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E-prescribing on Opioid-related Experiences and Outcomes: A Rapid Scoping Review

Report prepared for Canada Health Infoway

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We wish to acknowledge this land on which the University of Toronto operates. For thousands of years it has been the traditional land of the Huron-Wendat, the Seneca, and the Mississaugas of the Credit. Today, this meeting place is still the home to many Indigenous people from across Turtle Island and we are grateful to have the opportunity to work on this land.

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Table of Contents

Executive Summary

Objectives: 1) To examine how e-prescribing has been used clinically; 2) To examine the effects of e-prescribing on clinical outcomes, the patient/clinician experience, service delivery, and policy; and 3) To identify current gaps in present literature to inform future studies and/or recommendations.

Design: A rapid scoping review was completed.

Method: A comprehensive literature search was conducted by an expert librarian from the inception of selected databases (MEDLINE [Ovid], EMBASE [Ovid], and Scopus [Elsevier]) until November 16, 2022. Grey literature was searched using Google and ProQuest Theses and Dissertations via a string of key terms. The search criteria were as follows: 1) e-prescribing programs targeted to the use/misuse of opioids, including those that were complemented or accompanied by clinically focused initiatives, and 2) a primary research study of experimental, quasi-experimental, observational, qualitative, and/or mixed methods design. An additional criterion of an ambulatory component of e-prescribing (e.g., e-prescribing occurred upon discharge from acute care) was added at the full-text stage. No language limitations or filters were applied. All articles were double screened by trained reviewers using the inclusion criteria. All grey literature was manually searched by single reviewer. Data extracted included study characteristics, population characteristics, outcomes, and overall study findings. A quality assessment of articles was not performed. Data analysis of synthesized experiences and outcomes used a descriptive approach.

Results: Upon completion of screening, 32 full-text peer-reviewed articles and 2 grey literature documents (n=34) met the inclusion criteria. All of the studies had a quantitative components, with most highlighting e-prescribing from acute care settings to community or within closed hospital systems. The two main data systems used within an acute care setting were the Computerized Physician Order Entry system and the Electronic Prescribing for Controlled Substances system. Only a single study provided evidence on e-prescribing in a primary care setting and there was minimal reporting of prescriber and pharmacist characteristics, clinical populations, and socio-demographic information. The main outcomes identified were opioid prescribing rates, alerts (e.g., adverse drug events, drug-drug interactions), quantity and duration of opioid prescriptions, adoption of e-prescribing technology, attitudes towards e-prescribing and potential challenges with the implementation of e-prescribing into clinical practice. E-prescribing, including key features such as alerts and dose order sets, may reduce prescribing errors.

Conclusion: This rapid scoping review highlights initial promising results with e-prescribing and opioid therapy management. A key aspect for consideration is how e-prescribing might be used and related outcomes based on whether newly initiated or chronic. Among new prescriptions, there may be potential to decrease initiation, quantities, and doses as per guidelines to minimize short and long term risks. Conversely, there may be important and different considerations with e-prescribing for people who are taking opioids on a chronic basis to minimize disruptions with access and/or sudden dose changes. It is important that future work explores the experience of prescribers, pharmacists, and patients using e-prescribing for opioid therapy management, with an emphasis on prescribers in the community and primary care. Integrating the thoughts, perceptions, and beliefs of these parties into the literature is important as they are directly impacted by technology use in healthcare. Developing a common set of quality indicators for e-prescribing with opioids will help inform future research and build a stronger evidence base. Furthermore, understanding implementation considerations will be of importance as the technology is adopted and integrated into clinical practice and health systems.

Protocol/Topic Registration: https://osf.io/9zpcg/

Introduction

Over the past decade, rates of opioid-related harms have been increasing in North America.[1-3] Opioid-related harms may include poisoning, opioid use disorder, adverse drug reactions, neonatal withdrawal symptoms, and death.[4,5] Between January 2016 and March 2021, there were approximately 22,800 opioid-related deaths in Canada.[6] In 2020 alone, there were 6,306 opioid toxicity related deaths.[6] Specifically in Ontario, Canada's most populous province, there were 14.8 per 100,000 opioid poisoning hospitalizations,[5] most of which were accidental poisonings.[5] Concerningly, opioid-related harm increased dramatically during the COVID-19 pandemic, with Public Health Ontario reporting increases in emergency department visits, hospitalizations, and deaths.[7] Compared to the prior year, there was a 60% increase in opioid-related deaths in 2020, with a total of 2,426 deaths.[8]

Since the early 2010's, there has been growing awareness of opioid-related harms across Canada.[9] These harms were largely influenced by liberal prescribing of opioids for the treatment of both acute and chronic pain.[9] Evidence suggests that long-term use, particularly at higher doses, can lead to adverse events, including risk of opioid use disorder, opioid toxicities, falls, and motor vehicle collisions.[5,6,10,11] In response to the increasing numbers of opioid-related harms in Canada and the United States of America (USA), physician licensing bodies have revised professional standards for opioid prescriptions including recommendations for more conservative opioid prescription practices.[12,13] In the USA, national guidelines for chronic pain opioid prescribing were released in March 2016.[14] Just over one year later in Canada, a guideline for opioid therapy management was published in May 2017.[15] Strategies to address improvements in opioid management and safety have largely focused on improving knowledge of prescribers and patients, with many recommendations urging enhanced training and information for both groups.[16,17]

Electronic prescribing (or e-prescribing) is an approach designed to help facilitate safe and appropriate prescribing of medications. E-prescribing (in the Canadian context) is the secure electronic creation and transmission of a prescription between an authorized prescriber and a patient's pharmacy of choice, using clinical point-of-service solutions, in a manner that integrates clinical workflow and software.[18] E-prescribing has shown some promising benefits at the patient, clinician, and health system levels. At the patient level, e-prescribing has improved patient safety[19-24] and patient experiences with accessing medications.[25-27] For example, implementation of e-prescribing resulted in decreased rates of adverse drug events and prescribing errors,[19-24] and has also shown to improve an aspect of patient experience via easier access with reduced waiting times for dispensing.[21,25,26] At the clinician and health system levels, e-prescribing can improve workflow efficiency (e.g. facilitating communication between prescribers and dispensers,[28] and improven rates of medication adherence, as measured by prescriptions being filled),[29-33] resulting in both reduced healthcare costs and improved health outcomes.[34,35] While these benefits of e-prescribing have been well described, there remains a key gap in the literature: the extent to which e-prescribing can influence safe and appropriate opioid use, specifically relevant clinical outcomes.

To address this gap, a rapid scoping review was undertaken to answer the following question: *What direct impacts of e-prescribing have been experienced related to opioids?* The specific objectives of this rapid review were to: 1) examine how e-prescribing has been used clinically with opioids; 2) examine the effects of e-prescribing of opioids on clinical outcomes, patient/clinician experience, service delivery, and policy; and 3) identify any gaps in the literature to inform future studies and/or recommendations.

Methods

Protocol and registration

To answer the main research question, a rapid scoping review was conducted following the guidance of the JBI 2020 scoping review methodology[36] and the World Health Organization guide to rapid reviews.[37] Streamlined methods to conduct the rapid review followed the steps outlined by the Cochrane Rapid Reviews Methods Group in 2020.[38] Reporting aligns with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) statement.[39] The protocol for this review was registered with OSF Registries (https://osf.io/9zpcg/).

Eligibility criteria

Eligibility criteria for the review evolved during the screening stages. During the title and abstract screening, inclusion criteria were as follows: 1) e-prescribing programs that are targeted to opioid use/misuse, including those that are accompanied or complemented by clinically focused initiatives; and 2) a primary research study of experimental (e.g. randomized controlled trials), quasi-experimental (e.g. non-randomized controlled trials, controlled before and after studies, or interrupted time series), observational (e.g. cohort studies, case–control studies, or cross-sectional studies), qualitative, or mixed-method designs. At the full-text phase of screening, an additional inclusion criterion was added: an ambulatory component of e-prescribing (e.g. e-prescribing of opioids occurred at discharge from acute care, in the emergency department, or in the community). This criterion was not included until the full-text stage to ensure that all relevant articles were included for review, as abstracts were not likely to clearly specify involvement of an ambulatory component. The exclusion criteria for all stages of peer-reviewed article screening included: 1) prescribing that occurred within one hospital system (e.g. within an acute care ward); 2) articles that did not look at the impact of e-prescribing on opioid use; 3) digital solutions for prescribing that did not include e-prescribing (e.g. digital fax); 4) not a primary research study (e.g. commentaries, opinion piece) and 5) conference materials (e.g. abstracts). Grey literature was included if the criteria as outlined above were met; however, articles were not required to be a research study.

Information sources

A comprehensive literature search was conducted by an expert librarian (LB) on articles published from database inception until November 16th, 2022. Three databases were electronically searched: MEDLINE (Ovid), EMBASE (Ovid), and Scopus (Elsevier). Grey literature was searched using a string of key terms in Google and ProQuest Theses and Dissertations. No filters or language limitations were applied.

Search

The search strategies were developed based on two key concepts (e-prescribing and opioids) in consultation with the expert librarian who ran the search (LB). Previously published systematic reviews on opioids were also searched to identify relevant opioid-related terms.[40-42] Search strategies for the databases and grey literature can be found in Appendix A. The literature search was PRESS reviewed by another librarian.[43]

Selection of sources of evidence

Prior to de-duplication, records from MEDLINE and EMBASE were removed from the Scopus database search using the AND NOT function to ensure all relevant articles could be exported to EndNote (Scopus has an export limit of 2,000 records). De-duplication of the resulting list of articles from the three databases was then conducted in EndNote using the method developed by Bramer et al.[44] Literature review software, Covidence, was used to streamline the article screening process. At the title and abstract screening phase, a pilot test using 20 articles was

conducted by the reviewers (SRC, SG, JR, SM, SC, AY). Following the pilot test, the team met to review the inclusion criteria and the criteria were updated to ensure clarity. During this phase, eligibility criteria were kept broad to ensure as many relevant articles were included as possible (e.g. if uncertain about ambulatory component, articles were moved to full-text review). All articles were screened independently by two reviewers, with any conflicts resolved through team discussion.

Once the title and abstract screening was completed, 10 full-text articles were randomly selected for pilot-testing to ensure consistent application of the eligibility criteria across all reviewers. At this phase, articles that did not include an ambulatory component (i.e. did not involve opioids prescribed at acute care discharge, in the emergency department, or in the community) were excluded. All full-text articles were independently screened by two reviewers (from SRC, JR, SM, SC, AY) using the updated criteria, which included the ambulatory component.

Using Google, grey literature was manually searched by one reviewer (SRC). Following the last relevant citation, an additional 20 citations were reviewed to ensure all relevant materials were included. For dissertations and theses, this same process was completed using ProQuest by two reviewers (SRC and JR).

Data items and charting process

Data extraction, using the Covidence Data Extraction 2.0 form, was conducted once the full-text screening was completed. Key data from the articles that were collected included: study characteristics, population characteristics adapted from the Cochrane PROGRESS-Plus equity variable recommendations[45] (sample size, age, sex, gender, ethnicity/race, religion, income, education, geographical location, social capital), description of e-prescribing (design, prescriber context, intended recipients, indication for opioids, accompanied/not accompanied by clinical focused initiatives), study outcomes, and findings (e.g. descriptions of data driven activities or analysis for managing the prescribing of opioids or informing better policy and interventions, opioid dependency, opioid-related death, healthcare utilization due to opioids, economic costs due to opioids, fraud, transparency of prescription history) (see Appendix B for Data Extraction Codebook). A pilot test was conducted with each of the four reviewers (JR, SM, SC, AY) completing extraction using one article each. Each of the pilot articles was spot checked by an independent trained reviewer (SRC) to ensure consistency in extraction across reviewers. The remaining data extraction was conducted by the four reviewers (JR, SM, SC, AY) and spot checked by the independent reviewer (SRC). For the purposes of this rapid scoping review, a quality assessment of the articles was not conducted.

Synthesis of results

The findings from the included articles related to e-prescribing and opioid experiences and outcomes were synthesized. Data analysis used descriptive approaches. Descriptive summaries of the study characteristics, population characteristics, study outcomes, and findings were conducted. Summaries of the findings were developed by collating study findings that reported on similar topics (e.g. setting of e-prescribing, rates of prescribing opioids). Once the information was organized, a section header was developed based on the subject matter of each section. This organization process was done by two members of the authorship team (SRC and JR), in conjunction with members of the senior research team.

Results

The results of the literature searches yielded 1,183 articles (see Figure 1 for PRISMA diagram). Following the removal of duplicates, 939 articles were included in the title and abstract review. Following this initial screening phase, 161 reports were sought for retrieval. There was one article

for which the full-text could not be retrieved, leaving 160 full-text articles assessed for eligibility. With respect to grey literature, 12 dissertations or theses were identified, and four potentially relevant reports were found via Google. Following screening, 32 full-text articles[30,46-76] and two grey literature documents (one thesis and one report)[77,78] met the inclusion criteria and were included in the rapid review. The characteristics of the identified studies will be described below followed by a description of the grey literature report.

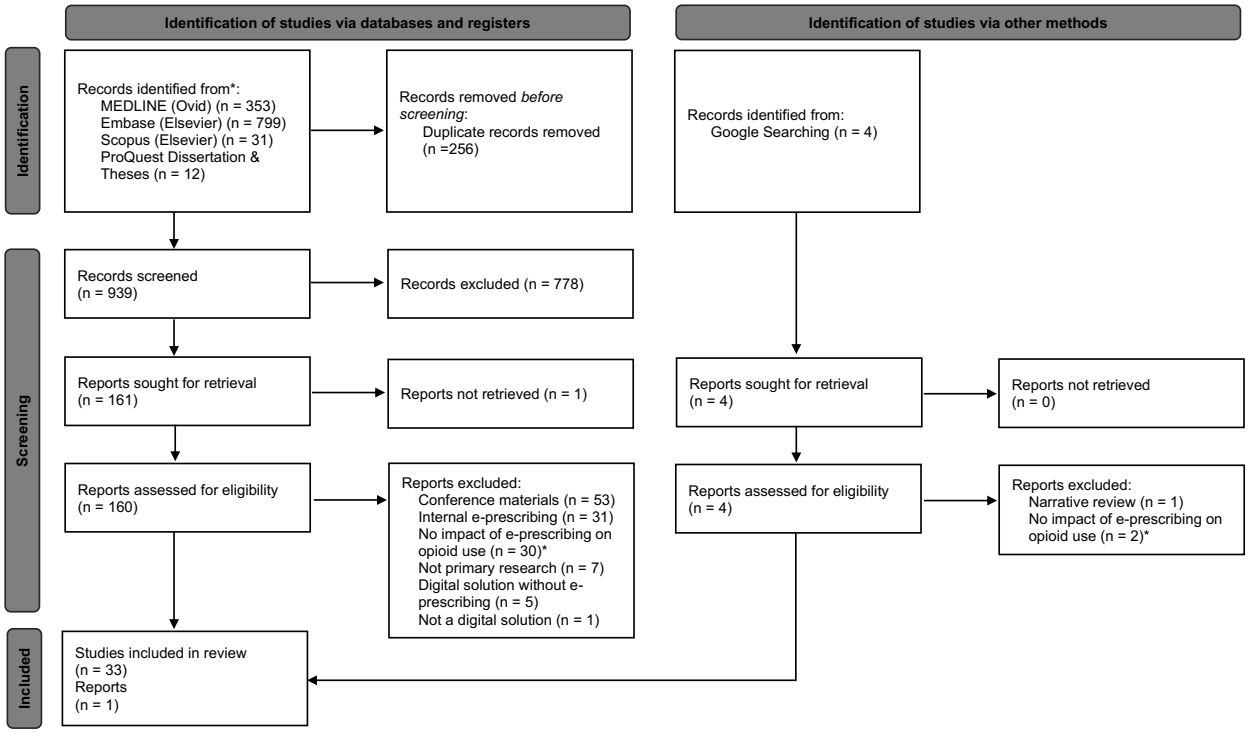

Figure 1. PRISMA Diagram displaying the screening process. *Note: Articles that were excluded did not study the influence of e-prescribing on opioid use.

Study Characteristics

The identified studies (n=33) were mostly conducted in the USA (n=25),[30,47-50,52-55,57-59,62,64-66,68-72,74-76,78] followed by Canada (n=2),[60,61] Australia (n=1),[67] and Brazil (n=1)[63] (see Appendix C). Publication dates ranged from 2005 to 2022. All studies had a quantitative component (n=33), with three being mixed methods.[55,71,72] The most common study designs were retrospective studies (n=9)[30,48,52,55,62,66,68,75,78] and prospective cohort studies (n=7),[51,60,65,69,73,74,76] followed by cross-sectional studies (n=4),[46,64,71,72] descriptive studies (n=3),[50,53,67] pre-post studies (n=3),[49,56,59] quasi-experimental studies (n=3),[61,63,70] quality improvement studies (n=3),[47,57,58] and a prospective controlled study (n=1).[54] Data were obtained through a variety of collection methods, with the most common being electronic medical records (n=13)[46-50,55-59,61,67,78] and hospital or healthcare setting databases (n=12).[53,54,60,62,63,65,68-70,73-75] Other data were obtained through a variety of methods and approaches, such as: surveys (n=5),[55,64,67,71,72] structured interviews (n=2),[60,67] opioid prescribing rate maps (n=1),[52] iScribe (an e-prescribing system used for outpatient settings; n=1),[30] data from the US Drug Enforcement Administration's Association of Electronic Prescribing of Controlled Substances With Opioid Prescribing Rates Administration's Automation of Reports and Consolidated Orders System,[52] computerized dataset,[66] large pharmacy benefits management company,[30] and treatment orders.[51]

With respect to populations being studied, most were clinical populations (n=24),[46-61,63,65,68,70,73,74,76,78] the general population (n=7),[30,62,64,66,67,69,75] and clinical prescribers (n=2).[71,72] E-prescribing settings varied among the included studies, with ambulatory settings (e.g. emergency department, outpatient) being the most common (n=16).[30,47-50,54,55,59,62,66-69,72,75,76] Other settings included: acute care discharge (n=12),[46,53,56-58,60,61,65,70,73,74,78] community pharmacy (n=1),[72] hospital pharmacy (n=2),[51,63] and primary care.[64] One study did not report the setting.[52]

For studies that specified the age of participants (n=13), seven studied adults (over the age of 18),[58,60,61,63,65-67] three studied a geriatric population (age 65 years and older),[54,56,59] and three included a strictly pediatric population (less than 18 years of age).[53,57,62] Of the populations characteristics, income, education, place of residence, social capital, and religion were not reported. Few studies reported ethnicity/race (n=10),[47,49,50,54,61,64,65,68,72,78] comorbidities (n=5),[46,60,64,67,68] marital status (n=1),[65] employment status (n=1),[65] or geographical location (n=1).[64]

The opioids being studied included oxycodone (n=14),[48,49,53,54,57-59,61,62,65-67,70,78] codeine (n=8),[46,49,53,58,61,62,70,78] morphine (Immediate Release,[48,53] Controlled Release,[48,53] Intravenous,[54,59] unknown[49,56,70,78]) (n=8), hydromorphone (n=7),[48,49,53,58,59,65,78] tramadol (n=6),[48,49,58,70,73,78] hydrocodone (n=6),[49,53,61,66,70,78] fentanyl (n=5),[48,59,61,63,78] meperidine (n=3),[61,70,78] oxycontin (n=2),[53,55] oxymorphone (n=2),[70,78] opioid in combination with acetaminophen (hydrocodone (n=3),[57,58,61] codeine (n=2),[58,61] and oxycodone (n=2)[57,61]), butorphanol (n=1),[78] dihydrocodeine (n=1),[78] and tapentadol (n=1).[70]

E-Prescribing Systems & Components of the Systems

Systems

The e-prescribing systems described in the articles included many components such as alerts, two-way communication, default ordering sets, and Computerized Physician Order Entry (CPOE) prescribing. CPOE prescribing was the most commonly included component (n=9).[30,47,51,56,60-62,64,66] A quasi-experimental study by Leung et al. (n=1,590; mean age 72.2, range 18-102 years) assessed the implementation of a CPOE system without clinical support in comparison to implementation of a CPOE system with either rudimentary or advanced support.[61] Specific to prescribing practices, an Electronic Prescribing for Controlled Substances (EPCS) system (n=6)[50,52,65,68,71,72] was integrated into some CPOE systems. EPCS is a secure online system specifically for controlled substances, which allows the direct transmission of prescriptions from a prescriber to a pharmacy.

Components

Dose quantity defaults and order sets were the most commonly described component of the e-prescribing systems (n=8).[49,54,57-59,66,67,70] Within the CPOE system specifically, both default duration (n=1)[70] and override or recommendations (n=1)[54] were mentioned. Alerts were the next most common component of e-prescribing software (n=7).[47,63,69,73,75,76,78] Two-way communication between prescribers and dispensers were discussed in five articles.[46,53,56,57,74] The types of communication included pharmacists reacting to a medication error and contacting medical prescribers (n=2),[46,74] medical reconciliation using enhanced computerized decision-making (i.e. comparing old prescriptions and performing potential duplicate medication checks),[56] and double validation (manual entry into electronic medical record system twice).[53] Other components of e-prescribing included drug-drug interaction screening software,[63] adherence tracking,[56] computerized calculations,[53] prescription printing,[53] and the addition of patient information into the system.[48]

Effects of E-Prescribing on Opioid Use

The overall effect of e-prescribing was described by 14 articles.[30,46,48,51-53,55,56,60-62,64,65,74] Articles examined the influence of e-prescribing on rates of opioid prescription, medication adherence, and prescription errors.

Rates of Prescribing, Discontinuation, Medication Adherence, and Adverse Drug Events

There were mixed findings regarding opioid prescribing rates related to e-prescribing. One recent retrospective study by Everson et al. (n=459; age not reported) identified that opioids were prescribed less often from 2013 to 2018 following the introduction of e-prescribing (from 78/100 people in 2013 to 43/100 people in 2018).[52] In contrast, a cross-sectional study by Ney and Weathers (n=233,390; aged 18+) reported that rates of primary care physician opioid prescribing increased after implementation of CPOE (from 7.5% to 10.4% overall, and 16.4% to 20.6% for non-cancer pain), with the odds of opioid prescription substantially higher in these ambulatory care visits.[64] With respect to opioid dose prescribed, two articles reported that the quantity of opioids being prescribed decreased following the implementation of e-prescribing.[52,65]

In Hickman et al.'s retrospective study of outpatient CPOE prescribing (n=312; age not reported), the leading reason prescribers discontinued medications was due to errors in prescribing.[55] Relatedly, Watterson et al. conducted a prospective cohort study (n=49,129; age not reported) to examine the impact of the CancelRx system on reducing discrepancies between the prescribing clinic's electronic health record and the pharmacy management software. CancelRx leverages the same electronic pathway as e-prescribing but focuses on discontinuation. Using secondary data from their single academic health system and interrupted time series analyses, Watterson et al. reported that 'successful' medication discontinuations increased, as defined by reduced discrepancies between clinics and pharmacies within a 72 hour period. Further, Watterson et al. found the time to medication discontinuation at the pharmacies decreased (e.g. from weeks to same day discontinuations) when discontinued at the prescribing clinic following its implementation. Watterson et al. concluded that CancelRx improved communication of medication discontinuations between clinics and pharmacies.[74]

Only one study examined the rate of nonadherence for opioids when using e-prescribing, where nonadherence was defined as prescriptions not filled.[30] Fischer et al. conducted a retrospective study (n=280,081 patients of all ages; n=3,634 prescribers) and reported that the nonadherence rate for newly prescribed opioid e-prescriptions was 23.9% of 12,625 opioid prescriptions.[30] Note, these authors only reported nonadherence for e-prescribing and did not compare nonadherence with non e-prescribing. Leung et al. found that the number of renally related preventable adverse drug events (defined as any drug related injury due to error at the time of order entry) decreased post implementation of an e-prescribing system.[61] Specific to opioids, an example of a renally related preventable adverse drug event found was the over sedation from morphine.[61]

Prescription Errors

There were eight articles that studied the influence of e-prescribing on prescription errors.[46,48,51,53,55,56,60,62] Of the articles that looked at prescription errors across various drug types, opioids, such as codeine, morphine, and oxycodone, were often associated with an error.[46,55,56,62] Typical errors for opioids included discontinuation errors (i.e. prescriptions were discontinued due to erroneous prescription entry as described by physicians), transcription errors, duplicated medications, or dosing errors.[51,53,55,56] Three articles compared the opioid error rates between e-prescriptions and hand-written prescriptions.[48,60,62] Compared with hand-written prescriptions, e-prescribing resulted in lower risk for medication errors (20.6% vs 1.2%)[60] and lower overall guideline deviations (100% of deviations were hand-written and not computer-generated).[48] However, one article, a retrospective study conducted by McPhillips et al. (n=1,933; age not

reported), reported no difference in potential error rates between hospitals that used CPOE and those that did not.[62]

Components of E-Prescribing that Influence Opioid Use

Specific components of e-prescribing were reported to influence opioid prescribing, including alerts, and default order sets.

Alerts

Seven articles described the influence of having alerts within the e-prescribing system.[47,63,69,73,75,76,78] The types of alerts included: allergy alerts,[78] naloxone alerts (i.e. an alert is triggered to prescribe naloxone when an opioid is being prescribed),[69] drug-drug interaction alerts,[63,73,75,76] and guideline concordance alerts.[47] Drug-drug interaction alerts were reported to prevent serious adverse drug events in one study,[75] but had no effect in another.[63] When looking at antiemetic drugs and their interaction with opioids, prescribers in one study were more likely to cancel the antiemetic drug order if the alert indicated an interaction with an opioid.[76] With respect to guideline concordance alert, one article reported that it did not influence the total number of opioid prescriptions in a two week interval.[47] However, there was an increase in prescriptions that aligned with the guidelines (from 12% to 31% of all prescriptions) at an academic multispecialty practice (where concordance was previously low). This increase in aligned prescriptions was not observed at a federally qualified health center (where concordance was already high). One article by Ariosto identified override rates and factors that contributed to high volume but relatively low value drug allergy alerts with e-prescibing.[69,78] A main opioid allergy alert was found to be gastrointestinal related such as nausea and constipation, contributing to 15% of the first alerts.[69,78]

Default Order Sets

The effect of including default order sets within the e-prescribing system was described by eight articles.[49,54,57-59,66,67,70] Default order sets were created within the e-prescribing system, such that when a prescriber indicates they would like to prescribe an opioid, a default quantity is provided. With respect to their effect on the prescribing patterns of opioids, six articles reported a reduction in the opioid dose being prescribed,[49,57,58,66,67,70] and one article also reported a reduction in duration of treatment.[70] While the quantity of opioids being prescribed decreased, one article reported no change in the number of opioid prescriptions per month.[70] Medication adherence following the implementation of default order sets was described by two studies.[49,67] Schwartz et al. found that e-prescribing assisted with the reduction of overall quantities but did not impact the proportion of patients who reported using half or less of their prescribed opioids.[67] Specifically, 58% of patients in their sample (n=106) reported using half or less of the medication prescribed and 21% (n=22) of participants did not fill their prescriptions following implementation of the default order set. In the study by Chiu et al., the authors reported no influence of default order set implementation on refill rates.[49]

At the provider level, four studies explored compliance with default order set implementation.[49,54,58,59] One study found that there was no change in compliance with the suggested opioid doses,[58] while another two studies found that agreement with recommendations had significantly improved following implementation.[54,59] However, Griffey et al. included a caveat: although overall agreement significantly improved from pre-implementation, it was still considered low (36%).[54] Deviations from recommended doses were reported by Chiu et al., who suggested that the type of prescriber (resident versus attending physician) and the type of procedure being done influenced whether the default dose was altered in new prescriptions.[49]

Experience and Perceptions with E-prescribing

There were two articles included in this review that described clinicians' experiences and perceptions with using e-prescribing for opioids.[71,72] Thomas et al., 2012, explored barriers

associated with the adoption and use of an EPCS system using a quantitative survey.[72] When asked about their expectations of e-prescribing systems for opioids, prescribers expected this technology to improve patient management and practice efficacy.[72] However, prescribers were hesitant to use new prescribing technologies due to their reservations with patient confidentiality or the learning curve to use e-prescribing systems.[72] In the second study by Thomas et al., 2013, a survey was conducted to understand the experiences of prescribers following EPCS implementation.[71] For prescribers currently using an e-prescribing system, they indicated that it was easy to use, improved the accuracy of prescriptions, improved workflow, improved coordination, and limited the number of calls from pharmacists.[71] With respect to satisfaction with the system, age, comfort with using a computer, number of patients per week, and belief that the system improved patient management were associated with increased odds of being satisfied with the system.[71] Both studies described technical issues, such as computer crashes, lag time between transmitting and receiving prescriptions, and pharmacist follow-up to confirm e-prescription details, as barriers to using the e-prescribing system for opioids.[71,72] Two additional barriers to implementation of the EPCS system identified were the need to keep a security token in their possession to access the system,[72] as well as the lack of community pharmacies using the e-prescribing system.[71] No studies explored the experiences and perspectives of patients or caregivers.

Influence of E-prescribing Policies/Mandates

E-prescribing mandates were associated with the reduction of both opioid prescriptions[50,68] and dose of opioids.[68] The mandates that were implemented were located in two states in the USA (New York and Massachusetts).[50,68]

The one report identified in the grey literature search suggested that mandatory national use of the e-prescribing system for controlled substances could save the USA government approximately $53 billion based on projections.[77] The cost savings were based on several factors including: reduced costs due to opioid-related fatalities (between $18 billion and $37 billion saved), decreased healthcare costs including treatment costs, increase in workplace productivity, reduced criminal justice costs ($7 billion to $14 billion saved), and savings from improved efficiencies in physician offices and pharmacies (e.g. reduced calls between prescribers and pharmacists regarding prescription clarifications, decreased wait times for patients to fill prescription; $1.6 billion saved).[77]

Discussion

This rapid scoping review had three main objectives: (1) to examine how e-prescribing has been used clinically for opioids; 2) to examine the impact of e-prescribing of opioids on opioid-related clinical outcomes, patient/clinician experience, service delivery, and policy; and 3) to identify any gaps in the literature. Each of the objectives are discussed further below.

Objective 1): To examine how e-prescribing has been used clinically for opioids

Overall, we identified a limited number of articles that met our inclusion criteria (n=34). Of these included articles, a limited number of e-prescribing settings were examined. The majority of studies examined e-prescribing being initiated within hospital-based care or an affiliated ambulatory clinic. Thus, most of the evidence found in this review reflects hospital settings and closed health systems. The main data systems used within the hospital systems were the CPOE system and the EPCS system. Only one study focused on e-prescribing in primary care. Additionally, there was minimal reporting of prescriber and pharmacist characteristics, clinical characteristics, or socio-demographic information.

Objective 2) To examine the effects of e-prescribing of opioids on clinical outcomes, patient/clinician experience, service delivery, and policy

We identified a large variation across included studies examining the effects of e-prescribing on clinical outcomes, experiences, service delivery, and policy. Several outcomes identified included opioid prescribing rates, quantity of opioids prescribed and duration of prescription, alerts (e.g. adverse drug events and drug-drug interaction), adoption of e-prescribing technology, attitudes toward e-prescribing, and challenges following implementation of e-prescribing technology. However, most of the outcomes were focused on prescription-level metrics such as prescription rates, prescription errors, and discontinuation rates.

Despite the variation in reported outcomes and results, there appears to be promising findings with respect to e-prescribing. For example, a few studies showed a reduction in prescribing errors when compared to handwritten notes (e.g., 20.6% handwritten errors vs 1.2% e-prescribing).[60] Several studies also highlighted promising effects of alerts and order sets on reducing errors. Two studies demonstrated the usefulness of e-prescribing mandates in reducing opioid prescriptions[50,68] and reducing dose.[68] Given rates of opioid-related harms have been increasing in North America,[1] these findings suggest e-prescribing may be a promising approach to address prescribing errors. However, it is important to understand the nature and related implications of reducing the number, dose, and rapid discontinuations as there may be unintended risks of reducing access to opioids or reducing doses too quickly.[79-81]

In the one report identified, mandatory national use of e-prescribing system for controlled substances has been projected to have a potential cost savings of approximately $53 billion annually for the USA government.[77] These potential cost savings could be re-allocated to fund programs for including education for prescribers, patients, and the general public. However, it is important to note that the unregulated opioid drug supply is the main cause of opioid-related deaths in Ontario and the generalizability of this report to the Canadian context should be made with caution.[82]

Objective 3) To identify any gaps in the literature to inform future studies and/or recommendations

Despite a comprehensive search, we identified minimal research examining e-prescribing for opioids and related outcomes. While results showed promising trends[1] toward impacting some outcomes, such as a reduction in prescription errors and identifying drug-drug interactions, there remain important clinical and policy-relevant areas for further exploration. A summary of important implementation and outcome considerations are outlined below.

Implementation Considerations

More studies are needed to understand implementation considerations such as barriers and facilitators for e-prescribing to inform adoption and larger scalability. There are well established factors that influence the implementation of interventions and their effectiveness. For example, the Consolidated Framework for Implementation Research[83] consists of five key domains which are known to influence implementation. These domains include: intervention characteristics (e.g. characteristics of e-prescribing), inner setting (features of the implementing organizations such as hospitals, community, and/or pharmacies), outer setting (external context/environment such as patient needs and resources), characteristics of the individuals involved (e.g. knowledge and attitudes of clinicians and patients; patient characteristics, such as first time opioid use versus repeated use, co-morbidities, acute or chronic pain, other prescribed medications), and the implementation process (strategies that might influence implementation, such as quality and

[1] Note: This rapid review did not critically appraise the strength of the evidence, thus caution is warranted with interpretation of the effect of e-prescribing on outcomes.

extent of planning, engagement of key stakeholders, impact on workflow). To inform adoption and uptake efforts of e-prescribing technology, it will be important for future work to understand for whom e-prescribing might be working, how, and in what circumstances. For example, this review identified important questions that remain, such as: Are there certain equity-seeking groups where this technology might be particularly useful to support safe and effective opioid therapy management? Are there certain prescribers and/or pharmacists that might benefit more from this technology, in what clinical settings? Are there certain aspects of the e-prescribing systems that are more beneficial and/or harmful (e.g. what are the alerts, order sets, interaction features). There are known risks to rapid dose reductions with opioids[79] and understanding potential harms would be important to further explore. A key aspect for consideration is how e-prescribing might be implemented for new prescriptions to prevent short term and long term risks among persons, compared to how it might be implemented for repeat prescriptions among those experiencing chronic pain. These implementation factors should be considered in future work examining e-prescribing.

Outcome Considerations

Overall, there was a lack of consistency in the types of outcomes reported and it is unclear whether the outcomes reported align with established quality indicators (e.g. consideration of dose within clinical context of acute or chronic care). Several of the outcomes may be problematic, such as nonadherence and discontinuation, as they may not accurately reflect improvement in outcomes. For example, with nonadherence, it is important to consider differences in "take medication when needed" versus taking the medication on a prescribed schedule regimen. With respect to discontinuation, the timing needs to be considered (e.g. discontinuing the same day versus discontinuing within the prescription period). Same-day discontinuations are likely due to errors by the prescriber, as seen in the study conducted by Hickman et al.[55] Tapering guidelines for chronic pain suggest the discontinuation of opioids may lead to the risk of inadvertent or unintentional overdose risk, if not done properly.[84,85] It is suggested that patients follow a gradual 5-10% morphine-equivalent dose decrease every 2 to 4 weeks with frequent follow-up. However, if the prescription is for acute pain, tapering is not necessarily needed.[84,85] Finally, there was an absence of studies exploring perceptions of e-prescribing for opioids from different stakeholder groups (e.g. clinicians, prescribers, patients) from a qualitative perspective, which would also inform meaningful outcomes and potential indicators of quality e-prescribing.

Recommendations for Future Research

One of the challenges in reviewing the opioid literature is the substantial shift in practice guidelines for opioid therapy management that occurred after 2016.[14,15] As such, studies published prior to this date examining e-prescribing and opioid use may not reflect current practices or needs. This review identified several gaps, particularly related to implementation and effectiveness considerations. Future research is warranted to address the gaps found and to expand the current knowledge of e-prescribing systems and opioid-related outcomes. Firstly, e-prescribing needs to be assessed across broader health systems and larger populations, such as in the community and in primary care. Only one study was found that assessed e-prescribing in primary care.[64] This study included data collected prior to 2016, when significant practice guideline changes were released that have impact on opioid prescribing and patterns, suggesting the only data available from primary care likely do not reflect current practice or need. Additionally, the perspectives, experiences, and healthcare outcomes from a wide variety of stakeholders (such as prescribers, clinicians, pharmacists, patients, and pharmacy managers) should be explored and examined through mixed-methods and qualitative studies. For example, qualitative studies with community stakeholders would provide insight into fear regarding e-prescribing of opioids that has previously been reported to impact prescribing rates of primary care physicians.[86-89] Finally, the development

of a common set of quality indicators to guide reporting of outcomes would likely be useful to ensure consistent implementation and evaluation of e-prescribing across varying studies.

Limitations

The limitations of the present study are consistent with those common to rapid reviews. It is possible articles were missed. Despite the time constraint, a rigorous selection process was undertaken with double screening present at each stage of the process and grey literature was searched. Of note, 15 studies were published 2016 or earlier, which would not reflect the dramatic shifts that occurred in opioid therapy management in the last several years. Additionally, the quality of the studies was not assessed, and as such, this report does not integrate the strength of the evidence.[37]

Conclusion

While relatively few studies were identified, this scoping review highlights initial promising results with e-prescribing and opioid therapy management. E-prescribing, including key features such as alerts and dose order sets, may reduce prescribing errors. A key aspect for consideration is how e-prescribing might be used and related outcomes based on whether newly initiated or chronic. Among *new prescriptions* there may be potential to decrease initiation, quantities, and doses as per guidelines to minimize short and long term risks. Conversely, there may be important and different considerations with e-prescribing for people who are taking opioids on a *chronic basis* to minimize disruptions with access and/or sudden dose changes. These important nuances were missed from the research reviewed and highlight gaps in the literature. It is important that future work explores the experience of prescribers, pharmacists, and patients using e-prescribing for opioid therapy management, with an emphasis on prescribers in the community and primary care. Integrating the thoughts, perceptions, and beliefs of these parties into the literature is important as they are directly impacted by technology use in healthcare. Developing a common set of quality indicators for e-prescribing with opioids will help inform future research and build a stronger evidence base. Furthermore, understanding implementation considerations will be of importance as the technology is adopted and integrated into clinical practice and health systems.

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Appendix A – Search Strategies

	MEDLINE All (Ovid)	Results
1	Drug Therapy, Computer-Assisted/	1691
2	Electronic Prescribing/	1162
3	Medical Order Entry Systems/	2439
4	(eprescrib* or eprescription*).ti,ab,kw.	106
5	(e prescrib* or e prescription*).ti,ab,kw.	573
6	(epharmacy or epharmacies).ti,ab,kw.	0
7	(e pharmacy or e pharmacies).ti,ab,kw.	29
8	((computeri?ed or digital* or electronic* or internet or online or virtual*) adj2 (prescrib* or prescription*)).ti,ab,kw.	2311
9	((computeri?ed or digital* or electronic* or internet or online or virtual*) adj2 (pharmacy or pharmacies)).ti,ab,kw.	916
10	(electronic* adj2 (transmit* or transmission or send* or sent) adj2 (prescrib* or prescription*)).ti,ab,kw.	55
11	(e medicine management or emedicine management).ti,ab,kw.	0
12	(computer* adj3 (entry system* or order system* or order entry or order management or drug therap*)).ti,ab,kw.	1911
13	(pharmac* management system* or order entry system* or order management system*).ti,ab,kw.	747
14	((pharmac* or prescrib* or prescription*) adj3 software*).ti,ab,kw.	696
15	or/1-14 [e-prescribing]	9008
16	exp Narcotics/	140632
17	exp Opioid-Related Disorders/	32948
18	Alphaprodine/ or exp Buprenorphine/ or Butorphanol/ or exp Codeine/ or Dextromoramide/ or Dextropropoxyphene/ or exp Enkephalins/ or exp Fentanyl/ or Hydromorphone/ or Levorphanol/ or exp Meperidine/ or Meptazinol/ or exp Methadone/ or Morphine/ or Nalbuphine/ or Oxymorphone/ or Pentazocine/ or Phenoperidine/ or Pirinitramide/ or Tramadol/	105016
19	(opioid* or opiate* or narcotic*).ti,ab,kw.	143111
20	(alphaprodine or nisentil or prodine).ti,ab,kw.	147
21	(buprenorphine or buprenorphine or buprenex or buprex or prefin or subutex or temgesic or 6029 m or 6029m or rx6029m or suboxone).ti,ab,kw.	8859
22	(butorphanol or dolorex or moradol or stadol or torbugesic or bc 2627 or bc2627).ti,ab,kw.	1733
23	(codeine or ardinex or idocodeine or n methylmorphine or hydrocodone or codinovo or dicodid or dihydrocodeinone or hycodan or hycon or hydrocodeinonebitartrate or robidone or oxycodone or dihydrohydroxycodeinone or dihydrone or dinarkon or eucodal or oxiconum or oxycodeinon or oxycone or oxycontin or pancodine or percocet or theocodin or vicodin).ti,ab,kw.	10300
24	(dextromoramide or d moramide or palfium or pyrrolamidol).ti,ab,kw.	272
25	(dextropropoxyphene or propoxyphene or d propoxyphene or darvon).ti,ab,kw.	1474
26	(enkephalin* or dago or dagol or damge or damgo or rx 783006 or dpdpe).ti,ab,kw.	17709

27	(fentanyl or duragesic or durogesic or fentanest or fentora or phentanyl or r 4263 or r4263 or sublimaze or alfenta or alfentanil or fanaxal or limifen or rapifen or r 39209 or r39209 or sufentanil* or sulfentanil or sulfentanyl or r 30730 or r30730).ti,ab,kw.	25228
28	(hydromorphon* or dihydromorphinone or dilaudid or laudacon or palladone).ti,ab,kw.	2016
29	(levorphanol or levodroman or levorphan or levo dromoran or l dromoran).ti,ab,kw.	490
30	medical heroin.ti,ab,kw.	7
31	(meperidine or demerol or dolantin or dolargan or dolcontral or dolin or dolosal or dolsin or isonipecain or lidol or lydol or operidine or pethidine or promedol or dimethylmeperidine or isopromedol or trimeperidine).ti,ab,kw.	6032
32	(meptazinol or meptid or wy 22811 or wy22811).ti,ab,kw.	227
33	(methadone or biodone or dolophine or metadol or metasedin or symoron or methadose or methex or phenadone or physeptone or phymet or pinadone or amidone or methaddict or methadyl or acetylmethadol or alphacetylmethadol or dimepheptanol or levomethadyl or levoacetylmethadol or laam or methadol or orlaam or acemethadone).ti,ab,kw.	15560
34	(morphin* or morphia or duramorph or ms contin or morphia or oramorph sr or sdz 202 250 or sdz202250 or sdz202 250).ti,ab,kw.	58262
35	(nalbuphine or nubain* or en 2234a or en2234a).ti,ab,kw.	1087
36	(oxymorphone or numorphan or opana).ti,ab,kw.	682
37	(pentazocine or fortral or lexir or talwin).ti,ab,kw.	2462
38	(phenoperidine or fenoperidine or lealgin or operidine or r 1406 or r1406).ti,ab,kw.	157
39	(pirinitramid* or piritramid* or dipidolor or dipydolor).ti,ab,kw.	475
40	(tramadol or adolonta or amadol or biodalgic or biokanol or contramal or jutadol or k 315 or k315 or mtwtramadol or nobligan or prontofort or ranitidin 1a pharma or takadol or theradol or tiral or topalgic or tradol or tradolpuren or tradonal or tralgiol or trama or tramadorsch or tramabeta or tramadin or tramadoc or tramadoldolgit or tramadolhameln or tramadolor or tramadolratiopharm or tramadura or tramagetic or tramagit or tramake or tramal or tramex or tramundin or trasedal or ultram or xymel 50 or zamudol or zumalgic or zydol or zytram).ti,ab,kw.	6340
41	(acetorophine or acetylcodeine or acetymethadol or anileridine or apadoline or azidomorphine or benzhydrocodone or bezitramide or bremazocine or brompton mixture or ciramadol or cocomadol or codydramol or conorfone or cyclazocine or dextrorphan or dezocine or diamorphine or diconal or dihydroetorphine or dihydromorphine or dimethylthiambutene or dipipanone or dynorphin or enadoline or eptazocine or ethylketazocine or ethylmorphine or etonitazene or etorphine or etoxeridine or faxeladol or furethidine or gelonida or isalmadol or isomethodone or ketazocine or ketobemidone or ketogan or kyotorphin or lefetamine or levacetylmethadol or levomethadone or levorphanol or metazocine or methylsamidorphan or tilidine or nicodine or nicomorphine or noracymethadol or bufigen pentor nalbufin* or nalcryn or nalpain or onfor or noracymethadol or norbuprenorphine or normorphine or norpethidine or norpropoxyphene or nortramadol or oliceridine or oripavine or pentamorphone or phenadoxone or phencyclidine or picenadol or piminodine or piritramide or profadol or propiram or sameridine or samidorphan or semorphone or tapentadol or thebaine or tifluadom or tilidine or tonazocine).ti,ab,kw.	16508
42	or/16-41 [opioids]	259653
43	**15 and 42**	**353**

	Embase (Elsevier Embase.com)	Results
1	'computer assisted drug therapy'/de	931
2	'computerized provider order entry'/exp	6194
3	'physician order entry system'/de	340
4	(eprescrib* OR eprescription*):ti,ab,kw	1195
5	('e prescrib*' OR 'e prescription*'):ti,ab,kw	1192
6	(epharmacy OR epharmacies):ti,ab,kw	64
7	('e pharmacy' OR 'e pharmacies'):ti,ab,kw	88
8	((computeri?ed OR digital* OR electronic* OR internet OR online OR virtual*) NEAR/2 (prescrib* OR prescription*)):ti,ab,kw	4675
9	((computeri?ed OR digital* OR electronic* OR internet OR online OR virtual*) NEAR/2 (pharmacy OR pharmacies)):ti,ab,kw	1633
10	(electronic* NEAR/2 (transmit* OR transmission OR send* OR sent) NEAR/2 (prescrib* OR prescription*)):ti,ab,kw	93
11	('e medicine management' OR 'emedicine management'):ti,ab,kw	0
12	(computer* NEAR/3 ('entry system*' OR 'order system*' OR 'order entry' OR 'order management' OR 'drug therap*')):ti,ab,kw	2951
13	('pharmac* management system*' OR 'order entry system*' OR 'order management system*'):ti,ab,kw	1291
14	((pharmac* OR prescrib* OR prescription*) NEAR/3 software*):ti,ab,kw	1607
15	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	14275
16	'narcotic agent'/de OR 'narcotic analgesic agent'/de	42025
17	'opiate agonist'/de	6504
18	'acetylmethadol'/de OR 'alfentanil'/de OR 'alphaprodine'/de OR 'buprenorphine'/de OR 'buprenorphine plus naloxone'/de OR 'butorphanol'/de OR 'codeine'/de OR 'dextromoramide'/de OR 'dextropropoxyphene'/de OR 'enkephalin'/exp OR 'fentanyl'/de OR 'hydrocodone'/de OR 'hydromorphone'/de OR 'levorphanol'/de OR 'meptazinol'/de OR 'methadone'/de OR 'morphine'/de OR 'nalbuphine'/exp OR 'oxycodone'/de OR 'oxymorphone'/de OR 'pethidine'/de OR 'pentazocine'/de OR 'phenoperidine'/de OR 'piritramide'/de OR 'sufentanil'/de OR 'tramadol'/de OR 'trimeperidine'/de	298233
19	(opioid* OR opiate* OR narcotic*):ti,ab,kw	201063
20	(alphaprodine OR nisentil OR prodine):ti,ab,kw	148
21	(buprenorphine OR buprenorphine OR buprenex OR buprex OR prefin OR subutex OR temgesic OR '6029 m' OR 6029m OR rx6029m OR suboxone):ti,ab,kw	12885
22	(butorphanol OR dolorex OR moradol OR stadol OR torbugesic OR 'bc 2627' OR bc2627):ti,ab,kw	2121
23	(codeine OR ardinex OR idocodeine OR 'n methylmorphine' OR hydrocodone OR codinovo OR dicodid OR dihydrocodeinone OR hycodan OR hycon OR hydrocodeinonebitartrate OR robidone OR oxycodone OR dihydrohydroxycodeinone OR dihydrone OR dinarkon OR eucodal OR oxiconum OR oxycodeinon OR oxycone OR oxycontin OR pancodine OR percocet OR theocodin OR vicodin):ti,ab,kw	16490
24	(dextromoramide OR 'd moramide' OR palfium OR pyrrolamidol):ti,ab,kw	262
25	(dextropropoxyphene OR propoxyphene OR 'd propoxyphene' OR darvon):ti,ab,kw	1931

26	(enkephalin* OR dago OR dagol OR damge OR damgo OR 'rx 783006' OR dpdpe):ti,ab,kw	20278
27	(fentanyl OR duragesic OR durogesic OR fentanest OR fentora OR phentanyl OR 'r 4263' OR r4263 OR sublimaze OR alfenta OR alfentanil OR fanaxal OR limifen OR rapifen OR 'r 39209' OR r39209 OR sufentanil* OR sulfentanil OR sulfentanyl OR 'r 30730' OR r30730):ti,ab,kw	37218
28	(hydromorphon* OR dihydromorphinone OR dilaudid OR laudacon OR palladone):ti,ab,kw	3570
29	(levorphanol OR levodroman OR levorphan OR 'levo dromoran' OR 'l dromoran'):ti,ab,kw	606
30	'medical heroin':ti,ab,kw	12
31	(meperidine OR demerol OR dolantin OR dolargan OR dolcontral OR dolin OR dolosal OR dolsin OR isonipecain OR lidol OR lydol OR operidine OR pethidine OR promedol OR dimethylmeperidine OR isopromedol OR trimeperidine):ti,ab,kw	7643
32	(meptazinol OR meptid OR 'wy 22811' OR wy22811):ti,ab,kw	267
33	(methadone OR biodone OR dolophine OR metadol OR metasedin OR symoron OR methadose OR methex OR phenadone OR physeptone OR phymet OR pinadone OR amidone OR methaddict OR methadyl OR acetylmethadol OR alphacetylmethadol OR dimepheptanol OR levomethadyl OR levoacetylmethadol OR laam OR methadol OR orlaam OR acemethadone):ti,ab,kw	21687
34	(morphin* OR morphia OR duramorph OR 'ms contin' OR morphia OR 'oramorph sr' OR 'sdz 202 250' OR sdz202250 OR 'sdz202 250'):ti,ab,kw	78039
35	(nalbuphine OR nubain* OR 'en 2234a' OR en2234a):ti,ab,kw	1422
36	(oxymorphone OR numorphan OR opana):ti,ab,kw	958
37	(pentazocine OR fortral OR lexir OR talwin):ti,ab,kw	3330
38	(phenoperidine OR fenoperidine OR lealgin OR operidine OR 'r 1406' OR r1406):ti,ab,kw	178
39	(pirinitramid* OR piritramid* OR dipidolor OR dipydolor):ti,ab,kw	622
40	(tramadol OR adolonta OR amadol OR biodalgic OR biokanol OR contramal OR jutadol OR 'k 315' OR k315 OR mtwtramadol OR nobligan OR prontofort OR 'ranitidin 1a pharma5' OR takadol OR theradol OR tiral OR topalgic OR tradol OR tradolpuren OR tradonal OR tralgiol OR trama OR tramadorsch OR tramabeta OR tramadin OR tramadoc OR tramadoldolgit OR tramadolhameln OR tramadolor OR tramadolratiopharm OR tramadura OR tramagetic OR tramagit OR tramake OR tramal OR tramex OR tramundin OR trasedal OR ultram OR 'xymel 50' OR zamudol OR zumalgic OR zydol OR zytram):ti,ab,kw	10737

41	(acetorophine OR acetylcodeine OR acetymethadol OR anileridine OR apadoline OR azidomorphine OR benzhydrocodone OR bezitramide OR bremazocine OR 'brompton mixture' OR ciramadol OR cocomadol OR codydramol OR conorfone OR cyclazocine OR dextrorphan OR dezocine OR diamorphine OR diconal OR dihydroetorphine OR dihydromorphine OR dimethylthiambutene OR dipipanone OR dynorphin OR enadoline OR eptazocine OR ethylketazocine OR ethylmorphine OR etonitazene OR etorphine OR etoxeridine OR faxeladol OR furethidine OR gelonida OR isalmadol OR isomethodone OR ketazocine OR ketobemidone OR ketogan OR kyotorphin OR lefetamine OR levacetylmethadol OR levomethadone OR levorphanol OR metazocine OR methylsamidorphan OR tilidine OR nicodine OR nicomorphine OR noracymethadol OR 'bufigen pentor nalbufin*' OR nalcryn OR nalpain OR onfor OR noracymethadol OR norbuprenorphine OR normorphine OR norpethidine OR norpropoxyphene OR nortramadol OR oliceridine OR oripavine OR pentamorphone OR phenadoxone OR phencyclidine OR picenadol OR piminodine OR piritramide OR profadol OR propiram OR sameridine OR samidorphan OR semorphone OR tapentadol OR thebaine OR tifluadom OR tilidine OR tonazocine):ti,ab,kw	21063
42	#16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41	445721
43	**#15 AND #42**	**799**

	Scopus (Elsevier Scopus.com)	Results
1	(TITLE-ABS-KEY(((computeri?ed OR digital* OR electronic* OR internet OR online OR virtual*) W/2 (prescrib* OR prescription* OR pharmacy OR pharmacies)) OR (electronic* W/2 (transmit* OR transmission OR send* OR sent) W/2 (prescrib* OR prescription*)) OR "e medicine management" OR "emedicine management" OR (computer* W/3 ("entry system*" OR "order system*" OR "order entry" OR "order management" OR "drug therap*")) OR "pharmac* management system*" OR "order entry system*" OR "order management system*" OR ((pharmac* OR prescrib* OR prescription*) W/3 software*))) AND NOT ((INDEX(medline)) OR (INDEX(embase)))	2182
2	(TITLE-ABS-KEY(opioid* OR opiate* OR narcotic* OR alphaprodine OR nisentil OR prodine OR buprenorphine OR buprenorphine OR buprenex OR buprex OR prefin OR subutex OR temgesic OR "6029 m" OR 6029m OR rx6029m OR suboxone OR butorphanol OR dolorex OR moradol OR stadol OR torbugesic OR "bc 2627" OR bc2627 OR codeine OR ardinex OR idocodeine OR "n methylmorphine" OR hydrocodone OR codinovo OR dicodid OR dihydrocodeinone OR hycodan OR hycon OR hydrocodeinonebitartrate OR robidone OR oxycodone OR dihydrohydroxycodeinone OR dihydrone OR dinarkon OR eucodal OR oxiconum OR oxycodeinon OR oxycone OR oxycontin OR pancodine OR percocet OR theocodin OR vicodin OR dextromoramide OR "d moramide" OR palfium OR pyrrolamidol OR dextropropoxyphene OR propoxyphene OR "d propoxyphene" OR darvon OR enkephalin* OR dago OR dagol OR damge OR damgo OR "rx 783006" OR dpdpe OR fentanyl OR duragesic OR durogesic OR fentanest OR fentora OR phentanyl OR "r 4263" OR r4263 OR sublimaze OR alfenta OR alfentanil OR fanaxal OR limifen OR rapifen OR "r 39209" OR r39209 OR sufentanil* OR sulfentanil OR sulfentanyl OR "r 30730" OR r30730 OR hydromorphon* OR dihydromorphinone OR dilaudid OR laudacon OR palladone OR levorphanol OR levodroman OR levorphan OR "levo dromoran" OR "l dromoran" OR "medical heroin" OR meperidine OR demerol OR dolantin OR dolargan OR dolcontral OR dolin OR dolosal OR dolsin OR isonipecain OR lidol OR lydol OR operidine OR pethidine OR promedol OR dimethylmeperidine OR isopromedol OR trimeperidine OR meptazinol OR meptid OR "wy 22811" OR wy22811 OR methadone OR biodone OR dolophine OR metadol OR metasedin OR symoron OR methadose OR methex OR phenadone OR physeptone OR phymet OR pinadone OR amidone OR methaddict OR methadyl OR acetylmethadol OR alphacetylmethadol OR dimepheptanol OR levomethadyl OR levoacetylmethadol OR laam OR methadol OR orlaam OR acemethadone OR morphin* OR morphia OR duramorph OR "ms contin" OR morphia OR "oramorph sr" OR "sdz 202 250" OR sdz202250 OR "sdz202 250" OR nalbuphine OR nubain* OR "en 2234a" OR en2234a OR oxymorphone OR numorphan OR opana OR pentazocine OR fortral OR lexir OR talwin OR phenoperidine OR fenoperidine OR lealgin OR operidine OR "r 1406" OR r1406 OR pirinitramid* OR piritramid* OR dipidolor OR dipydolor OR tramadol OR adolonta OR amadol OR biodalgic OR biokanol OR contramal OR jutadol OR "k 315" OR k315 OR mtwtramadol OR nobligan OR prontofort OR "ranitidin 1a pharma5" OR takadol OR theradol OR tiral OR topalgic OR tradol OR tradolpuren OR tradonal OR tralgiol OR trama OR tramadorsch OR tramabeta OR tramadin OR tramadoc OR tramadoldolgit OR tramadolhameln OR tramadolor OR tramadolratiopharm OR tramadura OR tramagetic OR tramagit OR tramake OR tramal OR tramex OR tramundin OR trasedal OR ultram OR "xymel 50" OR zamudol OR zumalgic OR zydol OR zytram OR acetorophine OR acetylcodeine OR acetymethadol OR anileridine OR apadoline OR azidomorphine OR benzhydrocodone OR bezitramide OR bremazocine OR "brompton mixture" OR ciramadol OR cocomadol OR codydramol OR conorfone OR cyclazocine OR dextrorphan OR dezocine OR diamorphine OR diconal OR dihydroetorphine OR dihydromorphine OR dimethylthiambutene OR dipipanone OR dynorphin OR enadoline OR eptazocine OR ethylketazocine OR ethylmorphine OR etonitazene OR etorphine OR etoxeridine OR faxeladol OR furethidine OR gelonida OR isalmadol OR isomethodone OR ketazocine OR ketobemidone OR ketogan OR kyotorphin OR lefetamine OR levacetylmethadol OR levomethadone OR levorphanol OR metazocine OR methylsamidorphan OR tilidine OR nicodine OR nicomorphine OR noracymethadol OR "bufigen pentor nalbufin*" OR nalcryn OR nalpain OR onfor OR noracymethadol OR	38287

	norbuprenorphine OR normorphine OR norpethidine OR norpropoxyphene OR nortramadol OR oliceridine OR oripavine OR pentamorphone OR phenadoxone OR phencyclidine OR picenadol OR piminodine OR piritramide OR profadol OR propiram OR sameridine OR samidorphan OR semorphone OR tapentadol OR thebaine OR tifluadom OR tilidine OR tonazocine)) AND NOT ((INDEX(medline)) OR (INDEX(embase)))	
3	**#1 and #2 *[using search history tool]***	**31**

	Dissertations & Theses Global (ProQuest)	Results
1	TITLE(((computeri?ed OR digital* OR electronic* OR internet OR online OR virtual*) N/2 (prescrib* OR prescription* OR pharmacy OR pharmacies)) OR (electronic* N/2 (transmit* OR transmission OR send* OR sent) N/2 (prescrib* OR prescription*)) OR "e medicine management" OR "emedicine management" OR (computer* N/3 ("entry system*" OR "order system*" OR "order entry" OR "order management" OR "drug therap*")) OR "pharmac* management system*" OR "order entry system*" OR "order management system*" OR ((pharmac* OR prescrib* OR prescription*) N/3 software*)) OR ABSTRACT(((computeri?ed OR digital* OR electronic* OR internet OR online OR virtual*) N/2 (prescrib* OR prescription* OR pharmacy OR pharmacies)) OR (electronic* N/2 (transmit* OR transmission OR send* OR sent) N/2 (prescrib* OR prescription*)) OR "e medicine management" OR "emedicine management" OR (computer* N/3 ("entry system*" OR "order system*" OR "order entry" OR "order management" OR "drug therap*")) OR "pharmac* management system*" OR "order entry system*" OR "order management system*" OR ((pharmac* OR prescrib* OR prescription*) N/3 software*))	391
2	TITLE(opioid* OR opiate* OR narcotic* OR alphaprodine OR nisentil OR prodine OR buprenorphine OR buprenorphine OR buprenex OR buprex OR prefin OR subutex OR temgesic OR "6029 m" OR 6029m OR rx6029m OR suboxone OR butorphanol OR dolorex OR moradol OR stadol OR torbugesic OR "bc 2627" OR bc2627 OR codeine OR ardinex OR idocodeine OR "n methylmorphine" OR hydrocodone OR codinovo OR dicodid OR dihydrocodeinone OR hycodan OR hycon OR hydrocodeinonebitartrate OR robidone OR oxycodone OR dihydrohydroxycodeinone OR dihydrone OR dinarkon OR eucodal OR oxiconum OR oxycodeinon OR oxycone OR oxycontin OR pancodine OR percocet OR theocodin OR vicodin OR dextromoramide OR "d moramide" OR palfium OR pyrrolamidol OR dextropropoxyphene OR propoxyphene OR "d propoxyphene" OR darvon OR enkephalin* OR dago OR dagol OR damge OR damgo OR "rx 783006" OR dpdpe OR fentanyl OR duragesic OR durogesic OR fentanest OR fentora OR phentanyl OR "r 4263" OR r4263 OR sublimaze OR alfenta OR alfentanil OR fanaxal OR limifen OR rapifen OR "r 39209" OR r39209 OR sufentanil* OR sulfentanil OR sulfentanyl OR "r 30730" OR r30730 OR hydromorphon* OR dihydromorphinone OR dilaudid OR laudacon OR palladone OR levorphanol OR levodroman OR levorphan OR "levo dromoran" OR "l dromoran" OR "medical heroin" OR meperidine OR demerol OR dolantin OR dolargan OR dolcontral OR dolin OR dolosal OR dolsin OR isonipecain OR lidol OR lydol OR operidine OR pethidine OR promedol OR dimethylmeperidine OR isopromedol OR trimeperidine OR meptazinol OR meptid OR "wy 22811" OR wy22811 OR methadone OR biodone OR dolophine OR metadol OR metasedin OR symoron OR methadose OR methex OR phenadone OR physeptone OR phymet OR pinadone OR amidone OR methaddict OR methadyl OR acetylmethadol OR alphacetylmethadol OR dimepheptanol OR levomethadyl OR levoacetylmethadol OR laam OR methadol OR orlaam OR acemethadone OR morphin* OR morphia OR duramorph OR "ms contin" OR morphia OR "oramorph sr" OR "sdz 202 250" OR sdz202250 OR "sdz202 250" OR nalbuphine OR nubain* OR "en 2234a" OR en2234a OR oxymorphone OR numorphan OR opana OR pentazocine OR fortral OR lexir OR talwin OR phenoperidine OR fenoperidine OR lealgin OR operidine OR "r 1406" OR r1406 OR pirinitramid* OR piritramid* OR dipidolor OR dipydolor OR tramadol OR adolonta OR amadol OR biodalgic OR biokanol OR contramal OR jutadol OR "k 315" OR k315 OR mtwtramadol OR nobligan OR prontofort OR "ranitidin 1a pharma5" OR takadol OR theradol OR tiral OR topalgic OR tradol OR tradolpuren OR tradonal OR tralgiol OR trama OR tramadorsch OR tramabeta OR tramadin OR tramadoc OR tramadoldolgit OR tramadolhameln OR tramadolor OR tramadolratiopharm OR tramadura OR tramagetic OR tramagit OR tramake OR tramal OR tramex OR tramundin OR trasedal OR ultram OR "xymel 50" OR zamudol OR zumalgic OR zydol OR zytram OR acetorophine OR acetylcodeine OR acetymethadol OR anileridine OR apadoline OR azidomorphine OR benzhydrocodone OR bezitramide OR bremazocine OR "brompton mixture" OR ciramadol OR cocomadol OR codydramol OR conorfone OR cyclazocine OR dextrorphan OR dezocine OR diamorphine OR diconal OR dihydroetorphine OR dihydromorphine OR dimethylthiambutene OR dipipanone OR dynorphin OR enadoline	12511

	OR eptazocine OR ethylketazocine OR ethylmorphine OR etonitazene OR etorphine OR etoxeridine OR faxeladol OR furethidine OR gelonida OR isalmadol OR isomethodone OR ketazocine OR ketobemidone OR ketogan OR kyotorphin OR lefetamine OR levacetylmethadol OR levomethadone OR levorphanol OR metazocine OR methylsamidorphan OR tilidine OR nicodine OR nicomorphine OR noracymethadol OR "bufigen pentor nalbufin*" OR nalcryn OR nalpain OR onfor OR noracymethadol OR norbuprenorphine OR normorphine OR norpethidine OR norpropoxyphene OR nortramadol OR oliceridine OR oripavine OR pentamorphone OR phenadoxone OR phencyclidine OR picenadol OR piminodine OR piritramide OR profadol OR propiram OR sameridine OR samidorphan OR semorphone OR tapentadol OR thebaine OR tifluadom OR tilidine OR tonazocine) OR ABSTRACT(opioid* OR opiate* OR narcotic* OR alphaprodine OR nisentil OR prodine OR buprenorphine OR buprenorphine OR buprenex OR buprex OR prefin OR subutex OR temgesic OR "6029 m" OR 6029m OR rx6029m OR suboxone OR butorphanol OR dolorex OR moradol OR stadol OR torbugesic OR "bc 2627" OR bc2627 OR codeine OR ardinex OR idocodeine OR "n methylmorphine" OR hydrocodone OR codinovo OR dicodid OR dihydrocodeinone OR hycodan OR hycon OR hydrocodeinonebitartrate OR robidone OR oxycodone OR dihydrohydroxycodeinone OR dihydrone OR dinarkon OR eucodal OR oxiconum OR oxycodeinon OR oxycone OR oxycontin OR pancodine OR percocet OR theocodin OR vicodin OR dextromoramide OR "d moramide" OR palfium OR pyrrolamidol OR dextropropoxyphene OR propoxyphene OR "d propoxyphene" OR darvon OR enkephalin* OR dago OR dagol OR damge OR damgo OR "rx 783006" OR dpdpe OR fentanyl OR duragesic OR durogesic OR fentanest OR fentora OR phentanyl OR "r 4263" OR r4263 OR sublimaze OR alfenta OR alfentanil OR fanaxal OR limifen OR rapifen OR "r 39209" OR r39209 OR sufentanil* OR sulfentanil OR sulfentanyl OR "r 30730" OR r30730 OR hydromorphon* OR dihydromorphinone OR dilaudid OR laudacon OR palladone OR levorphanol OR levodroman OR levorphan OR "levo dromoran" OR "l dromoran" OR "medical heroin" OR meperidine OR demerol OR dolantin OR dolargan OR dolcontral OR dolin OR dolosal OR dolsin OR isonipecain OR lidol OR lydol OR operidine OR pethidine OR promedol OR dimethylmeperidine OR isopromedol OR trimeperidine OR meptazinol OR meptid OR "wy 22811" OR wy22811 OR methadone OR biodone OR dolophine OR metadol OR metasedin OR symoron OR methadose OR methex OR phenadone OR physeptone OR phymet OR pinadone OR amidone OR methaddict OR methadyl OR acetylmethadol OR alphacetylmethadol OR dimepheptanol OR levomethadyl OR levoacetylmethadol OR laam OR methadol OR orlaam OR acemethadone OR morphin* OR morphia OR duramorph OR "ms contin" OR morphia OR "oramorph sr" OR "sdz 202 250" OR sdz202250 OR "sdz202 250" OR nalbuphine OR nubain* OR "en 2234a" OR en2234a OR oxymorphone OR numorphan OR opana OR pentazocine OR fortral OR lexir OR talwin OR phenoperidine OR fenoperidine OR lealgin OR operidine OR "r 1406" OR r1406 OR pirinitramid* OR piritramid* OR dipidolor OR dipydolor OR tramadol OR adolonta OR amadol OR biodalgic OR biokanol OR contramal OR jutadol OR "k 315" OR k315 OR mtwtramadol OR nobligan OR prontofort OR "ranitidin 1a pharma5" OR takadol OR theradol OR tiral OR topalgic OR tradol OR tradolpuren OR tradonal OR tralgiol OR trama OR tramadorsch OR tramabeta OR tramadin OR tramadoc OR tramadoldolgit OR tramadolhameln OR tramadolor OR tramadolratiopharm OR tramadura OR tramagetic OR tramagit OR tramake OR tramal OR tramex OR tramundin OR trasedal OR ultram OR "xymel 50" OR zamudol OR zumalgic OR zydol OR zytram OR acetorophine OR acetylcodeine OR acetymethadol OR anileridine OR apadoline OR azidomorphine OR benzhydrocodone OR bezitramide OR bremazocine OR "brompton mixture" OR ciramadol OR cocomadol OR codydramol OR conorfone OR cyclazocine OR dextrorphan OR dezocine OR diamorphine OR diconal OR dihydroetorphine OR dihydromorphine OR dimethylthiambutene OR dipipanone OR dynorphin OR enadoline OR eptazocine OR ethylketazocine OR ethylmorphine OR etonitazene OR etorphine OR etoxeridine OR faxeladol OR furethidine OR gelonida OR isalmadol OR isomethodone OR ketazocine OR ketobemidone OR ketogan OR kyotorphin OR lefetamine OR levacetylmethadol OR levomethadone OR levorphanol OR metazocine OR	

	methylsamidorphan OR tilidine OR nicodine OR nicomorphine OR noracymethadol OR "bufigen pentor nalbufin*" OR nalcryn OR nalpain OR onfor OR noracymethadol OR norbuprenorphine OR normorphine OR norpethidine OR norpropoxyphene OR nortramadol OR oliceridine OR oripavine OR pentamorphone OR phenadoxone OR phencyclidine OR picenadol OR piminodine OR piritramide OR profadol OR propiram OR sameridine OR samidorphan OR semorphone OR tapentadol OR thebaine OR tifluadom OR tilidine OR tonazocine)	
3	**#1 and #2 *[using search history tool]***	**12**

Google Search Used	Records Screened	Potentially Relevant Records
(electronic prescribing | e-prescribing | eprescribing) opioids filetype:pdf	Up to page 9	3
(electronic prescribing | e-prescribing | eprescribing) opiates filetype:pdf	Up to page 6	0
(electronic prescribing | e-prescribing | eprescribing) narcotics filetype:pdf	Up to page 7	0
(electronic prescribing | e-prescribing | eprescribing) (buprenorphine | suboxone) filetype:pdf	Up to page 3	1
(electronic prescribing | e-prescribing | eprescribing) (codeine | hydrocodone | oxycodone | oxycontin | vicodin)) filetype:pdf	Up to page 2	0
(electronic prescribing | e-prescribing | eprescribing) (dextropropoxyphene | propoxyphene) filetype:pdf	Up to page 3	0
(electronic prescribing | e-prescribing | eprescribing) (fentanyl | alfentanil | sufentanil) filetype:pdf	Up to page 5	0
(electronic prescribing | e-prescribing | eprescribing) (hydromorphone | dilaudid) filetype:pdf	Up to page 2	0
(electronic prescribing | e-prescribing | eprescribing) (levorphanol) filetype:pdf	Up to page 3	0
(electronic prescribing | e-prescribing | eprescribing) (meperidine | promedol) filetype:pdf	Up to page 2	0
(electronic prescribing | e-prescribing | eprescribing) (methadone | methadyl) filetype:pdf	Up to page 3	0
(electronic prescribing | e-prescribing | eprescribing) (morphine | morphia) filetype:pdf	Up to page 3	0
(electronic prescribing | e-prescribing | eprescribing) (oxymorphone | pentazocine | tramadol) filetype:pdf	Up to page 3	0
Included Resources: 1		

Appendix B – Data Extraction Codebook

NOTES

Please enter not applicable (NA) or not reported (NR) as needed instead of leaving blanks.

Copy-paste information directly from the article, no need to reword at this time.

Enter in information as presented in the article (e.g. no need to convert participant characteristics to percentages if not already provided).

Overview

SECTION 1. General Information

General Information	
Covidence Field	**Description**
Study ID	Covidence ID#
Title	Title of paper/report that data are extracted from
Authors	Enter the names of the authors [can be copied from Covidence]
Publishing source name	Enter the journal name or name of the publishing source (if the journal name is not available).
Year of publication	Enter the year the study was published. **Example:** 2015
Funding source name	Enter the source of funding support for the research. **Example:** CIHR; Bayer. Enter 'None' for no funding source.

SECTION 2. Characteristics of included studies

Characteristics of included studies	
Covidence Field	**Description**
Country in which the study was conducted	Select the country in which the study was conducted from drop down. Enter other country if not in drop down list.
Methods	
Objective	Copy-paste objective of study.
Method of Data Collection	Enter how data was collected. **Example:** Qualitative, quantitative
Data Sources	Enter where the participants or data are coming from. **Example:** Databases, charts, etc.
Study Design	Select type of study design from drop down menu.

Characteristics of included studies	
Covidence Field	**Description**
	Enter in other study design type if not available in list.
Type of qualitative methods	Enter type of qualitative methods if qualitative study. **Example:** Grounded theory, phenomenology, etc.
Main Outcome Being Measured	Copy-paste the main study outcome being measured. If the study is not clear about main vs secondary outcome, record outcome measures here. **Example:** Medication adherence via Patient Medication Adherence Questionnaire (PMAQ)
Secondary Outcome	Copy-paste the secondary outcome for the study (if applicable).
Participants	
Total number of participants	Enter the total number of participants enrolled in the study.
Sample size post intervention	Enter the number of participants in the sample following the intervention (if applicable)
Sample size pre intervention	Enter the number of participants in the sample prior to implementation of the intervention (if applicable)
Type of Population	Enter whether the population is general public or a clinical population. If clinical, include what type of condition. If mixed population, please include list of populations included. **Example:** Clinical (stroke) OR Clinical (stroke: 50%; spinal cord injury: 50%)
Inclusion criteria	Copy-paste the patient inclusion criteria for the study.
Exclusion criteria	Copy-paste the patient exclusion criteria for the study.
Population Characteristics	Enter in the population characteristics into the table provided on Covidence for the population of interest and control group (if applicable). Provide % breakdowns if available.
Age	Enter the age of the study participants as reported by the article. **Example:** Mean = 65.4 SD 2 years
Sex	Enter the sex of participants. Please denote if percentage. **Example:** Male: 54; Female: 50 OR Male: 55%; Female: 45%
Gender	Enter the gender of the participants. Please denote if percentage. **Example:** Men: 54; Women: 27; NB/Trans: 20
Ethnicity/Race	Copy and paste the breakdown of participants' race if provided. Please denote if percentage.
Income	Copy and paste the breakdown of participants' income if provided. Please denote if percentage.
Education	Copy and paste the breakdown of educational backgrounds if provided. Please denote if percentage.
Marital Status	Copy and paste the breakdown of participants' marital status if provided. Please denote if percentage.
Household Composition	Copy and paste the breakdown of household composition if provided. Please denote if percentage. **Example:** Living alone: 10; Living with spouse/partner: 13
Employment Status	Copy and paste the breakdown of participants' employment status if provided. Please denote if percentage.
Geographical Location	Copy and paste if the breakdown of the participants' geographical location. Please denote if percentage. **Example:** Rural: 50; Urban: 25
Comorbidities	Enter details of any comorbid conditions present in the study sample. If a comorbidity scale/index was used report the results.

Characteristics of included studies	
Covidence Field	**Description**
	Example: Heart disease (45%), COPD (13%), Cancer (8%); Charlson Comorbidity Index (1.2)
Where are they residing at time of study	Enter in details of where participants are living at the type of the study. **Example:** Community: 45; In-patient rehabilitation: 60
Religion	Copy and paste the breakdown of participants' religion if provided. Please denote if percentage.
Social Capital	Copy and paste the breakdown of participants' social networks if provided. Please denote if percentage. **Example**: Number of contacts: 4; Frequency of contact: 3x a week
Comorbidities	Enter details of any comorbid conditions present in the treatment group. If a comorbidity scale/index was used report the results. **Example:** Heart disease (45%), COPD (13%), Cancer (8%); Charlson Comorbidity Index (1.2)
Note: *Adopted from PROGRESS-PLUS equity variables (https://methods.cochrane.org/equity/projects/evidence-equity/progress-plus).	

SECTION 3. E-Prescribing Characteristics

E-PRESCRIBING CHARACTERISTICS	
Covidence Field	**Description**
E-Prescribing Setting	Enter in where the e-prescribing is taking place. **Example:** Emergency department, community
Type of Opioid Being Prescribed	Enter the type of opioid being prescribing using e-prescription software. **Example:** Morphine, Percocet, etc.
Other drugs being reported on	Copy-paste any other drugs that are mentioned in relation to e-prescribing.
Components of E-Prescribing	Enter in any components of e-prescribing that are being used in the study. **Example**: Alerts, two-way communication, etc.

SECTION 4. Intervention Characteristics

INTERVENTION CHARACTERISTICS	
Covidence Field	**Description**
Description/aim of intervention.	Copy and paste the description or aim of the intervention
Content	Copy and paste what the intervention includes. **Example**: Training program on how to use e-prescribing
Description of treatment arms	Enter or copy and paste the description of the treatment arms in the study. **Example:** Patients randomized into following groups: Aged 65-75 years to placebo, aged 65-75 years to Flublok
Frequency	Enter number of times intervention occurs. **Example:** How many times per week or month.

INTERVENTION CHARACTERISTICS	
Covidence Field	**Description**
Duration	Enter the duration of the intervention. **Example:** How many weeks or months did the intervention last.
Stand alone or multi-component program	Enter whether or not the intervention is a stand alone or part of a larger intervention. **Example:** Multicomponent would included e-prescribing and an educational component.
Format	Enter if the format of the intervention is individual (one-to-one) or in a group setting.
Delivery	Enter who administer the program. **Example:** Community pharmacist
Method of Delivery	Enter in how the program was delivered. **Example:** In-person, online, etc.
Technology	Enter in the method and type of delivery if technology was used. Enter in if the intervention took place in real time. **Example:** Education sessions took place via Zoom.
Tailoring	Enter if the intervention was planned to be personalized, titrated, or adapted. Describe what, why, when, and how.
Modification	Enter if the intervention was modified during the course of the study. Include the changes (what, why, when, and how).
Setting	Enter where the intervention took place.

SECTION 5. Study Outcomes & Findings

OUTCOMES *Only report outcomes & findings related to e-prescribing and opioids*	
Covidence Field	**Description**
Results from abstract	Copy and paste the results written in the abstract.
Conclusions from abstract	Copy and paste the conclusions from the abstract.
Results/Key findings from main text	Copy and paste the results written in the main text.
Conclusion from main text	Copy and paste the conclusions from the main text.

Appendix C – Descriptive summary of included studies (n=33)

Article[†] Author, Year Country	**Sample Size**	**Sample**		**Main Outcome Related to Opioid Use & E-prescribing**	**E-Prescribing Setting**	**Key Findings/Results related to Opioid Use & E-prescribing**
		Socio-demographic Information	**Clinical Characteristics**			
Abdel-Qader et al., 2010[46] United Kingdom	N=1,038 people	Age: NR Sex: Females: 540 Males: 498	Clinical (Acute Care Discharge)	Prescribing errors	Discharge (Acute Care)	- The most frequently recorded individual medications associated with an error included codeine (n=18 [2.9%]). - The most frequent high-risk medications (associated with erroneous orders) included codeine (n=18 [22.2%] and morphine (n=7 [8.6%])
Ancker et al., 2021[47] USA	N=22,113 patients (Weill Cornell Medicine: n=18,218; Institute for Family Health: n=3895)	Age: NR Sex: Weill Cornell Medicine: 49.4% Female (n=9139) Institute for Family Health: 68.6% Female (n=2705)	Clinical	Proportion of guideline-concordant (contained 12 pills or fewer, i.e., a 3-day supply) prescriptions and number of mouse clicks and keystrokes to place order	Ambulatory[*]	- At Weill Cornell Medicine, guideline-concordant prescriptions immediately rose from an average of 12% to 31% of all prescriptions - At Institute for Family Health, guideline-concordant prescriptions remained at 44% - The intervention (to test the effect of a default prescription order intervention on opioid prescribing choices) was not associated with any change in total volume of opioid prescriptions - There was a 62.7% decrease in total keystroke (3,552 in the 6 months before the default prescription order intervention to 1,323 in the 6 months afterward)
Ariosto et al., 2011[78] USA	N=30,321 patients; N=2767 alerts	Override: Mean Age: 54.5 years SD 16.4 No override: Mean Age: 54.7 years SD 16.7	Clinical (Acute Care Discharge)	Prescribing rate for prescriptions with allergy alerts triggered and overwritten	Discharge (Acute Care)	- The override rate for the patient's first opiate alerts was 89% - Opiate allergy override rate was 93% for all admissions and re-admissions - Over half of all discharges had opiates ordered during their stay and of those, patients with recorded

Article[†] Author, Year Country	**Sample Size**	**Sample**		**Main Outcome Related to Opioid Use & E-prescribing**	**E-Prescribing Setting**	**Key Findings/Results related to Opioid Use & E-prescribing**
		Socio-demographic Information	**Clinical Characteristics**			
		Sex: Female: n=1900 (69%) Male: n=867 (31%)				opiate allergies (9.1%), 25461 CPOE opiate allergy alerts were triggered. - Override rates remained high, with 80% for advanced practice nurses (APN) and 90% for physicians, with APNs less likely to override the patient's first opiate alert compared to physicians (P=.001)
Bicket et al., 2017[48] USA	N=451 patients	Mean Age: 47.5 SD 17.4 years Range (18-100 years) Sex: NR	Clinical Outpatient	Prescribing rate and errors	Ambulatory	- The most prescribed opioid was oxycodone immediate release (IR) (71%) with other opioids being prescribed less often (hydromorphone IR (10%), morphine IR (3%), oxycodone continuous release (CR; 3%), fentanyl patches (3%), tramadol IR (3%), and morphine CR (2%)) - 92% of formulation of opioid prescribed to adults was in tablet form - A similar number of handwritten (47%) and hospital computer-generated (47%) prescriptions was found for the opioid prescriptions; however, fewer prescriptions were generated by non-hospital computer software (7%). - All prescriptions containing a best-practice deviation or lacking two patient identifiers were written by hand and not computer-generated
Chiu et al., 2018[49] USA	N=2,910 patients	Pre-implementation: Mean Age: 54.4 years SD 17.3	Clinical (Outpatient surgery)	Prescribing quantity and dose and refill rate	Outpatient (Surgical)	- The median number of opioid pills prescribed decreased from 30 to 20 per prescription post – implementation (P<.001).

Article[†] Author, Year Country	**Sample Size**	**Sample**		**Main Outcome Related to Opioid Use & E-prescribing**	**E-Prescribing Setting**	**Key Findings/Results related to Opioid Use & E-prescribing**
		Socio-demographic Information	**Clinical Characteristics**			
		Sex: Male 479 (33.1%) Female 968 (66.9%) Post-implementation: Mean Age: 54.5 years SD 16.4 Sex: Male: 483 (33.0%) Female: 980 (67.0%)				- The percentage of prescriptions written for 30 pills decreased, from before to after the default change, from 39.7% to 12.9% (P<.001) - The percentage of prescriptions written for 12 pills increased, from before to after the default change, from 2.1% to 24.6% (P<.001) - No statistical difference was found in opioid refill rates from before to after the default change (3.0% vs 1.5%; P=.41). - Results from adjusted linear regression analysis indicated that the number of opioid pills decreased by 5.22 (95% CI, −6.12 to −4.32) per prescription - After the default change, total opioid MME prescribed decreased by 34.41 (95% CI, −41.36 to −27.47) after the default change
Danovich et al., 2019[50] USA	N=44,626 patients	Pre-implementation: Mean Age: 47.5 years SD 16.7 Sex: Males: 48% Females: 52% Post-implementation: 48.2 years SD 16.8 Sex:	Clinical (Emergency Department)	Prescribing rate	Emergency Department	- Between the pre- and post-implementation stage of the New York State Electronic Prescribing Mandate, there was an absolute decrease of 724 (53%) opioid prescriptions (1,366 vs. 642; P<.0001), which is an absolute difference of 2.3% (95% CI 2.0% - 2.6%).

Article[†] Author, Year Country	**Sample Size**	**Sample**		**Main Outcome Related to Opioid Use & E-prescribing**	**E-Prescribing Setting**	**Key Findings/Results related to Opioid Use & E-prescribing**
		Socio-demographic Information	**Clinical Characteristics**			
		Males: 54% Females: 46%				
Delgado Sánchez et al., 2005[51] Spain	N=41,931 treatment orders	Age: NR Sex: NR	Clinical	Prescribing errors	Hospital Pharmacy	- 62 of 1,183 (3.7%) prescription and transcription errors involved opioid pain relievers.
Everson et al., 2020[52] USA	N=459 observations	Age: NR Sex: NR	Clinical	Prescribing rates	Not Reported	- The population-weighted percent of opioids prescribed using EPCS increased from 0% in 2013 to 27% in 2018 - From 2013 to 2018, national rates of opioid prescriptions decreased from 78 to 53 prescriptions per 100 persons - By 2018, EPCS increased to 69.4% in mandated states and 23.6% in non-mandated states - In multivariable models, it was found that a 10 percentage-point increase in the use of EPCS was associated with an additional 2 prescriptions per 100 persons (95% CI, 1.3 - 2.8) and a 0.8% (95% CI, 0.06% - 1.5%) increase in MME per 100 persons
Fischer et al., 2011[30] USA	N=280,081 patients; N=3,634 prescribers	N per Age: <1 year 1,108 (0.4%) 1-18 years 42,372 (15.1%) 19-44 years 68,449 (24.4%) 45-54 years 53,147 (19.0%) 55-65 years	General Public	Primary nonadherence	Outpatient	- Of all e-prescriptions, opioids made up 3% - The rate of primary nonadherence for opioids was 23.9%

Article[†] Author, Year Country	**Sample Size**	**Sample**		**Main Outcome Related to Opioid Use & E-prescribing**	**E-Prescribing Setting**	**Key Findings/Results related to Opioid Use & E-prescribing**
		Socio-demographic Information	**Clinical Characteristics**			
		60,611 (21.6%) 65 years 54,389 (19.4%) Sex: Males: 111,003 (39.6%) Females: 169,021 (60.3%)				
George et al., 2016[53] USA	N=4,218 CS discharge pediatric prescriptions	Mean Age: 9 years SD 6.1 Range (0–21) Sex: NR	Clinical (Pediatric)	Prescribing trends and errors	Discharge (Pediatric)	- The most prescribed opioid was oxycodone (uncombined) (73%) - Codeine was prescribed in combination with acetaminophen (7%) - 98% of children under 6 years, and 16% of children over 12 years were prescribed liquid formulations - A subset of 700 regenerated prescriptions were legible (drug, amount dispensed, dose, patient demographics, and provider name) and used best prescribing practice - 25 of the 700 regenerated prescriptions had incorrect weights - 14 varied by 10% or less, 2 varied by >15%, 1 resulted in underdosing, and the other in overdosing
Griffey et al., 2012[54] USA	N=1,407 patients; N=2,398 orders	Intervention: Mean Age: 74 years SD 7.4 Sex: Female: 61% Control:	Clinical (Emergency Department)	Medication ordering consistent with recommendations	Emergency Department	- There was a significant difference in agreement with recommendations between the ON and OFF periods (36% vs. 26%; P<.001) for opioids - Hydromorphone was the second most common drug that was written at 10-fold orders (10x preferred dose) (6 of 38 orders)

Article[†] Author, Year Country	**Sample Size**	**Sample**		**Main Outcome Related to Opioid Use & E-prescribing**	**E-Prescribing Setting**	**Key Findings/Results related to Opioid Use & E-prescribing**
		Socio-demographic Information	**Clinical Characteristics**			
		Mean Age: 75 years SD 7.2 Sex: Female: 60%				
Hickman et al., 2018[55] USA	N=312 prescriber responses	Age: NR Sex: NR	Clinical (Outpatient)	Prescribing errors	Outpatient	- Top reasons for the discontinued erroneous orders were medication ordered for wrong patient (27.8%, n=60); wrong drug ordered (18.5%, n=40); and duplicate order placed (14.4%, n=31) - Oxycodone was the most frequent drug discontinued error (3%)
Hung et al., 2021[56] Taiwan	N=1,719,478 prescriptions	Age: NR Sex: NR	Clinical (Outpatient)	Prescribing errors	Discharge	- Morphine was the third most common potential duplicated medication for the nervous system category (3.8%, n=2472) following the intervention.
Jones et al., 2021[57] USA	N=5,776 surgeries	Mean Age: 13 years, IQR (9-16) Sex: Males: 53% Females: 47%	Clinical (Pediatric Orthopaedic Surgery)	Provider compliance and prescribing quantity	Discharge (Pediatric Surgery)	- Greater than 90% compliance with the opioid guidelines was achieved and sustained for 20 months - There was a 54% reduction in opioids prescribed, from 71 MME per patient to 33 MME per patient in opioids prescribed and the reduction was sustained for 12 months
Kearney et al., 2022[58] USA	N=1,208 surgeries; N=1,134 patients	Age: NR Sex: NR	Clinical (Outpatient for hand, orthopedic, plastic, and spine surgery)	Prescribing compliance to pill quantities and MME	Discharge (Surgical)	- The mean compliance with prescribing at or below the suggested opioid pill quantities and MMEs improved by less than 5% - Post-implementation of the prescribing tool, the number of MMEs prescribed significantly decreased by 26% (100 vs. 75 MME) in a subgroup of hand surgeries

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Kim et al., 2017[59] USA	N=1,946 patients	Pre-implementation: Mean Age: 73.3 years SD 7.5 Sex: Females: 497 (49.6%) Males: 505 (50.4%) Post - implementation: Mean Age: 73.1 years SD 7.4 Sex: Females: 434 (46.0%) Males: 510 (54.0%)	Clinical (Emergency Department)	Recommended dose rate	Emergency Department	- The recommended dosing of opioids significantly increased post-implementation of default geriatric dosing in CPOE template (29.0% vs. 35.2%; P<.001) - Of the opioids, fentanyl (adjusted risk difference 13%, 95% CI 2% -23%), morphine (adjusted risk difference 11%, 95% CI, 4% - 19%), and hydromorphone (adjusted risk difference 7%, 95% CI, 4% - 10%) showed the greatest increases
Kurteva et al., 2021[60] Canada	N=3,486 patients	Opioid on discharge: Mean Age: 66.6 years SD 13 Sex: Male: 927 (60.6%) No opioid on discharge: Mean Age: 71.8 years SD 15.5 Sex:	Clinical (acute care discharge)	Prescribing errors	Discharge (acute care)	- A total of 1,530 (43.9%) of 3,486 patients were prescribed opioids, of which 205 (13.4%) patients had at least 1 opioid-related medication error - There is a 69% lower risk of having an opioid medication error when the discharge prescription was finalized with the electronic reconciliation software (adjusted OR 0.31, 95% CI, 0.14 - 0.65) - The medication error rate is higher for handwritten vs electronic prescriptions (20.6% vs 1.2%) - There is a 2.3 times increased risk of healthcare utilization in the 30 days

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		Male: 1,083 (55.4%)				post discharge period associated with opioid-related medication errors (adjusted OR: 2.32, 95% CI, 1.24-4.32).
Leung et al., 2013[61] Canada	N=1,590 patients	Mean Age: 72.2 years Range (18.0-102.0) Sex: Males: 427 (57.0%) Females: 321 (43.0%)	Clinical (Renal)	Rate of preventable ADEs	Discharge (Renal Failure)	- Preventable ADEs for opioids decreased significantly from pre- vs. post-implementation of CPOE systems with clinical decision support (28 vs. 4; P=.0002) but not non-preventable ADE's (1 vs. 5; P=.15)
McPhillips et al., 2005[62] USA	N=1,933 patients	Age: NR Sex: NR	General Public	Potential drug errors	Ambulatory (Pediatrics)	- 15% of analgesic dispensing events were above the maximum recommended dose, with most occurring for oxycodone (28 of 51 potential overdoses) - Of the 18 dispensing events associated with potential overdosing in adolescents, 17 were for oxycodone
Moura et al., 2012[63] Brazil	N=2,147 patients	Phase 1: Mean Age: 52.7 years SD 20.9 Sex: Male:1,032 (56%) Phase 2: Mean Age: 53.4 years SD 21.3 Sex:	Clinical	DDI rates	Hospital Pharmacy	- Incident rate per 1,000 patient-days for high-severity drug-drug interaction pair amiodarone x fentanyl was not significantly different pre-post intervention (0.36 vs. 0.18, P=.99) - Overall, there was a 71% reduction in high-severity DDIs (P<.01)

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		Male: 105 (36%)				
Ney et al., 2019[64] USA	N=233,390 office-based medical visits	CPOE: Age: 18-64 years (53%), 65 years and older (30%), 0-17 years (17%) Sex: Female: 58% No CPOE: Age: 18-64 years (57%), 65 and older years (23%), 0-17 (20%) Sex: Female: 58%	General Public	Prescribing rate	Ambulatory (Primary care)	- Comparing physicians with access to CPOE vs. without CPOE, opiates were prescribed 10.4% compared to 7.5% - The adjusted odds of opiate prescription were significantly greater in visits to physicians who had access to CPOE (OR 1.35, 95% CI, 1.14 - 1.58; P=.001) - Among patients visits citing pain, the adjusted odds of opioid prescription were significantly greater when physicians had access to CPOE compared to those without access to CPOE (OR 1.28, 95% CI, 1.02 - 1.61; P=.035)
Ramaseshan et al., 2020[65] USA	N=113 people	Mean Age: 63.2 years SD 11.0 Sex: Females: 100%	Clinical (Outpatient Pelvic Reconstructive Surgery)	Post-discharge narcotic use (PDNU), refill rate, pain scores	Discharge (Surgical)	- The median PDNU was 24.0 (0-82.5) MME (equivalent to fewer than 4 oxycodone 5 mg tablets or 5 hydrocodone 5 mg tablets) - Fewer than 11 oxycodone tablets were required by about 75% of patients - 29.2% did not use any narcotics after discharge - Median unused MME was 90.0 (45-112.5) - At the postoperative week 1 and postoperative weeks 4 - 6 timepoints, about 88.5% of patients felt their

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						prescribed narcotic amount was sufficient for their pain needs - 10.6% of patients needed a narcotic refill
Santistevan et al., 2018[66] USA	N= 6,478 adult patients	Age: NR Sex: NR	General Public	Prescribing rate and quantity	Emergency Department	- Pre-intervention, 4,104 adult patients received opioid discharge prescriptions and 2,464 received these post-intervention - The median quantity of opioid tablets prescribed decreased from 20 to 15 (P<.0001) after the removal of the default quantity - The proportion of patients receiving 20 tablets was reduced from 0.5 (95% C,I 0.48 - 0.52) to 0.23 (95% CI, 0.21 - 0.24) after default quantity removal (P<.001), despite 20 tablets being the most frequent quantity of tablets received in both groups
Schwartz et al., 2019[67] Australia	N=208 patients	Pre-implementation: Mean Age: 49 years SD 17 Sex: Male: 52 (51%) Post-implementation: Mean Age: 44 years SD 15 Sex: Male: 60 (57%)	General Public	Prescribing quantity	Emergency Department	- Oxycodone quantity of 5 tablets increased from 3% to 32% post-intervention - Oxycodone quantity of 20 tablets fell from 40% to 24% post-intervention - The mean number of oxycodone tablets prescribed per patient fell from 13.8 (SD 5.1) to 10.8 (SD 5.6) - Paracetamol with codeine quantity of 10 tablets increased from 2% to 24% while it fell from 98% to 76% for quantity 20 tablets - The mean number of paracetamol with codeine tablets prescribed per patient fell from 19.8 (SD 1.5) to 17.6 (SD 4.2)

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Shoji et al., 2022[68] USA	N=428 patients	Pre-implementation: Mean Age: 58 years SD 16 Sex: Females: 156 (72%) Males: 60 (28%) Post-implementation: Mean Age: 57 years SD 15 Sex: Females: 159 (75%) Males: 53 (25%)	Clinical (Outpatient surgery for carpal tunnel release (CTR), ganglion excision, distal radius fracture (DRF), open reduction internal fixation (ORIF), and carpometacarpal (CMC))	Prescribing rate and amount	Outpatient	- Significant decrease in MME prescribed for ganglion excision (P=0.03) and CMC arthroplasty (P<.01) - Significant decrease in the total number of tablets prescribed for ganglion excision (P<.01), CMC arthroplasty (P<.01), and DRF ORIF (P=.04) - No significant decrease in opioid tablet amount (P=.27) or average MME(P=.44) for CTR - Across the whole population, there was a significant increase in the number of patients not receiving opioid prescriptions after surgery (P<.01)
Siff et al., 2021[69] USA	N=82,463 opioid prescriptions	Age: NR Sex: NR	General Public	Prescribing rates	Outpatient	- General medicine (adult, pediatric, and family) accounted for 41.0% of opioid prescriptions and surgery accounted for 23.0% - Opioid prescriptions with overridden naloxone prompts were due to reasons including: 57% naloxone not indicated, 30% of patients declined naloxone, 4% of patients already had a prescription for naloxone, and 9% other.
Slovis et al., 2021[70] USA	N=30,975 patients and N=78,246 prescriptions	Median Age: 59 years Sex: Female: 17,344 of 30,975, 56%	Clinical (Outpatient)	Prescribing quantity and duration	Discharge (Outpatient)	- Overall median quantity of opioid tablets dispensed before versus after the intervention was significantly reduced (54 vs 42; P<.001).

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						- Median duration of opioid treatment significantly reduced (10.5 days vs 7.5 days; P<.001) - There were small but significant reductions in the proportion of prescriptions for morphine (6.30% to 5.95%; P=.04) and oxymorphone (0.37% to 0.24%; P=.002) - Although there was no change in the median 45 MME/day per prescription before and after the intervention, there was a significant reduction in the proportion of prescriptions greater than 90 MME/day (27.46% vs 22.86%; P<.001)
Thomas et al., 2012[72] USA	N=246 prescribers	Mean Age: 52 years Sex: 63% male, 37% female	Clinical Prescribers (internal medicine/ primary care 20.3%, neurology/ psychiatry/ substance abuse 12.5%, 10.2% dentistry, 8.1% emergency medicine, 6.9% pediatrics, 16.9% surgery, 34.6% other)	Expectations of EPCS	Ambulatory	- Although many prescribers reported recurrent technical issues with their system, 76% felt comfortable with their e-prescribing system - The features most frequently used by prescribers were automated renewals (59.8% used it >1 per day) and viewing prescribing (52.5% used it >1 per day) - Comparing users and non-users of the EPCS, users were more likely to expect EPCS to: improve work flow and practice efficiency (69.6% vs 58.8%, P<.10); improve management of pharmaceutical therapy within the practice (74.3% vs 58.1%, P<.01); be easy to use (69.6% vs 54.8%, P<.05); and were less likely to expect EPCS to cause system breaches of patient confidentiality (6.9% vs 14.7%,

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						P<.05) or involve a learning curve that is disruptive to the practice (14.7% vs 33.4%, P<.001) - Although certain security measures were seen as a burden and potential barrier, prescribers viewed EPCS as a tool to improve their practice
Thomas et al., 2013[71] USA	N=102 prescribers	Age: NR Sex: NR	Clinical Prescribers (internal medicine/ family practice (45.1%) and neurology or psychiatry (18.6%))	Adoption, attitudes, and challenges following EPCS implementation	Community Pharmacy	- 62% of total CS prescriptions (electronic and paper) were electronically sent to prescribers - Prescribers found EPCS easy to use (72.9%); improved accuracy of prescriptions (69.5%); improved workflow (66.1%); improved monitoring of medications in the practice (59.3%); improved coordination with pharmacists (55.9%), and led to fewer calls to pharmacists (54.2%), - But EPCS experience did not meet the high expectations reported before implementation - Providers using EPCS reported safety problems (e.g. Prescribing errors) occurred less often post-implementation of EPCS - Barriers included limited pharmacy participation and unreliability of the technology
Tora et al., 2014 Sweden	N=180,059 patients	Mean Age: 75.8 years SD 17.5 Range (1-110) Sex: Females: 62.0%	Clinical	Prevalence of DRP	Discharge	- Tramadol accounted for 1.6% of all alerts and had one of highest proportion of alerts in comparison to other drugs (Proportion (frequency alert/ frequency all drugs) 1.92)

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Watterson et al., 2022[74] USA	N=49,129 CS discontinuations	Age: NR Sex: NR	Clinical	Successful discontinuation and time difference between discontinuation in clinic/ pharmacy	Discharge (acute care)	- Post-implementation of CancelRx (discontinuation e-prescribing tool), there was an immediate and significant (P<.001) increase in the number of CS medications that were successfully discontinued at the pharmacy after being discontinued in the clinic - A year following implementation, the change was sustained (slope = 0.03 percent point, 95% CI, − 0.050 to 0.110) and did not revert to pre-CancelRx levels - After CancelRx implementation, medication discontinuations in the pharmacy and clinic were all completed on the same day (all values were = 0) with a stable trend and almost no variation
Weingart et al., 2014[76] USA	N=29,592 alerts	Age: NR Sex: NR	Clinical (Oncology)	Clinical behaviour responding to alerts	Ambulatory	- The majority (68.1%) of the antiemetic-triggered alerts were attributed to their interactions with analgesic opioids. - Prescribers sometimes canceled the new order when an alert indicated an interaction between antiemetics and opioid analgesics, antiarrhythmics, and antidepressants - Prescribers were often prompted to cancel the order when there was an interaction between opioids and antiretrovirals, antiparkinson medications, antibiotics, antidepressants, and antineoplastic agents

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Weingart et al., 2009[75] USA	N= 60,352 patients; N=2,321 prescribers	Age: NR Sex: NR	General Public	ADE alerts	Ambulatory	- DDI alerts involving narcotic- narcotic and narcotic- benzodiazepine anti-convulsant combinations were judged to have prevented serious ADEs (2 for acetaminophen-propoxyphene combination with acetaminophen-hydrocodone combination annually, 1 for acetaminophen-propoxyphene combination with lorazepam annually).

[†] Only research studies are included in this table; the grey literature report is not reflected in this table due to inability to extract the relevant information.
[*]Ambulatory was defined as e-prescribing occurring outside of a single system (e.g. within a single hospital system). Prescriptions within the emergency department, outpatient and during transitions of care were included.
Abbreviations: ADE= Adverse Drug Events; CI= Confidence Interval; CR= Continuous Release; CS= Controlled Substances; CPOE= Computerized Physician Order Entry System; DDI= Drug-drug Interaction; DRP= Drug-Related Problem; EPCS= Electronic Prescriptions for Controlled Substances; IQR= Interquartile Range; IR= Immediate Release; MME= Morphine Milligram Equivalents; OR= Odds Ratio;
PDNU= Post-discharge narcotic use; SD= Standard Deviation; USA= United States of America.