: 35 years N/A 8 64% Male Mean: 35 years 77% Black 9 65.0% Male 66.9% older than 30 years N/A 10 50% Male 71% White Mean: 36.8 years

Table 6: Patient Demographics

*Age and racial/ethnic groups with the greatest representation in the study population

**Subjects with complete data (no missing information)

***Percentages represented in gender-exclusive group (compared to all males only; females not included in calculation)

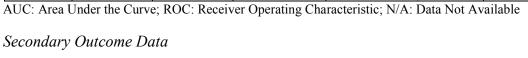
Validity and Reliability: Primary Outcome Data

None of the 10 studies provide inter-rater reliability and test-retest analyses. Only three studies report on the internal consistency of their screening instruments. Studies 1 and 4 have the same statistical values, because both studies use the same patient population data.^{59,62} Studies 3, 7 and 9 do not report on any validity testing; Studies 5, 8, 9 and 10 do not report on any reliability testing. The majority of the studies provide qualitative analyses of their instruments' validity. Studies 1, 3 and 4 provide quantitative data for the SOAPP-R. Study 2 provides quantitative data for the ASSIST. Study 3 states: "the reliability test was conducted. Studies 1 and 4 report on the item-total correlations of individual questions in the SOAPP-R. Additional qualitative statements, regarding the validity and reliability of the screening instruments assessed in this review, are included in Table 7.

Study Number	Test- Retest Reliability	Inter- Rater Reliability	Internal Consistency (Cronbach's Alpha)	Validity Measures	Other Reliability Measures
1	N/A	N/A	.91	Unadjusted ROC analysis: AUC of 0.64; adjusted analysis: AUC of 0.81	Item-total correlations: from 0.21 (question 21) to 0.71 (question 10)
2	N/A	N/A	0.81 - 0.95	"Good discriminative validity": AUC of 0.95	N/A
3	N/A	N/A	N/A	N/A	Reliability statistic: 0.786
4	N/A	N/A	.91	Unadjusted ROC analysis: AUC of 0.64; adjusted analysis: AUC of 0.81	Item-total correlations: from 0.21 (question 21) to 0.71 (question 10)
5	N/A	N/A	N/A	Face-value validity	N/A
6	N/A	N/A	N/A	"Self-report of peritrauma alcohol and other drug use is valid in this context; the screen also performed moderately well in discriminating between	"Self-report of peritrauma alcohol and other drug use: may be even more reliable than toxicology screens"

Table 7: Validity and Reliability Data

				those who had or had	
7	N/A	N/A	N/A	not used illegal drugs" N/A	"Overall, self-reporting is reliable at the moment of inclusion in the treatment program and its reliability decreases over time, as substance use may induce negative consequences for the patients."
8	N/A	N/A	N/A	"The data overwhelmingly backed the validity of self- reported illicit drug and ethanol consumption."	N/A
9	N/A	N/A	N/A	N/A	N/A
10	N/A	N/A	N/A	"Protocol balanced internal versus external validity"	N/A



Although the data in Table 8 is more extensive than the lack of reliability and validity data in Table 7, there are missing statistics for specificity, sensitivity and predictive value (positive and negative) for the majority of the studies. Specificity, sensitivity and predictive values validate the use of screening instruments in comparison to the reference standard and provide information concerning the usefulness and utility of screening instruments in the chosen study environment. Studies 3 and 10 provide no specificity, sensitivity or predictive value data. There are no positive and negative predictive values for Studies 1, 2, 3, 5 and 10. There is no negative predictive value data for Study 9.

Table 9 includes analyses of the effects on morbidity/mortality, clinical utility/feasibility and accuracy data. There are two statistics provided: 64% for the utility of SOAPP-R and 91% for the accuracy of the medical history and physical/patient self-reporting in medical charts.^{59,66} The remaining data in Table 9 consists of qualitative assessments.

Study Number	Specificity	Sensitivity	Positive Predictive Value	Negative Predictive Value
1	71%	54%	N/A	N/A
2	Use/abuse: 93%; Abuse/dependence: 87%	Use/abuse: 93%; Abuse/dependence: 90%	N/A	N/A
3	N/A	N/A	N/A	N/A
4	71.0% (95% CI: 58.8–81.3%)	53.9% (95% CI: 25.2–80.7%)	25.9% (95% CI: 11.2– 46.3%)	89.1% (95% CI: 77.7– 95.9%)
5	98.8% (95% CI: 98.3–99.4%)	40.3% (95% CI: 32.5–48.0%)	N/A	N/A
6	63% - 67%	47%	3 - 8%	94 - 99%
7	95.7% (95% CI: 93.3–98.1%)	4.0% (95% CI: 1.7–6.3%)	8.3% (95% CI: 5.1– 11.6%)	91.1% (95% CI: 87.8– 94.4%)
8	91%	92%	88%	94%
9	N/A	N/A	89%	N/A
10	N/A	N/A	N/A	N/A

 Table 8: Specificity, Sensitivity and Predictive Value Data

CI: Confidence Interval; N/A: Data Not Available

Table 9: Effect on Morbidity/Mortality, Clinical Utility/Feasibility and Accuracy Data

Study Number	Effect on Morbidity/Mortality	Clinical Utility/Feasibility	Accuracy Data
1	N/A	64% (95% CI: 48–80%)	N/A
2	"Screening tools are a necessary component to reduce morbidity and mortality in healthcare populations and could play a role in reducing the burden of disease and treatment gap"	N/A	N/A
3	N/A	"Screening for opioid misuse in the ED is feasible"	N/A
4	N/A	"From a clinical perspective: the negative predictive value of the SOAPP-R confirmed its use as a viable screening tool in the ED	N/A

		settingfeasible screening tool"	
5	N/A	"As a result, this tool does not exhibit sufficient sensitivity to be used as a screening tool in clinical settings"	N/A
6	N/A	"Single item screener is useful for identifying patients who might benefit from more extensive assessments; depending on the illicit drug, the binge item screen identifies between half and three quarters of patients who used drugs in the past 12-months, with the strongest sensitivity estimates for hallucinogens and ecstasy"	N/A
7	N/A	"The use of a structured interview is time-consuming and not compatible with medical activity, results obtained using such instruments would be of little interest for clinical practice"	"Only a half of the subjects positive for toxicological assays were identified as substance users in the medical chart, and two thirds of subjects recorded as substance users were positive for toxicological assays"
8	N/A	"Screening all patients is a prohibitive and unnecessary investment of time, money, and manpower; past clinical experience reinforces the accuracy of patient self-reporting"	91%
9	N/A	"Our screening and clinical decision rule provides a rapid and simple method of identifying patients on whom more comprehensive ED-based SBIRT should be focused as part of emergency care practice"	N/A
10	N/A	"A computerized SBIRT system that can be integrated successfully into the ED setting will likely be feasible in most other medical settings, such as inpatient floors and primary care clinics"	N/A

CI: Confidence Interval; ED: Emergency Department; N/A: Data Not Available

DISCUSSION

Reference Standard Credibility

For this systematic review, we finalized 10 articles for qualitative analysis. Each study used a different reference standard with the exception of Studies 3, 6, and 9; which did not include reference standards within their study design. This undermines the quality of research presented in these three studies. It is important to note that using reference standards without knowledge of the standard's limitations and biases can lead to misinformation and errors in identifying patients with and without the disorder. Reference standards are expected to have 100% accuracy in determining which patients have the disorder or not; however, this is rarely achieved for screening instruments. Therefore, extensive validation of the reference standard is vital before use.⁷⁰

The remaining seven studies do include reference standards for comparison; however, the credibility and accuracy of the reference standards are questionable. Studies 1 and 4 used PDMP data containing both \geq 4 opioid prescriptions and \geq 4 providers in a 12-month period for the study reference standard and to characterize high-risk drug use behavior.^{59,62} As stated in Study 4, the PDMP data was considered as "objective" data as it captures all prescriptions for medications prescribed in a state. The study authors claim that they used AUC analysis to determine that \geq 4 opioid prescriptions and \geq 4 providers is an appropriate fit for high-risk SOAPP-R scores. However, this was only one validation test conducted in one study population. This reference standard is limited in that there is not enough data to support the use of PDMP data as a reference standard for SOAPP-R validation.⁶² Study 1 states, within its "Limitations" section, that "the use of PDMP data to identify ADB may have been imperfect,"⁵⁹ demonstrating that this

reference standard does not have 100% accuracy.⁵⁹ The results presented in Studies 1 and 4 may be affected by this imperfect reference standard.

Study 2 uses the Mini International Neuropsychiatric Interview version 6.0 (MINI) as its reference standard. According to this study, the MINI has been validated and used in clinical environments and for research purposes in the past.⁶⁰ The MINI has good inter-rater reliability and test-retest reliability data as well as good specificity and sensitivity. The psychometric data is reported in a 1997 validation study of the MINI.⁷¹ Although it is not a perfect reference standard, the MINI does have previously established validity and reliability data and has been used as a reference standard for the ASSIST instrument in a multi-country study.^{60,71} This reference standard is stronger, due to the prevalence of existing data, than other reference standards used by the studies in this review.

Study 5 uses the ASSIST instrument as its reference standard. According to the article, the reliability and validity of the ASSIST establish this instrument as a gold standard for determining psychoactive substance use.⁶³ASSIST has been previously validated in primary healthcare settings; the validation study found good internal consistency (Cronbach's alpha: .77-.94) and good discriminative validity; however, these values are also not perfect and show a wide range of possible psychometrics for this screening instrument.⁷² To establish the ASSIST as a gold standard, additional data for the screening instrument, in different patient populations, is necessary.

Studies 7 and 8 use toxicological tests as reference standards. This is problematic, because different statistics and analyses are used for survey instruments versus toxicological tests. Due to the heterogeneity between the two screening tools, it is difficult to compare and contrast surveys and toxicological tests. Additionally, there are limitations to toxicological tests,

such as the occurrence of false positives, cross-contaminations, and mislabeling.^{10,73,74} These limitations undermine the use of toxicological tests as viable reference standards and further limit the data presented in Studies 7 and 8.

Study 10 uses two reference standards: AUDIT and DAST-10. Similar to ASSIST, the AUDIT and DAST-10 are previously validated drug abuse screening instruments. The AUDIT has been validated for alcohol use disorders and the DAST-10 has been validated in drug and alcohol abuse patients.⁷⁵ The DAST-10 has good internal consistency (Cronbach's alpha: .92) and the instrument is considered as a unidimensional scale from item inter-correlation analysis. The validation study for DAST states that further validation studies are needed in various patient populations and clinical settings, which indicate that the DAST-10 is an imperfect reference standard for drug abuse screening as well.⁷⁶ Although these seven studies incorporate reference standards into their study design, all of the reference standards contain limitations; therefore, the data presented in each study are subject to limitations and biases.

Analysis of Study Characteristics

Six of the 10 studies used the prospective and/or cross-sectional study design. The prospective, cross-sectional design is used for most survey-based studies and allows researchers to interact with patients and determine in a timely manner if substance abuse is a concern for these patients.⁴³ As discussed previously, opioids are used for pain management and certain populations, such as cancer patients or patients with serious injuries. They are susceptible to opioid misuse due to prescribed opioid use.²⁴ These patients may be first seen in EM settings; which is why it is vital to screen EM patients for drug abuse.

Studies 1 and 4 report small sample sizes (n = 82). The sample size is vital for statistical analysis and interpretation. Low sample sizes may not accurately represent the population at

large due to the prevalence of exceptions and biases that occur within smaller numbers of patients. Larger sample sizes, typically greater than 50-100 patients, are encouraged for these studies to ensure accurate results and reporting for various population groups that filter through EM settings.¹⁰ Additionally, the demographics presented in Table 6 generally correspond with data present in the medical literature for demographic opioid abuse patterns.^{33,35,38} *Validity and Reliability: Primary Outcome Data Analysis*

There is an overwhelming lack of psychometric analyses for almost all the screening instruments within this review. None of the studies provide inter-rater reliability and test-retest reliability analyses. The internal consistency of SOAPP-R is high (Cronbach's alpha: .91) and indicates good reliability of the instrument in screening for opioid use in EM settings.^{59,62} The internal consistency of ASSIST is also high (Cronbach's alpha: .81-.95) for the study conducted in South African communities.⁶⁰ High AUC values, as shown for SOAPP-R and ASSIST, indicate goodness of fit with the chosen reference standard and discriminative validity.^{59,60,62} For the adjusted analysis, the AUC value (.81) for the high-risk SOAPP-R score of 18 was a good fit for the PDMP data reference standard.^{59,62} For the ASSIST, the AUC value (.95) illustrated good discriminative validity when assessing differences between use and abuse of illicit drugs.⁶⁰ Studies 1 and 4 also report on the item-total correlations of individual questions in the SOAPP-R instrument, indicating that the question items correlate well with each other and ask different questions related to drug use within the instrument.^{59,62} The remaining studies provide qualitative analyses of their respective instrument's validity and it is difficult to ascertain meaningful results without concrete data available to support these statements.

Secondary Outcomes: Data Analysis

Specificity, sensitivity and predictive values validate the use of screening instruments in comparison to the chosen reference standards and provide information concerning the usefulness and utility of the screening instruments in the designated study environment. The ASSIST; two, single-item screening questions; patient medical charts; and medical history and physical/patient self-reporting in medical charts all report high specificity values (87% - 98.8%).^{60,63,65,66} The SOAPP-R and the single-item binge-drinking screening question report moderate specificity values (63% - 71%).^{59,62,64} The sensitivities of the instruments differ across the studies. As mentioned in Study 7, there is poor sensitivity for the patient medical charts (4%).⁶⁵ The ASSIST and medical history and physical/patient self-reporting in medical charts report high sensitivity (90% - 93%), whereas the remaining screening instruments report moderate sensitivity values.^{60,66} Only the medical history and physical/patient self-reporting in medical charts and Drug Abuse Screening Test report high positive predictive values (88% and 89% respectively).^{66,67} The SOAPP-R; single-item binge-drinking screener question; patient medical charts; and medical history and physical/patient self-reporting in medical charts report high negative predictive values (89.1%, 94 - 99%, 91.1% and 94% respectively).^{62,64,65,66}

Table 9 includes qualitative analyses of the effects on morbidity/mortality, clinical utility/feasibility and accuracy data. There is a lack of concrete data for these variables as well. Two statistics are provided to indicate the moderate clinical utility of SOAPP-R (64%) and the high accuracy rate of the medical history and physical/patient self-reporting in medical charts (91%).^{59,66} The clinical utility/feasibility and accuracy data correspond with the respective study conclusions for all studies that report this data.

Limitations

There are copious limitations for each of the 10 studies reported in this review. The most prevalent limitation is the lack of screening instrument data and methodology in majority of the studies. Previously validated screening tools, such as SOAPP-R and ASSIST, do have reliability and validity data from studies conducted in primary care and pain management settings; however, this data does not necessarily extrapolate to EM settings.^{59,60,62} Primary care and EM settings differ in their patient populations and delivery of healthcare. Due to the amount of pain-related cases presented to the ED in comparison to other medical specialties, it is vital to validate screening instruments through the use of pilot studies to ensure that the instruments truly serve their purpose in a new environment with different patient populations.^{77,78} The studies also state within their "Limitations" sections that further validation studies and psychometric tests should be conducted to determine if the screening instruments are appropriate for use in EM settings.

We rated the quality of each study using the pre-established grading scales from the USPSTF. Studies 3, 6 and 9 were rated as "poor" due to the exclusion of reference standards in these studies.^{61,64,67} Studies 1 and 4 were rated as "fair" due to the use of an imperfect reference standard and use of a sample size less than 100 subjects (n = 82).^{59,62} Studies 7 and 8 were also rated as "fair"; although toxicology screening is an imperfect reference standard, the sample sizes for both studies exceeded the 100-subject criterion for quality assessment.^{65,66} Studies 2, 5 and 10 were rated as "good" due to the use of reference standards with previous validation data, the use of the reference standard as a comparison with the main screening instrument, and the large sample sizes reported for each study.^{60,63,68} There are limitations for this quality assessment, but the aim was to objectively consider all data presented in the 10 studies and to minimize the existence of personal bias and interpretation by referencing the USPSTF criteria for each study.¹⁰

For the two studies conducted in South Africa and France, although there is significant data presented in each study, it is difficult to extrapolate these results to U.S. EM settings due to population, public health and medical practice differences.

Regarding limitations for this systematic review, we may not have screened for all relevant studies due to limitations in the number of search terms and synonyms we were able to use for the study, and barriers such as language differences and unpublished studies that do not have reportable data at this time for analysis.¹⁸

Conclusions

The lack of validity and reliability data hinder the selection of appropriate screening instruments for use in EM settings. Of the screening instruments presented within this systematic literature review, the SOAPP-R and ASSIST provide the most amount of data and promise for use in EM settings; however, the lack of studies and screening instrument data indicate that none of the screening instruments presented in this study are suitable for all EM settings. Additionally, there is a lack of information concerning the utility of the screening instruments for use by the clinician to ensure timeliness within the face-paced EM setting.

For the data provided in the 10 studies, there was a lack of background information concerning calculations of specificity and sensitivity and how qualitative analyses were determined. Due to differences in reference standards and statistics used for the majority of the outcome variables, it is difficult to conduct any meta-analysis.

Due to the lack of meaningful evidence for comparison and analysis, we cannot answer our hypothesis at this time. Extensive studies that test a majority of the psychometric properties of opioid-use screening instruments in EM settings are needed. To advance the science in this field, more data and testing is required. As mentioned previously, screening tools can provide

time-sensitive information in fast-paced medical environments. Self-administered instruments can save time for the clinician and provide meaningful information for further treatments and interventions needed for at-risk population groups.⁴³

When conducting survey-based studies, clinicians and researchers should include all possible psychometric data in their articles. Clinicians must conduct pilot tests before starting the primary study to test the reliability and validity of the screening instrument in EM settings and share this information with the medical community. A study conducted in the United Kingdom, which analyzed the validity and reliability of a questionnaire that aimed to capture patient satisfaction with intermediate care, includes test-retest reliability, face validity and construct validity quantitative data.⁷⁹ Although it is impossible to include all reliability and validity testing in one study, clinicians should consider consulting statisticians/experts in the field of psychometrics to determine which tests would provide useful reliability and validity data to the medical community. As per this review, there is a need for studies that test test-retest, inter-rater, and internal consistency reliability; and construct, convergent, divergent, and discriminative validity.^{56,57} Clinicians should consider including most, if not all, of these reliability and validity tests in order to provide more information concerning the screening instruments in circulation within the medical field and provide more credibility for the instruments that are used as reference standards and for various settings in which they have not yet been validated in.

A Primer on the Validity of Assessment Instruments article includes more information on which reliability and validity tests researchers should consider. This includes test-retest reliability, inter-rater reliability, internal consistency (Cronbach's alpha) reliability; and validity tests such as face validity, content validity, criterion validity, construct validity and various other validity tests. The article states that researchers should first conduct "a literature search and use

previously developed outcome measures. If the instrument must be modified...with your subjects and setting, modify and describe how...if no assessment instruments are available, [you] use content experts to create your own and pilot the instrument prior to using it in your study. Test reliability and include as many sources of validity evidence as possible...discuss the limitations...openly".⁸⁰ We encourage EM researchers to follow these guidelines, consult the existing literature and determine which psychometric tests are appropriate to include within their study publications.

After clinicians use screening tools to determine which patients may have opioid use disorders and which may be at risk for opioid dependency, they may refer patients to treatment programs or begin treatment within the ED by providing brief interventions to patients in realtime, as explained in the HERA/SBIRT study.⁶⁸ According to SAMHSA-HRSA, SBIRT is evidence-based and identifies patients who use, abuse and depend on alcohol and illicit drugs. This tool is used for community-based screening and can be used in any healthcare settings. The SBIRT contains screening, brief intervention and referral to treatment components. The brief intervention allows a clinician to converse with the patient, and to provide information concerning the risks of illicit drug use and provide feedback to assist the patient. The referral to treatment component allows the clinician to provide a referral to patients who may need therapy or other treatment services for their drug use behaviors. The SBIRT can be used to screen both adults and adolescents.⁸¹ We chose to highlight SBIRT as there is more literature now explaining the benefits of the SBIRT program; however, further studies need to test SBIRT in EM settings as well as other treatment programs that can provide assistance to patients in a timely manner.

For high-risk opioid dependent patients, treatment initiation can begin in the ED. A randomized clinical trial, conducted from 2009 to 2013 in an urban-teaching hospital ED,

assessed the efficacy of three opioid treatment interventions. These interventions include the following: screening and referral to treatment; screening, brief intervention and facilitated referral to community-based treatment services; and screening, brief intervention and treatment with buprenorphine/naloxone with referral to primary care for a 10-week follow-up.⁸²

According to this study, one of the only options available to ED patients who exhibit opioid dependency is referral to addiction treatment programs. The initiation of buprenorphine in the ED can provide effective medication treatment to patients who need assistance immediately along with the use of brief interventions and referral to other treatments.⁸³ This study found that the buprenorphine group, compared to the brief intervention and referral group, significantly increased participation in addiction treatment, reduced self-reported opioid use and decreased use of inpatient addiction treatment services. However, the study did not find significant decreases in the rates of positive urine samples for opioids.⁸² It is important to continue researching the benefits of naloxone and buprenorphine to counteract the adverse effects of opioid drug dependency.

As a result of this review, we know that there is a lack in opioid screening instrument validation studies within EM settings. If this knowledge gap is filled, we can retrieve useful data to conduct screening in fast-paced settings and implement innovative instruments to ensure that all patients at risk for opioid abuse are captured before adverse health outcomes and further drug dependency manifest. Due to the rise in the rate of heroin overdose as a result of the opioid epidemic, it is vital to implement validated screening instruments in the EM setting and capture as many patients as possible for education, intervention and treatment.

REFERENCES/BIBLIOGRAPHY

- Rudd RA, Seth P, David F, Scholl L. Increases in drug and opioid-involved overdose deaths — united states, 2010–2015. *MMWR Morb Mortal Wkly Rep.* 2016;65:1445–1452. DOI: http://dx.doi.org/10.15585/mmwr.mm655051e1.
- Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in drug and opioid overdose deaths—united states, 2000–2014. *MMWR Morb Mortal Wkly Rep*. 2016;64:1378– 82. DOI: 10.15585/mmwr.mm6450a3.
- Centers for Disease Control and Prevention. National Center for Health Statistics: Alcohol Use. https://www.cdc.gov/nchs/fastats/alcohol.htm. Accessed July 19, 2017.
- Centers for Disease Control and Prevention. National Center for Health Statistics: Accidents or Unintentional Injuries. https://www.cdc.gov/nchs/fastats/accidentalinjury.htm. Accessed July 19, 2017.
- Gladden RM, Martinez P, Seth P. Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths—27 states, 2013–2014. MMWR Morb Mortal Wkly Rep. 2016;65:837–43. DOI: http://dx.doi.org/10.15585/mmwr.mm6533a2.
- Peterson AB, Gladden RM, Delcher C. Increases in fentanyl-related overdose deaths florida and ohio, 2013–2015. *MMWR Morb Mortal Wkly Rep.* 2016;65:844-9. DOI: 10.15585/mmwr.mm6533a3.
- Substance Abuse and Mental Health Services Administration. Substance Use Disorders. https://www.samhsa.gov/disorders/substance-use. Accessed May 22, 2017.
- Florence CS, Zhou C, Luo F, Xu L. The economic burden of prescription opioid overdose, abuse, and dependence in the united states, 2013. *Med Care*. 2016;54(10):901-6. DOI: 10.1097/MLR.000000000000625.

- United States Preventative Services Task Force. Drug Use, Illicit: Screening. https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/dr ug-use-illicit-screening. Accessed May 22, 2017.
- Lanier D, Ko S. Screening in Primary Care Settings for Illicit Drug Use: Assessment of Screening Instruments — A Supplemental Evidence Update for the U.S. Preventive Services Task Force. Evidence Synthesis No. 58, Part 2. AHRQ Publication No. 08-05108-EF-2. Rockville, Maryland: Agency for Healthcare Research and Quality. 2008.
- Substance Abuse and Mental Health Services Administration-Health Resources and Services Administration Center for Integrated Health Solutions. Screening Tools. http://www.integration.samhsa.gov/clinical-practice/screening-tools. Accessed May 20, 2017.
- Cordell WH, Keene KK, Giles BK, Jones JB, Jones JH, Brizendine EJ. The high prevalence of pain in emergency medical care. *Am J Emerg Med.* 2002;20(3):165-9. https://doi.org/10.1053/ajem.2002.32643.
- Rosenblum A, Marsch LA, Joseph H, Portenoy RK. Opioids and the treatment of chronic pain: controversies, current status, and future directions. *Experimental and clinical psychopharmacology*. 2008;16(5):405-416. DOI: 10.1037/a0013628.
- 14. Jones LA. Systematic review of alcohol screening tools for use in the emergency department. *Emergency Medicine Journal*. 2011;28:182-191. DOI: 10.1136/emj.2009.085324.
- 15. Feldhaus KM, Koziol-McLain J, Amsbury HL, Norton LM, Lowenstein SR, Abbott JT. Accuracy of 3 brief screening questions for detecting partner violence in the emergency

department. JAMA. 1997;277(17):1357-1361. DOI:

10.1001/jama.1997.03540410035027.

- Stewart SH, Connors GJ. Screening for alcohol problems: what makes a test effective? *Alcohol Research & Health*. 2004/2005;28(1):5–16.
- Hodgson R, Alwyn T, John B, Thom B, Smith A. The FAST alcohol screening test. *Alcohol Alcohol.* 2002;37(1):61-6.
- Denison HJ, Dodds RM, Ntani G, Cooper R, Cooper C, Sayer AA, Baird J. How to get started with a systematic review in epidemiology: an introductory guide for early career researchers. *Arch Public Health*. 2013;71(1):21. DOI: 10.1186/0778-7367-71-21.
- 19. Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Welcome to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) website! http://www.prisma-statement.org. Accessed July 04, 2017.
- NIH: National Institute on Drug Abuse. Opioids: Brief Description. https://www.drugabuse.gov/drugs-abuse/opioids. Accessed June 22, 2017.
- Australian Pain Management Association. Opioids. https://www.painmanagement.org.au/2014-09-11-13-35-53/2014-09-11-13-36-47/164opiods.html. Accessed June 22, 2017.
- 22. Smith HS. Opioid metabolism. Mayo Clinic Proceedings. 2009;84(7):613-624.
- 23. American Addiction Centers. How Long Do Opiates Stay in Your System? http://americanaddictioncenters.org/prescription-drugs/how-long-in-system/. Accessed June 22, 2017.

- NIH Medline Plus. Opioids and Chronic Pain. https://medlineplus.gov/magazine/issues/spring11/articles/spring11pg9.html. Accessed June 22, 2017.
- 25. American Academy of Pain Medicine. Use of Opioids for the Treatment of Chronic Pain. http://www.painmed.org/files/use-of-opioids-for-the-treatment-of-chronic-pain.pdf. Accessed June 22, 2017.
- 26. The National Alliance of Advocates for Buprenorphine Treatment. Physical Dependence and Addiction: An Important Distinction. http://www.naabt.org/addiction_physicaldependence.cfm. Accessed June 22, 2017.
- 27. NIH: U.S. National Library of Medicine-Medline Plus. Substance use disorder. https://medlineplus.gov/ency/article/001522.htm. Accessed June 22, 2017.
- 28. Substance Abuse and Mental Health Services Administration (SAMHSA). Substance Use Disorders. https://www.samhsa.gov/disorders/substance-use. Accessed June 22, 2017.
- 29. Harm Reduction Coalition. Understanding Naloxone. http://harmreduction.org/issues/overdose-prevention/overview/overdosebasics/understanding-naloxone/. Accessed June 22, 2017.
- Centers for Disease Control and Prevention. Opioid Overdose: Overdose Prevention. https://www.cdc.gov/drugoverdose/opioids/odprevention.html. Accessed June 22, 2017.
- Savage SR. Management of opioid medications in patients with chronic pain and risk of substance misuse. *Current Psychiatry Reports*. 2009;11(5):377-84. PMID: 19785979.
- Centers for Disease Control and Prevention. Opioid Overdose: Understanding the Epidemic. https://www.cdc.gov/drugoverdose/epidemic/index.html. Accessed June 22, 2017.

- Rudd RA, Paulozzi LJ, Bauer MJ. Increases in heroin overdose death rates—28 states,
 2010 to 2012. *Morbidity and Mortality Weekly Report*. 2014;63(39):849-854.
- 34. Lev R, Petro S, Lee O, Lucas J, Stuck A, Vilke GM, Castillo EM. A description of medical examiner prescription-related deaths and prescription drug monitoring program data. *American Journal of Emergency Medicine*. 2016;34(3):510-4. DOI: 10.1016/j.ajem.2015.12.023.
- 35. Pletcher MJ, Kertesz SG, Kohn MA, Gonzales R. Trends in opioid prescribing by race/ethnicity for patients seeking care in US emergency departments. *JAMA*. 2008;299(1):70-78. DOI: 10.1001/jama.2007.64.
- 36. McCabe SE, Boyd CJ, Cranford JA, Teter CJ. Motives for nonmedical use of prescription opioids among high school seniors in the united states: self-treatment and beyond. *Archives of Pediatrics & Adolescent Medicine*. 2009;163(8):739-744. DOI: 10.1001/archpediatrics.2009.120.
- 37. Mazer-Amirshahi M, Mullins PM, Rasooly IR, Van den Anker J, Pines JM. Trends in prescription opioid use in pediatric emergency department patients. *Pediatric Emergency Care*. 2014;30(4):230-5. DOI: 10.1097/PEC.00000000000102.
- Vaughn MG, Nelson EJ, Salas-Wright CP, Qian Z, Schootman M. Racial and ethnic trends and correlates of non-medical use of prescription opioids among adolescents in the united states 2004-2013. *Journal of Psychiatric Research*. 2016;73:17-24. DOI: 10.1016/j.jpsychires.2015.11.003.
- 39. Cerdá M, Santaella J, Marshall BDL, Kim JH, Martins SS. Nonmedical prescription opioid use in childhood and early adolescence predicts transitions to heroin use in young

adulthood: a national study. *The Journal of Pediatrics*. 2015;167(3):605-12. DOI: 10.1016/j.jpeds.2015.04.071.

- Compton WM, Jones CM, Baldwin GT. Relationship between nonmedical prescriptionopioid use and heroin use. *New England Journal of Medicine*. 2016;374(2):154-63. DOI: 10.1056/NEJMra1508490.
- 41. Center for Behavioral Health Statistics and Quality. 2014 National Survey on Drug Use and Health: detailed tables. Rockville, MD: Substance Abuse and Mental Health Services Administration. http://www.samhsa.gov/data/sites/default/files/NSDUH-FRR1-2014/NSDUH-FRR1-2014.pdf. 2015.
- 42. Centers for Disease Control and Prevention. Wide-ranging Online Data for Epidemiologic Research (WONDER), Multiple-Cause-of-Death file, 2000–2014. http://www.cdc.gov/nchs/data/health_policy/AADR_drug_poisoning_involving_OA_Her oin US 2000-2014.pdf. 2015.
- 43. Center for Substance Abuse Treatment. Substance Abuse Treatment: Addressing the Specific Needs of Women. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2009. (Treatment Improvement Protocol (TIP) Series, No. 51.) Chapter 4: Screening and Assessment.

https://www.ncbi.nlm.nih.gov/books/NBK83253/. Accessed June 22, 2017.

- 44. Austin Peay State University. Writing a Systematic Literature Review: Resources for Students and Trainees. http://www.apsu.org.au/assets/Resources/Writing-a-Systematic-Literature-Review.pdf. Accessed July 04, 2017.
- 45. University of Stirling. What is a Systematic Literature Review and How Do I Do One? https://www.stir.ac.uk/media/schools/management/documents/centregradresearch/How%

20to%20do%20a%20systematic%20literature%20review%20and%20meta-analysis.pdf. Accessed July 04, 2017.

- 46. Alcohol and Drug Abuse Institute Library: University of Washington. ADAI Library. http://lib.adai.washington.edu. Accessed July 04, 2017.
- 47. NIH: National Institute on Drug Abuse. Chart of Evidence-Based Screening Tools for Adults and Adolescents. https://www.drugabuse.gov/nidamed-medical-healthprofessionals/tool-resources-your-practice/screening-assessment-drug-testingresources/chart-evidence-based-screening-tools-adults. Accessed July 04, 2017.
- National Center for Biotechnology Information: U.S. National Library of Medicine.
 PubMed.gov. https://www.ncbi.nlm.nih.gov/pubmed/. Accessed July 04, 2017.
- American Psychological Association. PsycINFO. http://www.apa.org/pubs/databases/psycinfo/index.aspx. Accessed July 04, 2017.
- 50. John Wiley & Sons, Inc. Cochrane Database of Systematic Reviews. http://www.cochranelibrary.com/cochrane-database-of-systematic-reviews/. Accessed July 04, 2017.
- 51. Clarivate Analytics. Web of Science. https://apps.webofknowledge.com/WOS_GeneralSearch_input.do?product=WOS&searc h_mode=GeneralSearch&SID=4DjkJWjyouo2X1ExJ8I&preferencesSaved=. Accessed July 04, 2017.
- John Wiley & Sons, Inc. Cochrane Central Register of Controlled Trials (CENTRAL). http://www.cochranelibrary.com/about/central-landing-page.html. Accessed July 04, 2017.

- 53. EBSCO Industries, Inc. CINAHL Complete. https://www.ebscohost.com/nursing/products/cinahl-databases/cinahl-complete. Accessed July 04, 2017.
- University of York. Centre for Reviews and Dissemination. https://www.york.ac.uk/crd/.
 Accessed July 04, 2017.
- U.S. National Institutes of Health. ClinicalTrials.gov. https://clinicaltrials.gov. Accessed July 04, 2017.
- 56. Mdege ND, Lang J. Screening instruments for detecting illicit drug use/abuse that could be useful in general hospital wards: a systematic review. *Addict Behav*. 2011;36(12):1111-9. DOI: 10.1016/j.addbeh.2011.07.007.
- 57. Tiet QQ, Finney JW, Moos RH. Screening psychiatric patients for illicit drug use disorders and problems. *Clin Psychol Rev.* 2008;28(4):578-91. DOI: 10.1016/j.cpr.2007.08.002.
- Joober R, Schmitz N, Annable L, Boksa P. Publication bias: what are the challenges and can they be overcome? *Journal of Psychiatry & Neuroscience: JPN*. 2012;37(3):149-152. DOI: 10.1503/jpn.120065.
- 59. Finkelman MD, Kulich RJ, Butler SF, Jackson WC, Friedman FD, Smits N, Weiner SG. An investigation of completion times on the screener and opioid assessment for patients with pain - revised (SOAPP-R). *J Pain Res.* 2016;9:1163-1171.
- 60. van der Westhuizen C, Wyatt G, Williams JK, Stein DJ, Sorsdahl K. Validation of the alcohol, smoking and substance involvement screening test in a low- and middle-income country cross-sectional emergency centre study. *Drug Alcohol Rev.* 2016;35(6):702-709. DOI: 10.1111/dar.12424.

- Reyes-Gibby CC, Anderson KO, Todd KH. Risk for opioid misuse among emergency department cancer patients. *Acad Emerg Med.* 2016;23(2):151-8. DOI: 10.1111/acem.12861.
- 62. Weiner SG, Horton LC, Green TC, Butler SF. A comparison of an opioid abuse screening tool and prescription drug monitoring data in the emergency department. *Drug Alcohol Depend*. 2016;159:152-7. DOI: 10.1016/j.drugalcdep.2015.12.007.
- Broderick KB, Richmond MK, Fagan J, Long AW. Pilot validation of a brief screen tool for substance use detection in emergency care. *J Emerg Med.* 2015;49(3):369-74. DOI: 10.1016/j.jemermed.2015.03.011.
- 64. Ramchand R, Marshall GN, Schell TL, Jaycox LH, Hambarsoomians K, Shetty V, Hinika GS, Cryer HG, Meade P, Belzberg H. Alcohol abuse and illegal drug use among Los Angeles County trauma patients: prevalence and evaluation of single item screener. *J Trauma*. 2009;66(5):1461-7. DOI: 10.1097/TA.0b013e318184821d.
- 65. Tournier M, Molimard M, Titier K, Cougnard A, Bégaud B, Gbikpi-Benissan G, Verdoux H. Accuracy of information on substance use recorded in medical charts of patients with intentional drug overdose. *Psychiatry Res.* 2007;152(1):73-9.
- 66. Olshaker JS, Browne B, Jerrard DA, Prendergast H, Stair TO. Medical clearance and screening of psychiatric patients in the emergency department. *Acad Emerg Med*. 1997;4(2):124-8.
- 67. Macias Konstantopoulos WL, Dreifuss JA, McDermott KA, Parry BA, Howell ML, Mandler RN, Fitzmaurice GM, Bogenschutz MP, Weiss RD. Identifying patients with problematic drug use in the emergency department: results of a multisite study. *Ann Emerg Med.* 2014;64(5):516-25. DOI: 10.1016/j.annemergmed.2014.05.012.

- Boudreaux ED, Abar B, Baumann BM, Grissom G. A randomized clinical trial of the health evaluation and referral assistant (HERA): research methods. *Contemp Clin Trials*. 2013;35(2):87-96. DOI: 10.1016/j.cct.2013.04.010.
- Horizon Discovery Group. What is a Reference Standard? https://www.horizondiscovery.com/reference-standards/what-are-reference-standards. Accessed July 06, 2017.
- 70. Gold R, Reichman M, Greenberg E, Ivanidze J, Elias E, Tsiouris AJ, Comunale JP, Johnson CE, Sanelli PC. Developing a new reference standard: is validation necessary? *Acad Radiol.* 2010;17(9):1079-82. DOI: 10.1016/j.acra.2010.05.021.
- Lecrubier Y, Sheehan DV, Weiller E. The mini international neuropsychiatric interview (MINI). a short diagnostic structured interview: reliability and validity according to the CIDI. *Eur Psychiatry*. 1997;12:224–231.
- 72. Humeniuk R, Ali R, Babor TF. Validation of the alcohol, smoking and substance involvement screening test (ASSIST). *Addiction*. 2008;103:1039–47.
- Beck O, Carlsson S, Tusic M, Olsson R, Franzen L, Hulten P. Laboratory and clinical evaluation of on-site urine drug testing. *Scand J Clin Lab Invest*. 2014;74(8):681-6. DOI: 10.3109/00365513.2014.939995.
- 74. O'Neal CL, Poklis A. An evaluation of the role of ROC plots in the prediction of heroin use from total codeine and total morphine concentrations in urine. *J Anal Toxicol*. 1998;22(6):487-92.
- 75. Saunders JB, Aasland OG, Babor TF, De La Fuente JR, Grant M. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. *Addiction*. 1993;88:791–804.

- 76. Skinner HA. The drug abuse screening test. Addict Behav. 1982;7:363-71.
- 77. American College of Emergency Physicians. Urgent Care Fact Sheet. http://newsroom.acep.org/fact_sheets?item=30033. Accessed July 15, 2017.
- 78. Centers for Medicare and Medicaid Services. Differences Between Your Provider's Office and the Emergency Department. https://marketplace.cms.gov/outreach-andeducation/downloads/c2c-emergency-department.pdf. Accessed July 15, 2017.
- 79. Wilson A, Hewitt G, Matthews R, Richards SH, Shepperd S. Development and testing of a questionnaire to measure patient satisfaction with intermediate care. *Quality & Safety in Health Care*. 2006;15(5):314-319. DOI: 10.1136/qshc.2005.016642.
- Sullivan GM. A primer on the validity of assessment instruments. *Journal of Graduate Medical Education*. 2011;3(2):119-120. DOI: 10.4300/JGME-D-11-00075.1.
- 81. SAMHSA-HRSA Center for Integrated Health Solutions. SBIRT. https://www.integration.samhsa.gov/clinical-practice/sbirt. Accessed July 15, 2017.
- 82. D'Onofrio G, O'Connor PG, Pantalon MV, Chawarski MC, Busch SH, Owens PH, Bernstein SL, Fiellin DA. Emergency department–initiated buprenorphine/naloxone treatment for opioid dependence, a randomized clinical trial. *JAMA*. 2015;313(16):1636-1644. DOI: 10.1001/jama.2015.3474.
- Sullivan LE, Fiellin DA. Narrative review: buprenorphine for opioid-dependent patients in office practice. *Ann Intern Med.* 2008;148(9):662-670.