Designing a Patient-Centered Opioid Misuse Screening and Brief Intervention for the Community Pharmacy

By

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DEDICATION

To those who believed in me, even when I didn't

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There are several people who have been invaluable in my journey to completing this dissertation. First and foremost my advisors, Drs. Olayinka Shiyanbola and James Ford, without whom this dissertation would be impossible. I have been very fortunate to have mentors who can provide critical feedback and support in equal measure. A special thanks to my committee members Drs. Michelle Chui, Randall Brown, and Gina Bryan for guiding this work and going the extra mile when I needed it.

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ABSTRACT

While opioids are effective analgesics when taken correctly, long – term opioid usage carries some safety risks, including risk of misuse, development of opioid use disorders, or overdose death. However, stringent opioid prescribing guidelines may lead to reduced prescriptions and lack of access to opioids for patients who need them. Prevention of opioid use disorders and opioid safety initiatives must be balanced with patient needs. Screening and brief interventions (SBI) can offer opportunities to identify opioid misuse and safety risks and accordingly intervene without a significant increase in workload for healthcare professionals. As pharmacists are one of the most accessible healthcare professionals and medication experts, they are uniquely positioned to offer patient-centered SBI.

We conducted a scoping literature review to identify gaps in current literature on pharmacy-based screening and brief interventions. We found that existing studies did not involve patient perceptions, lacked implementation focus, and did not involve robust qualitative methodologies. Therefore, the objective of our study was to develop a patient-centered opioid misuse SBI for the community pharmacy setting.

We used the Consolidated Framework for Implementation Research (CFIR) to design the study instruments, guide analysis, and interpret findings. Using qualitative interviews of patients and pharmacists, we explored their perceptions, needs, and barriers to participating in the SBI. We also used a building approach to mixed methods integration to develop a quantitative implementation measure based on qualitative pharmacist themes and quotes. The quantitative questionnaire was then evaluated for

initial face and construct validity. Finally, we used a template analysis approach to compare themes from pharmacist and patient interviews and interpret the results for future implementation of the SBI.

The study resulted in several important pharmacist themes categorized according to the CFIR domains of individual characteristics, inner setting, innovation characteristics, and outer setting. Analysis of patient interviews resulted in four main themes: opioid and care experience, knowledge and beliefs, SBI and care needs, and implementation barriers and solutions. A 36- item questionnaire was developed based on pharmacist interviews specific to the SBI and setting, with good face and initial construct validity. Template analysis of patient and pharmacist interviews resulted in SBI features and implications for its implementation.

Overall, the study is an important exploration into pharmacy-based opioid misuse SBI with a focus on patient centeredness and implementation. Barriers and facilitators of SBI participation from both stakeholder groups were identified. The findings from the study can be used to implement and pilot test a SBI within pharmacy settings in the future.

CHAPTER I

INTRODUCTION

Prescription Opioids and Opioid Use Disorder: Balancing Safety and Acceptability

Opioid analgesics are routinely prescribed for the treatment of moderate to severe pain. Despite a decline in the overall opioid prescribing rate in Wisconsin since 2012, the opioid dispensing rate in 2020 was 39.6 per 100 persons.[1] High prescribing rates coupled with inappropriate prescribing for opioids has contributed to an increased prevalence of misuse/abuse, and opioid use disorder (OUD). In the US, about 29% of patients on opioid prescriptions misuse them, 12% of people using an opioid for pain subsequently develop an OUD, and 6% of people misusing opioids transition to heroin use.[2] Approximately 46 people die due to an overdose involving a prescription opioid in the US every day.[3] The age-adjusted death rate due to a prescription opioid overdose was in Wisconsin 5.8 per 100,000 population in 2020.[1]

In response, the Centers for Disease Control and Prevention (CDC) released opioid prescribing guidelines in 2016.[4] While these stricter opioid prescribing guidelines led to the declining trend in opioid prescribing rates, the fear of potential misuse and development of OUDs have led to patient issues with access to even appropriate opioid prescriptions.[5] Research suggests that non-white minorities, especially Blacks, are prescribed opioids at half the rate of white patients.[6] Provider bias, media portrayal of the opioid epidemic, and governmental regulations have led to significant racial inequities.[6] In contrast, white patients and people with private insurance tend to have substantially higher access to treatment for OUDs.[7] These opioid-related disparities have worsened over the years. In 2020, rate of deaths due to prescription opioid overdose increased among Blacks (8.0 per 100,000) and American Indians (10.2 per

100,000) in Wisconsin as compared to the statewide rate of 5.8 deaths.[1] Therefore, development of patient-centered interventions that can prevent OUDs and overdose deaths while maintaining adequate access to pain medications is critical.

Opioid Use Disorder Prevention

Prevention interventions are categorized as primary, secondary, or tertiary based on when the intervention occurs: primary is before the behavior occurs (before opioid misuse), secondary is after it occurs but before the behavior becomes habitual (before patient develops an OUD), and tertiary is after the patient is diagnosed with the disorder (reducing harms of OUD).[8] Primary prevention seeks to prevent the onset of disease while secondary prevention comprises screening for or identifying early stages of the disease. Secondary prevention also includes reversing early effects of the disease if possible such as addressing symptoms including tolerance or withdrawal. Tertiary prevention, also known as harm reduction, attempts to reduce the consequences of the disease (preventing overdose deaths or infections) and achieve disease remission when possible.[8] Although each type of prevention strategy has distinct advantages and disadvantages, many interventions combine different strategies for a more comprehensive approach to prevention.[8,9] This leads to interventions that address risk for OUD at multiple levels such as universal efforts (education on opioids), selective efforts (interventions for patients with family history of substance use disorders) and indicated efforts (counseling patients who are misusing).[9] Therefore, designing prevention interventions that address risks at multiple levels can target a broader population and increase effectiveness of preventive efforts.

Pharmacists and Opioid Use Disorder Prevention

Community pharmacists are one of the most accessible healthcare professionals who routinely interact with patients, providing opportunity for primary, secondary and tertiary prevention, as well as improved access to treatment for OUD.[10] Pharmacists can use their expertise in medications to improve access to treatments and providers. Moreover, pharmacists can aid in primary prevention of OUD. They can contribute to developing pain management plans and counseling patients regarding medications to avoid opioid misuse.[11] Pharmacists can also play roles in secondary and tertiary prevention strategies such as screening and harm reduction. As patients typically do not disclose having a disorder or even admit to having problems with opioid use, screening for opioid misuse becomes a necessary step before they can receive any treatment. However, in the US, the role of the community pharmacist in OUD prevention and treatment has been mostly limited to dispensing medications such as buprenorphine, naltrexone, etc., and even then not at optimal levels.[12] There is a need to expand the role of the pharmacist in providing prevention interventions for OUD.

Screening and Brief Intervention (SBI)

One type of secondary-tertiary prevention model for substance misuse is the SBI, or its more comprehensive version the Screening, Brief Intervention, and Referral to Treatment (SBIRT) model. SBIRT as defined by the Substance Abuse and Mental Health Services Administration (SAMHSA) is a comprehensive, early intervention for individuals at risk for substance misuse that may involve referral to more intensive treatment depending on the individual's needs.[13] According to SAMHSA's model description, any SBIRT intervention must

be brief (5-10 minutes screening), must include a universal screening (ex. all patients with opioid prescriptions are screened), must address a specific behavior (ex. opioid misuse), must occur in a non-substance abuse treatment facility (ex. pharmacy), must be comprehensive i.e. include all three components, and must have supportive evidence of its effectiveness.[13] However, based on this definition, SBIRT has only demonstrated effectiveness for intervening upon risky alcohol use.[14]

The less comprehensive version i.e., only the SBI (without referral to treatment), has been studied more extensively in a variety of settings. SBI for people who have unhealthy drinking habits in outpatient settings has strong evidence for effectiveness.[15] While some brief interventions for patients with alcohol use disorders in primary care settings have not shown to be highly effective,[16] others report positive findings.[17] Alternate formats of delivery such as using digital health technologies for alcohol misuse SBI have shown to have moderate effect in reducing misuse behaviors such as binge drinking.[18,19]

A potential reason for the mixed evidence is while SBI has shown efficacy in reducing risky alcohol use, there are gaps in its effectiveness when translated into clinical care settings.[20] Another potential reason could be that many patients having risky alcohol use have already developed an alcohol use disorder and need intensive treatment;[21] which is not included in the SBI model. However, the more comprehensive SBIRT model provides opportunity for patient referral to intensive treatment, but again with mixed effectiveness data of the SBIRT on utilization of intensive treatment services.[22,23] Finally, a recent systematic review identified barriers and facilitators of alcohol SBI in primary care and found setting specific factors such as costs, available resources, and individual characteristics such as beliefs and self-efficacy were important.[24] However, patient acceptability was rarely studied as an important factor.

Although some studies have reported effectiveness of SBI programs for drug misuse,[25] the evidence is not consistent across different settings.[26] Moreover, most SBIRT programs have mostly focused on illicit drug use and not prescription opioid misuse. One study evaluated a SBI for prescription drug use, but it was part of a randomized controlled trial in a hospital setting.[27] Effectiveness of the SBI model for OUD prevention in pharmacy settings has not been studied extensively. Finally, brief interventions have mainly involved counseling using motivational interviewing techniques to reduce misuse. Other types of brief interventions that focus on harm reduction, rather than only addressing misuse behaviors, have not been studied.

In summary, this mixed evidence of the SBI/SBIRT model effectiveness, has raised four concerns, mainly: 1) patient population already meeting criteria for diagnosis of a disorder will need more intensive treatment than brief interventions, 2) efficacy evidence for alcohol based SBI is strong but effectiveness data (in real world settings) is mixed i.e., gaps in translation 3) patient perspectives of the SBI may be a barrier, but is not explored, and 4) inpatient primary care and emergency settings have been studied, but pharmacy settings have not.

Therefore, there is a need to design a novel SBI as a primary, secondary, and tertiary prevention effort rather than only focusing on patients who have already developed a disorder. Additionally, different brief interventions other than counseling must be evaluated. We must also consider future translation of the SBI into actual practice because efficacy may not equal effectiveness. Patients who may benefit the most from the SBI need to be comfortable participating in it. Considering most data is for alcohol SBIs, evaluating prescription opioid misuse may show different results, especially if packaged as a ‘medication safety intervention’, rather than as an illicit drug use intervention. Finally, outpatient community settings such as the

pharmacy may show different results than inpatient clinical setting, especially when the substance under consideration is a prescribed medication.

Pharmacists and SBI

Recently, many interventions have been designed to be primary prevention initiatives focusing on improving opioid prescribing practices. In a study by Cox et al, an intervention that involved a clinical pharmacist review of opioid prescriptions successfully reduced the amount of opioids utilized without an increase in pain scores.[28] The success of the intervention heavily depended on the interdisciplinary focus of the setting where clinical pharmacists worked with prescribers from the same organization, indicating the need to explore community pharmacist specific views before such interventions can be disseminated to new settings. Additionally, more comprehensive interventions targeting opioid prescription, commonly called 'opioid stewardship' initiatives, often led by clinical pharmacists, have been developed and successfully implemented.[29,30] While these initiatives reduce the number of opioid prescriptions, they do not offer secondary prevention options (screening) or tertiary prevention (naloxone or other brief interventions). Finally, community pharmacists are typically more accessible than clinical pharmacists, especially in rural areas or for underinsured populations.[31] Therefore, OUD prevention research in community pharmacy settings is necessary to reach more patients and improve their health outcomes.

There has been an increasing focus on leveraging community pharmacists as a resource in all types of OUD prevention, including screening and brief interventions.[10] Screening using prescription drug monitoring programs (PDMP)[32,33] and brief interventions such as naloxone

dispensing[34,35] or opioid counseling[36] have been studied in pharmacy settings, but have not been incorporated into one comprehensive SBI model.[37] Using a comprehensive SBI model to implement the interventions would increase their effectiveness and be more patient-centered. However, issues such as lack of clinical information and discomfort in talking to patients can act as barriers for such interventions.[38] Community pharmacists can be a valuable resource in prevention and treatment of OUD, if barriers to effective practice are addressed. Therefore, it is essential to first explore needs and barriers among community pharmacists and accordingly design SBIs.

Need for the study

Although opioid prescribing rates are decreasing, 335 overdose deaths due involving a prescription opioid occurred in Wisconsin in 2020, about 19% higher than previous years.[39] To take preventative actions to reduce overdose deaths and the risk of developing an opioid use disorder, healthcare professionals must recognize opioid misuse behaviors early. Efforts to address opioid misuse must not lead to inadequate pain management, especially among groups that receive disproportionately fewer opioid prescriptions, such as members of the Black community.[40] These disparities can be addressed by leveraging community pharmacists who are highly accessible healthcare professionals, especially in rural areas with underinsured patients. They have training in medication counseling, believe that screening for opioid misuse is important, and are interested in providing screening interventions.[11,41] However, patients are not screened for opioid misuse behaviors when picking up their prescription opioids at the pharmacy. With an increase in overdose deaths in 2020 attributed to the COVID-19 pandemic, and a predicted increased of 28.5% in 2021,[42] there is a critical need to develop a pharmacy-based

screening and brief intervention to address opioid misuse while maintaining access to opioid medications for patients who need them. In the absence of such an intervention, pharmacists as a resource will remain underutilized and prevention efforts to address the opioid epidemic will continue to be inadequate.

CHAPTER 2

LITERATURE REVIEW

Rationale for Literature Review

Exploring the role of pharmacists in OUD prevention interventions is an emerging topic of interest. While some narrative reviews have explored the broader topic,[10,43] literature pharmacy-based or pharmacist-led SBI has not been appraised. To design an effective SBI, it is important to consolidate all the literature on SBIs involving pharmacists and examine its strengths and weaknesses. Using a systematic approach to this literature review would ensure that all relevant literature is captured and inferences on these studies can be made without a high risk of bias.

Screening interventions require inclusion of patient preferences and needs in their design, to ensure that patients find the intervention acceptable. Additionally, patient involvement in development of screening interventions for misuse or abuse behaviors is particularly important because of the delicate nature of the topic of addiction. It is also important to view opioid misuse behaviors as symptoms of a disease, and not as an immoral choice made by the patient, thereby viewing the patient holistically and the disease as only one aspect of their life. If patients screen positive for opioid abuse, treatment referrals and harm reduction strategies can be employed, without stigmatizing patients or hindering patient's autonomy to choose treatment. Attitudes and behavior of the pharmacist should not change, irrespective of patient's decision regarding treatment. Additionally, these interventions must address implementation science principles to ensure optimum translation of the intervention into pharmacy practice. Therefore, screening interventions must be implementation-focused and patient-centered. Development of such

interventions will require review of the literature to explore current research in the area, evaluation of the effectiveness of existing interventions, and assessment of the patient-centeredness and implementation focus of existing interventions based on the criteria described above.

Purpose of Review

To conduct a scoping review of the literature regarding pharmacy-based screening of opioid misuse to 1) identify all experimental and observational studies and grey literature that explore the topic or involve design and implementation of SBI, 2) to evaluate the patient-centeredness of included studies, and 3) to explore the use of dissemination and implementation science in the literature.

The specific questions that guided the review are:

- What is the state of science with regards to pharmacy-based SBI for opioid misuse?
- What types of pharmacy-based SBI exist? What are their characteristics?
    - Were patient perspectives included in development or evaluation of these interventions?
    - Were D&I principles[44] used in developing and implementing these interventions?
- Are the interventions and research in the field patient-centered? If yes, to what extent?
    - Criteria used were based on attributes defined by Morgan and Yader of patient-centered care[45]: holistic, individualized, respect for autonomy, and empowerment.
- What are some limitations of the studies?
    - How can inclusion of patient-centeredness have helped with these limitations?

- How can addressing D&I science principles have improved these limitations?

Methods of Scoping Review

The search was carried out according to Preferred Reporting of Systematic Reviews and Meta-analyses –Scoping reviews (PRISMA-Sc) guidelines.[46] The search protocol was registered as an open-ended registration at Open Science Framework, OSF Registries (Registration DOI: 10.17605/OSF.IO/FPGN6) and is publicly accessible.[47]

Eligibility

The initial eligibility criteria (using search limits) were years, language, and publication status. As literature on the topic is spread out over the last 20 years without any large change attributable to a particular time frame, literature published after the year 2000 was included. No geographical limits were placed but only English publications were included. Both published literature and all papers with full texts available online were selected. Papers without freely available full texts were requested through the university library. Grey literature search was conducted separately to avoid publication bias.

Additional eligibility criteria used during the screening and extraction stage were study populations, study designs, publication types, and full-text access. Studies that included patients prescribed opioids who received screening (ex. chronic non-cancer pain patients on opioids) were included. Studies with only patients who had a formal diagnosis of an opioid use disorder or those that did not receive screening were excluded. Although pharmacists were most likely to be community based, studies including other pharmacists (clinical/hospital/specialized) who interact with patients were also included. Eligible study designs were case studies/ quality

improvement (QI) initiatives, observational studies, and experimental intervention studies. Studies that described SBIs (even if not using the term) for opioid misuse in community pharmacy or were related to such interventions were included. Systematic reviews, commentaries, and editorials were also included. Other types of reviews such as narrative literature reviews that did not generate novel results beyond summarizing the literature were initially included. At the extraction stage, the bibliography of these reviews were checked for relevant studies. The relevant studies from the bibliography were included in the final extraction instead of the original study. As full texts are essential for complete qualitative synthesis of the article, papers with only abstracts were excluded. Any full texts that were not accessible, even from the library one-month after the request was made, or after contact with author, were not included.

Information Sources

Four databases were searched for published literature: PubMed (Medline), Scopus, PsycInfo, CINAHL. Cochrane was searched for other reviews and relevant registered trials if any. Although Web of Science was searched, the results were not included because they were mostly duplicates. For the included reviews, the bibliography was scanned for additional articles. Contact with authors was made only for articles unavailable through the library for their full texts.

For grey literature, 24 sources were purposefully searched or browsed. These included grey literature repositories such as GreyNet, Grey Literature Report, repositories such as Google Scholar, ProQuest Dissertations &Theses, government document sources such as WorldCat, NIH Publications list, and individual organizations such as SAMHSA, American Pharmacists Association and College of Psychiatric and Neurologic Pharmacy. A general Google search in

incognito mode was also conducted and first two pages of the search results were browsed. The full list of grey sources is provided in Appendix 1.

Search

The keywords included in the search were ‘pharmacist’, ‘substance use disorder’, ‘opioid use disorder’, ‘screening’, ‘attitude’, ‘stigma’, ‘perceptions’, ‘patient satisfaction’, and ‘patient-centered’. MeSH terms for these keywords were included in the syntax and formulated for PubMed. Then the syntax was adapted for other databases. The full search strategy for all databases with accompanying limits has also been included in Appendix 2. The overall search was last conducted in March 2021. Filters such as human subjects and English language were activated. Search terms for grey literature search included ‘opioid misuse’, ‘screening’, and ‘pharmacy’ for all sources. The grey literature sources were searched from August to October 2021.

Selection of Sources of Evidence (Search Process)

Covidence software was used for the review. Initially, title-abstracts were screened to remove irrelevant articles by three reviewers. Two reviewers screened each abstract individually. Conflicts were resolved after discussion between the two reviewers or by the third reviewer. Abstracts that met the criteria discussed above were included for further review. Full texts were then scanned for relevancy by two reviewers independently. Reasons for exclusion for each full-text were documented by each reviewer. Conflicts were resolved after discussion among all three reviewers. Grey literature search was conducted by only one reviewer. Relevant results from the grey literature search were added to the list of included articles.

Data Charting Process

Data charting began at the full-text screening stage. All reviewers independently made note of the specific type of screening and the brief intervention type described in each of the full-texts determined to be eligible for inclusion. Finally, one reviewer conducted qualitative synthesis of the last eligible and relevant articles. Although the other two reviewers did not duplicate this charting process, they reviewed the final extracted data for accuracy and completeness. This extraction table also included data synopsized from the grey literature search.

Data Items

Information about all study characteristics, methods, outcomes, and the SBI components were extracted in the charting process. This synthesis included extraction of key data and exploring how papers fared according to the patient centered attributes conceptualized by Morgan and Yader[45] and designing for dissemination and implementation science principles.[44] Studies that included a component elucidating patient perceptions/views regarding the interventions as well as any mention of implementation outcomes were also included in the charting process. This also applied to the grey literature included in final synthesis. All data were charted in Covidence.

Critical appraisal of individual sources of evidence

Critical appraisal of individual studies is typically conducted to reduce information overload by eliminating weak studies or to evaluate the evidence collected for validity and usefulness. As the studies included for final synthesis were not a large number, critical appraisal was only done for assessment of the quality of the included studies. The LEGEND evaluation tool system[48] for intervention research was used for the quality assessment. Studies that were of low quality were not eliminated. Each study was assessed for the validity of its findings,

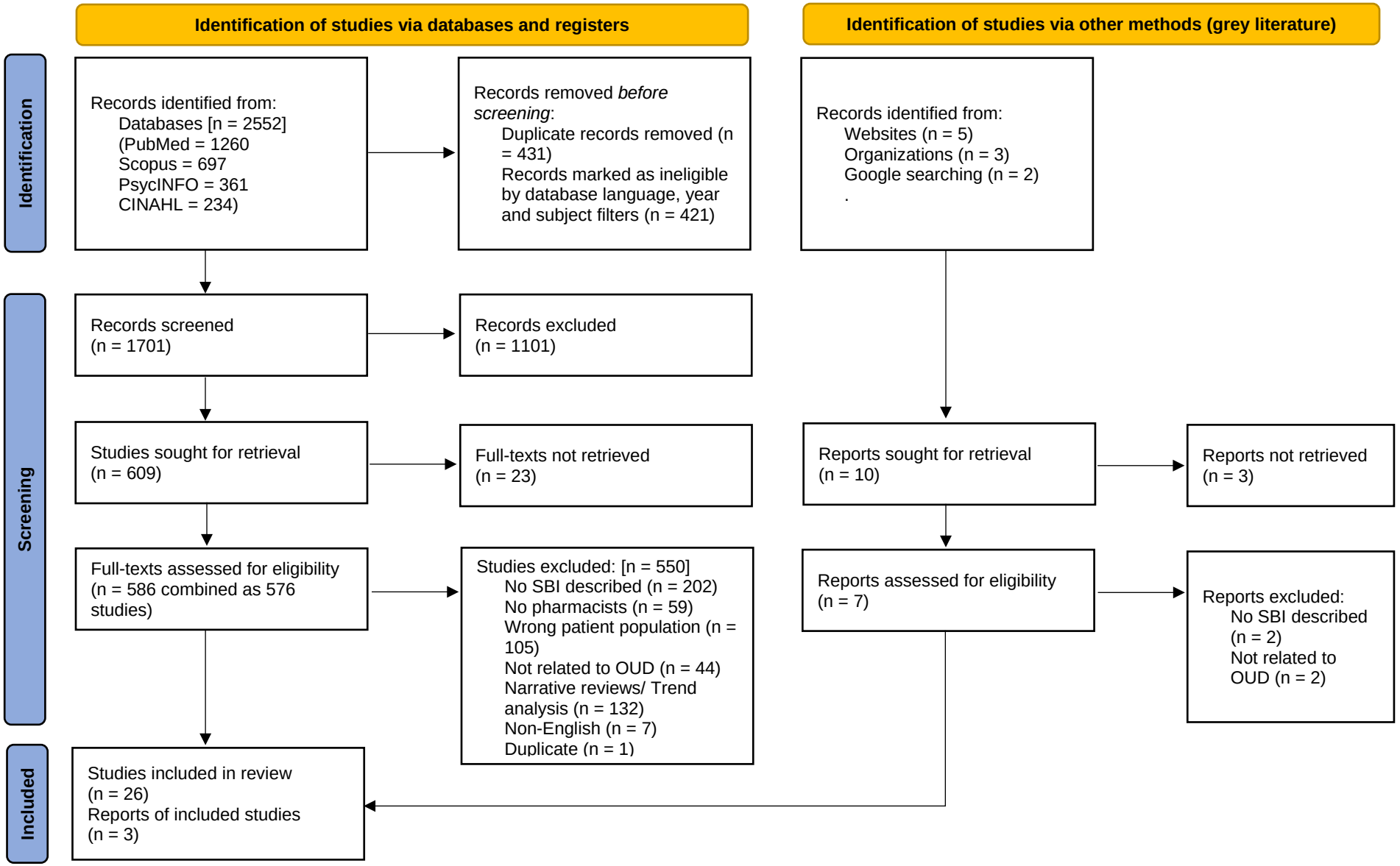
reliability of the reporting, and its applicability for our overall project. Only one reviewer conducted the assessment, but reasons behind each decision were reported for clarity. For each study a specific tool within the system of tools was selected based on its study design. Covidence was also used for logging and organizing this information.

Synthesis of results

All data items from included papers were organized into two extraction tables. The first table included information about the studies immediately relevant to our search i.e., the SBI components and patient - centered, D&I focus. The second table provided detailed information about methods and outcomes of each study. The results of the quality assessment table were organized in a separate table. All the studies in the final extraction were categorized as interventions (quasi-experimental), case either series/QI initiatives, or observational research.

Results of the review

The search resulted in 2552 records, of which 1701 title-abstracts were screened for relevance. Of those, 586 full-texts were assessed for eligibility and combined as 576 studies (when full-texts were part of the same overall project). Finally, 26 studies were included for qualitative synthesis. The grey literature search identified 10 reports, of which 7 were assessed (3 full texts were unavailable) and 3 were included in the final synthesis. The full results of the search process are shown in the PRISMA diagram (Fig 1) below. The results of the individual studies relevant to relevant to our research questions are provided in Table 1 and study characteristics of the charted data are presented in Table 2. Finally, results of the critical appraisal are presented in Table 3.



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Fig 1: PRISMA Diagram

Table 1: Extraction Table (Part 1)

Ref ID	Title	Lead author last name	Year	Country	Study funding sources	Possible conflicts of interest for study authors	Screening Method	Brief Intervention	Patient Centeredness	D&I focus
Intervention Studies										
01[49]	Opioid Overdose Prevention Through Pharmacy-based Naloxone Prescription Program: Innovations in Healthcare Delivery	Bachyrycz	2017	United States	National Center for Research Resources and the National Center for Advancing Translational Sciences of the National Institutes of Health (NIH) through Grant Number 8UL1TR000041, the University of New Mexico (UNM) College of Pharmacy, and the New Mexico Pharmacists Association, NIH/NIAAA R01 AA021771 and R15 AA022242 grants.	None declared	Screening criteria established by program including red flags, high-risk situations and households, high doses, elderly patients, rural and underserved areas, professional judgement of pharmacist.	Naloxone	Not patient-centered	D&I Principles not used
02[50]	Pharmacist Consult Reports to Support Pharmacogenomics Report Interpretation	Bright	2020	United States	Michigan Department of Health and Human Services.	Patent pending related to this study. Authors have an ownership interest/ employee of Genemarkers, LLC	Pharmacogenomics information regarding risk for opioid use disorders	Pharmacist medication recommendations including naloxone	Individualized	D&I Principles not used
03[51]	Development of a targeted naloxone co-prescribing program in a	Wilson	2017/ 2019	United States	Health Resources and Services Administration (HRSA) of the U.S.	None declared	Chart review	Naloxone	Not patient-centered	D&I Principles not used

	primary care practice & Evaluation of a pharmacist-led naloxone co-prescribing program in primary care				Department of Health and Human Services (HHS) as part of an award totaling $1,656,886 with 0%financed with non-governmental sources					
04[52, 53]	A community pharmacy-led intervention for opioid medication misuse: A small-scale randomized clinical trial	Cochran	2018/ 2019	United States	National Institute on Drug Abuse (R21DA043735)	None declared	Prescription Opioid Misuse Index	MTM, motivational interviewing, referral to treatment and patient-navigation - naloxone sessions	Other: Holistic, Autonomous, Individualized	Other: Fidelity, feasibility and acceptability evaluated, findings from all research summarized using CFIR
05[54]	Preparing pharmacists to increase naloxone dispensing within community pharmacies under the Pennsylvania standing order	Santa	2021	United States	Pennsylvania Commission on Crime and Delinquency, Substance Abuse Education & Demand Reduction (PCCD SAEDR Grant #2017-SE-01 29485)		Not specified	Naloxone	Not patient-centered	Other: Implemented within pharmacy workflow, stakeholders engaged in implementation
06[55-57]	A pilot study of community pharmacists screening for opioid misuse risk & statewide study of patient acceptance of naloxone	Strand/ Skoy	2019/ 2020	United States	FM Area Foundation and the North Dakota Board of Pharmacy, North Department of Human Services [FAR0029570], the Blue Cross Blue Shield Caring Foundation [FAR0029437], and	None declared	Opioid Risk Tool (ORT), red flags (patient unknown to the pharmacy, history of early refills, requesting a particular	Naloxone, counseling, referral, partial prescription fill, medication take-back	Not patient-centered	Other: Training materials disseminated widely

					the Alex Stern Foundation [FAR0029481]		brand, or cash paying), risk of accidental overdose, and PDMP			
07[58, 59]	Routine opioid outcome monitoring in community pharmacy: Pilot implementation study protocol and Secondary analysis predicting pharmacists' engagement	Nielsen	2019	Australia	Mindgardens Seedfunding Grant (UNSW), WentWest, NHMRC Research Fellowships (#1163961, #1136944), Victorian Pharmacotherapy Area Based Networks of Latrobe Community Health Service, Hume Area Pharmacotherapy Network" Primary Care Connect, Area Four Pharmacotherapy Network, Orticare Grampians Loddon Mallee Pharmacotherapy Network, Western Victoria PHN and Co-Health, and Substance Misuse Prevention and Service Improvements Grant Fund.	Unrelated grants from Indivior and Seqirus. Honoraria for providing training on identification and treatment of codeine dependence (Indivior). Untied education grant from Mundipharma to conduct postmarketing surveillance on oxycodone.	Routine Opioid Outcome Monitoring Tool, five overdose risk indicators from chart review	Printed patient summary, verbal reinforcement of information by pharmacist, summary letter for prescriber, and naloxone (if indicated)	Other: Individualized	Other: Intervention implemented within workflow and setting. REAIM used to measure outcomes
Case Series/Reports/ QI Initiatives										
08[60]	The innovative role of an opioid overdose prevention pharmacists' at a mental health teaching hospital	Costa	2021	Canada	Centre for Addiction and Mental Health	None declared	Clinican led - standardized tool: 'Ask, advise, assist' approach	Pharmacist-led Naloxone training	Not patient-centered	D&I Principles not used
09[61]	Indian Health Service pharmacists engaged in opioid	Duvivier	2017	United States	Not reported	None	Brief Risk Interview, PDMP,	Naloxone, MAT	Not patient-centered	D&I Principles not used

	safety initiatives and expanding access to naloxone						Opioid Risk Tool			
10[62]	Impact of a pharmacist-driven intervention on the outpatient dispensing of naloxone	Griffin	2019	United States	Wake Forest Baptist Health.	None declared	Patients scoring a 14% or greater overdose risk based on the Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD) or patients prescribed greater than or equal to 50 MME per day.	Naloxone	Not patient-centered	D&I Principles not used
11[63]	A standardized team-based approach for identifying naloxone-eligible patients in a grocery store pharmacy	Sexton	2019	United States	None declared	Author's spouse is employed by the American Pharmacists Association	Chart review for naloxone eligibility criteria (>50 MME per day, concurrent use of a benzodiazepine with an opioid, Fentanyl patch>25mg/h, have a documented or verbally reported	Naloxone counseling with educational handout	Not patient-centered	D&I Principles not used

							history of over-dose or SUD)			
12[64]	Establishment of a pharmacist-led service for patients at high risk for opioid overdose	Tewell	2018	United States	Not reported	None declared	Chart review for CDC at-risk criteria	Naloxone	Other: Holistic	D&I Principles not used
13[65]	The substance use intervention team: A hospital-based intervention and outpatient clinic to improve care for patients with substance use disorders	Tran	2021	United States	Rush University Medical Center from the Division of Substance Use Prevention and Recovery of the Illinois Department of Human Services as part of the Illinois Opioid-State Targeted Response (STR) Grant (TI-080231) and Illinois State Opioid Response (SOR) Grant (TI-081699) from the US Substance Abuse and Mental Health Services Administration (SAMSHA)	ACCELERAT (A Chicago Center of Excellence in Learning Health Systems Research Training) (K12-HS026385) from the Agency for Healthcare Research and Quality (AHRQ), National Center for Advancing Translational Sciences (UL1-TR002398, KL2-TR002387), the National Institute on Drug Abuse (R01-DA041071, UG1-DA049467), and the Cynthia Oudejans Harris, MD, Endowment Fund at Rush University Medical Center.	Medical record, Alcohol Use Disorder Identification Test (AUDIT) and/or Drug Abuse Screening Tests (DAST).	Clinical consult, motivational interviewing by social worker, SUD treatment, naloxone	Not patient-centered	D&I Principles not used

14[66]	Assessing the impact of clinical pharmacists on naloxone coprescribing in the primary care setting	Watson	2020	United States	Not reported	Not reported	Risk Index for Overdose or Serious Opioid-induced Respiratory Depression (RIOSORD), Chart review	Naloxone education handout	Not patient-centered	D&I Principles not used
15[67]	Development and implementation of procedures for outpatient naloxone prescribing at a large academic medical center	Zschoche	2018	United States	Not reported	None declared	Patient risk factors	Naloxone education	Not patient-centered	D&I Principles not used
Observational Studies										
16[68]	Naloxone for Opioid Overdose Prevention: Pharmacists' Role in Community-Based Practice Settings	Bailey	2014	United States	National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health (NIH) UL1TR000117, and STTR grant (NIDA DA 4R42DA030001-02) from the National Institute on Drug Abuse.	Daniel P. Wermeling, owner of AntiOp Inc, is developing a naloxone nasal spray.	High risk patients, prescription and medical records	Naloxone	Not patient-centered	D&I Principles not used
17[69]	A Comparative Exploration of Community Pharmacists' Views on the Nature and Management of Over-the-Counter (OTC) and	Carney	2016	Other: Ireland, South Africa and the UK	The research leading to these results has received funding from the European Community's Seventh Framework Programme FP7/2007-	None declared	No specific method mentioned	Counseling and opioid tapering discussed	Not patient-centered	D&I Principles not used

	Prescription Codeine Misuse in Three Regulatory Regimes				2013under grant agreement no 611736.					
18[11, 70]	Pharmacists' knowledge, attitudes and beliefs regarding screening and brief intervention for prescription opioid abuse	Cochran	2013/ 2015	United States	Not reported	None declared	No specific screening	No specific intervention but indicates counseling	Not patient-centered	D&I Principles not used
19[71]	Pharmacists' perspective on the Take home naloxone program (The PHANTOM Study)	Edwards	2017	Canada	None	None declared	Not specified	Naloxone	Not patient-centered	D&I Principles not used
20[72, 73]	Changes in Pharmacists' Perceptions / Practice and Outcomes After a Training in Opioid Misuse and Accidental Overdose Prevention	Eukel	2019/ 2020	United States	North Dakota Board of Pharmacy, FM Area Foundation, North Dakota Department of Human Services, Blue Cross BlueShield Caring Foundation, and Alex Stern Foundation	None declared	Chart review, PDMP, Opioid Risk Tool	Naloxone, Patient-Centered Counseling	Not patient-centered	D&I Principles not used
21[74]	Using the theory of planned behavior to investigate community pharmacists' beliefs regarding engaging patients about prescription drug misuse	Fleming	2019	United States	New Investigator Award provided by the American Association of Colleges of Pharmacy (AACP).	None declared	PDMP	Counseling	Not patient-centered	D&I Principles not used
22[75]	Pharmacists' training, perceived roles, and actions	Fleming	2014	United States	Unrestricted educational grant from	None declared	PDMP	Document incident, refuse to dispense,	Not patient-centered	D&I Principles not used

	associated with dispensing controlled substance prescriptions				Reckitt Benckiser Pharmaceuticals, Inc.			contact prescriber or law enforcement, counsel patients		
23[76]	How does use of a prescription monitoring program change pharmacy practice?	Green	2013	United States	Centers for Disease Control and Prevention (CDC 5R21CE001846)	None declared	PDMP	Contacting prescribers, counseling patients, referral to treatment	Not patient-centered	D&I Principles not used
24[77]	Attitudes and perceptions of naloxone dispensing among a sample of Massachusetts community pharmacy technicians	Kurian	2019	United States	Agency for Healthcare Research and Quality (R18 HS024021-Green (PI))	None declared	Chart review for high risk prescriptions	Naloxone	Not patient-centered	D&I Principles not used
25[78]	Feasibility and acceptability of a proposed pharmacy-based harm reduction intervention to reduce opioid overdose, HIV and Hepatitis-C	Meyerson	2020	United States	Indiana University Grand Challenge: Responding to the Addictions Crisis.	None declared	PainCas [(Inflexxion, Inc Newton, MA)] tool	Motivational interviewing, Naloxone, syringe services, referral	Not patient-centered	Other: CFIR used to design study
26[79]	An opioid dispensing and misuse prevention algorithm for community pharmacy practice	Rickles	2019	United States	Not reported	Not reported	Prescription review, PDMP, clinical and observational patient profile review	Contact prescriber	Not patient-centered	D&I Principles not used
Grey Literature										
27[80]	Pharmacists' role in addressing opioid abuse, addiction, and diversion	Lofton (APhA)	2013	United States	The American Pharmacists Association meeting, Purdue Pharma LP, Teva Pharmaceutical	None declared	Red Flags, VIGIL (verification, identification, generalization	MTM, Opioid Education, Referral	Not patient-centered	D&I Principles not used

					Industries Ltd., Endo Pharmaceuticals, and Mallinckrodt, The Pharmaceuticals business of Covidien.		, interpretation, and legalization), PDMP			
28[81]	Opioid Use Disorders: Interventions for Community Pharmacists	DiPaula (CPNP)		United States	Providers' Clinical Support System for Opioid Therapies (5H79TI025595) from SAMHSA	Not reported	Verify prescription, red flags, PDMP	Naloxone, counseling regarding medications	Not patient-centered	Includes resources for implementation
29[82, 83]	Role of Community Pharmacy in Improving Public Health	Pringle	2018	United States	National Association of Chain Drug Stores Foundation (NACDSF)	Not reported	Validated tool	Naloxone, counseling, referral	Not patient centered	Stakeholders involved, integrated into workflow

Table 2: Extraction Table (Part 2)

Ref ID	Aim of study	Study design	Population description	Inclusion criteria	Exclusion criteria	Method of recruitment	Sample Size	Data Collection Method	Results/ Outcomes	Main Finding/ Conclusion
Intervention Studies										
01[49]	To describe emerging trends in Naloxone Rescue Kit prescription patterns by pharmacists	Cross sectional study	Pharmacists practicing in New Mexico	Pharmacists certified in the protocol training and who submitted a summary form to the state registry	None	Other: No direct recruitment	133	Secondary data analysis	89.5% patients received their first naloxone prescription through the program. 62% of the prescriptions were prescribed per patient's request.	Polysubstance use was common. Patients were receptive to naloxone. But the SBI was underutilized because majority of patients were not screened by pharmacists.
02[50]	To describe how pharmacists can help further personalize pharmacogenomics (PGx) information and identify clinical recommendations for patients	Cross sectional study	Patients outpatient medical practices and addiction clinics in southwest Michigan.	English-speaking, adult patients without a prior PGx test, received either buprenorphine or naltrexone for at least 6 months, or at least one long acting opioid for 6months or longer	Patients taking opioids for managing cancer-related pain	Clinic patients	252	PGx reports, chart review	PGx reports for 198 (78.6%) contained red and/or yellow flags for medications with actionable or informative PGx guidance for currently prescribed medications. Pharmacists made 13 (5.16%) recommendations related to opioids.	Pharmacists streamlined the PGx report flags and identified other pharmacotherapy interventions following application of patient-specific data, thereby developing a brief report of recommendations for the patients' prescriber(s).
03[51]	To develop a targeted pharmacist-led naloxone co-	Cohort study	Patients from clinical practice on chronic	Adult patients taking morphine-equivalent	Pregnant patients or patients currently receiving	Clinic patients	1297 screened, 350 met criteria	Chart review	The percentage of naloxone co-prescribing increased from 3.4% to 37.2% ($p<0.01$). Of the 87	Pharmacist-led naloxone co-prescribing program increased the rate of naloxone prescriptions, but the number of

	prescribing program in a primary care practice and evaluate it.		opioid therapy	daily dosage (MED) of 50 mg or more, taking concomitant benzodiazepine, with a history of substance use disorder, or with a history of overdose.	treatment for OUD		for naloxone		patients who received a naloxone prescription at follow-up, 31.4% of patients filled it.	prescriptions dispensed remained low.
04[52, 53]	To examine feasibility and acceptability of a Brief Motivational Intervention -Medication Therapy Management (BMI-MTM)intervention along with its impact on medication misuse and concomitant health conditions.	Pilot RCT	Pharmacy patients picking up opioid prescriptions	English speakers,18 years of age or older, screened positive for opioid misuse	Receiving cancer treatment, pregnant, psychotic and manic episode in the past 30 days, filling buprenorphine only, do not have a reliable landline or mobile phone, cannot provide collateral contact information for at least 2 contact persons,	Clinic patients	387 approached, 65 eligible, 32 recruited	Self-reported telephone survey	Compared to control group at 3-months, intervention recipients reported greater improvements in misuse ([AOR]=0.13;95% CI=0.05,0.35,p<0.001), pain (B =8.8,95%CI=-0.95,18.5,p=0.08) and depression (B=-0.44;95%CI=-0.65,-0.22;p<0.001).	It is a feasible misuse intervention associated with superior patient satisfaction and outcomes than standard medication counseling.

					or plan to leave the area for an extended period of time in the next 3 months					
05[54]	To describe implementation of a pharmacy-led naloxone distribution program	Cohort study	Community pharmacists in Philadelphia	Practicing in study pharmacies	None	Voluntary	24 pharmacists from 11 community pharmacies (6 chain and 5 independent) recruited, 22 surveys collected	Survey	Pre-post survey results showed a reduction in stigmatizing attitudes regarding naloxone dispensing and an increase in pharmacists' understanding of the standing order and appropriate naloxone use. There was an increase in pharmacists' self-reported confidence in their ability to appropriately identify, discuss, and dispense naloxone to patients. All pharmacies increased their average monthly dispensing rate following protocol implementation	Pharmacists who received both trainings were more likely to change naloxone dispensing practices, leading to an overall increase in naloxone dispensing by community pharmacists
06[55-57]	To design, implement, and evaluate the Opioid Misuse Risk Prevention Toolkit	Cohort study	Community pharmacists and patients receiving opioid prescriptions	N/A	N/A	Clinic patients	11 pharmacists (pilot), 2716 patients (statewide)	Chart review, data capture	107(26%) patients receiving opioid prescriptions were identified as at some risk of misuse and 30% at risk of an accidental overdose. Pharmacist-initiated naloxone	Utility and the feasibility of screening for opioid misuse risk at the community pharmacy level was demonstrated. Patient acceptance of naloxone at the community pharmacy level was notably higher

									recommendations based on risk screening resulted in a 5.81% take-home naloxone acceptance rate. Individuals that were taking multiple opioid medications were most likely to accept the naloxone (20.45%). Concurrent disease states or medications (COPD, anxiety/depression medication, sleep aid) were associated with a statistically significant increase in the rate of naloxone acceptance. Acceptance of take-home naloxone increased as a patient risk for opioid misuse and/or accidental overdose increased.	compared to national naloxone dispensing rates when pharmacists implemented the SBI.
07[58, 59]	To test the implementation of a computer-facilitated SBI (Routine Opioid Outcome Monitoring [ROOM]) and examine pharmacist characteristics associated	Cohort study	Pharmacists working in New South Wales and Victoria. Patients receiving opioid prescriptions from study pharmacies	Pharmacists working in pharmacies that reported dispensing at least five opioid prescriptions /day, were willing for up to 3 pharmacists to perform study-related tasks	Patients not physically picking up their prescriptions	Other: Professional pharmacy networks and targeted pharmacist advertising through participating Primary Health Network regions and word of mouth.	64 (23 pharmacies) recruited, 44 (21 pharmacies) completed study	Online surveys	On average, each additional decade of practice was associated with a 31% (95% CI 0%, 53%) reduction in the number of screenings undertaken by pharmacists. Each additional decade practicing, lower knowledge of naloxone and lower confidence in identifying unmanaged	Findings from this pilot study identified potential barriers to implementing opioid outcome monitoring.

	with implementation of ROOM.			including recruiting 20 patients, had a computer device. Adult patients receiving a repeat supply of opioids for non-cancer pain from a enrolled pharmacy, who are able to provide voluntary informed consent and willing and able to self-complete the screening tool in the pharmacy.					pain were all independently associated with reduced engagement in screening.	
Case Series/Reports/ QI Initiatives										
08[60]	To describe the development and implementation of an opioid overdose prevention initiative	Case report	N/A	N/A	N/A	Other: Hospital staff	N/A	N/A	From August 2017 through January 2020, 7,997 standardized assessments were documented in the electronic health record.	The pharmacist acted as the central developer and coordinator of key deliverables, including an opioid overdose risk assessment tool, as well as providing much of the education and training regarding naloxone across the organization.
09[61]	To develop effective pharmacy-	Case series	Clinical pharmacists practicing at	N/A	N/A	Other: N/A	Unknown	N/A	N/A	Pharmacist involvement in key initiatives including responsible

	based interventions to mitigate harm from opioid use disorders.		Indian Health Services locations							opioid prescribing, expanded access to MAT and naloxone, coupled with an emphasis on enhanced education, illustrated pharmacists' impact on the opioid epidemic.
10[62]	To evaluate a pharmacist-driven intervention on naloxone prescriptions dispensed in outpatient pharmacies within an academic medical center	Cohort study	Patients at five pharmacy sites associated with Wake Forest Baptist Health	Adult patients who received a buprenorphine or buprenorphine-naloxone prescription in the last 30 days for opioid dependence or patients who received 3 or more subsequent opioid prescriptions in the last 90 days	Active cancer patients, in hospice or palliative care, lacking current information in the electronic medical record. Outpatient pharmacy locations were excluded for a lack of a data analytics platform or point-of-sale system, or serving majority of patients who meet exclusion criteria.	Clinic patients	386	Chart review	Only 41 (30%) of eligible patients were offered naloxone and 11 prescriptions were dispensed.	A pharmacist-led intervention surrounding the outpatient dispensing of naloxone was successfully implemented across five outpatient pharmacies.

11[63]	To define a standardized team-based approach to identify naloxone-eligible patients in a community pharmacy and to evaluate the impact of the approach on the number of naloxone orders dispensed	Case control study	Patients at two pharmacy stores	Adult patients (or caregivers) of participating pharmacies	Younger than 18 years or did not speak English, or received a less than a 5-day supply of opioid prescription and had no exposure to any other opioids within the previous 30 days.	Clinic patients	N/A	Chart review	During the study period, 39 persons were identified as eligible for naloxone, and 11 naloxone orders were dispensed at the intervention store (28.2%); 2 naloxone orders were dispensed at the control store.	A standardized team-based approach was successfully implemented in a grocery store pharmacy and resulted in increased naloxone dispensing to naloxone-eligible patients.
12[64]	To describe a program at a family medicine clinic to provide naloxone prescriptions with education on naloxone use and opioid hazards to patients at risk for opioid overdose	Case series	Patients with active opioid prescription	Adult patients prescribed long-term opioid therapy for at least 3 months and at least one at-risk CDC criteria	Pregnant	Clinic patients	138	Chart review	During the first 6 months of program, 49 patients were identified as being at risk for opioid overdose; pharmacists educated 84% of those patients and subsequently confirmed that 69% had filled a naloxone prescription.	Naloxone prescribing and provision of education on naloxone use to at-risk patients in a family medicine clinic by pharmacists can help ensure access to life-saving medication and reinforce CDC recommendations on safe prescribing of opioids

13[65]	To describe development and implementation of a team-based SBI	Case series	All hospitalized patients at the medical center	None	Pediatric patients, emergency department patients, and those admitted to the obstetrics and gynecology unit	Clinic patients	35,541	Chart review	87.2% of patients admitted to the hospital received initial SUD screening. Of the patients who screened positive, 1,400 received a brief intervention by a unit social worker; the SUIT service was consulted on 880 patients, and multiple medications for SUD were started during inpatient care.	screening, brief intervention, and referral to treatment service was successfully implemented in our hospital, with the SUIT pro-gram in place to provide interdisciplinary addiction care and initiate medications for SUD in appropriate patients.
14[66]	To evaluate the impact of pharmacist-led naloxone intervention	Case series	Clinic patients on opioid therapy	Patients from 5 family practice and 2 internal medicine practice sites who were receiving chronic opioid therapy	Patients with do not resuscitate (DNR) order in place, short duration of opioid therapy, or who have been prescribed naloxone previously	Clinic patients	230	Chart review	During the naloxone co-prescribing initiative, 230 patients were identified by clinical pharmacists as being at elevated risk for opioid overdose. Of these, 86 (37%) were deemed ineligible for naloxone. Out of the 144 patients determined to be eligible, 63 (44%) were agreeable to receiving naloxone and 7 additional patients were agreeable after a follow-up conversation with their PCP. Of the patients that agreed to receive naloxone, 48 (76%) confirmed that they	The pharmacy-driven approach highlighted the importance of having pharmacists within an ambulatory care setting and allowed high-level pharmacist practice without adding to the workload of other members of the healthcare team.

									had picked up naloxone from their pharmacy.	
15[67]	To describe an inter-professional initiative to operationalize outpatient naloxone prescribing at a large academic medical center	Case series	Patients at risk of overdose and patients with OUD	Not reported	Not reported	Clinic patients	Not reported	Chart review	588 discharge prescriptions for naloxone were written throughout the institution. Of those prescriptions, 32% were from the ED, 28% were from the inpatient detoxification unit, 26% were from medical, surgical, and oncology inpatient units, 13% were from outpatient clinics within the institution, and 1% were from pediatric units.	The implementation of an outpatient naloxone prescribing policy created a streamlined approach for the team to use in providing naloxone education and improved naloxone access to patients at high risk for opioid overdose.
Observational Studies										
16[68]	To describe outpatient naloxone dispensing practices in community settings	Case report	Pharmacists practicing in community- and clinic-based settings in large metropolitan cities	Pharmacists who have collaborated with physician specialists in the area of opioid abuse and overdose prevention in order to initiate outpatient naloxone dispensing	None	Other: Not described	6	Structured Interviews i.e. face to face survey	No relevant outcomes	Pharmacists were enthusiastic but education, reimbursement, and ethical issues were barriers. Dispensing naloxone required a provider's prescription in 5 of the 6 locations included.

17[69]	To explore the perspectives of community pharmacists in three regulatory regimes on issues of customer misuse of over-the-counter (OTC) and prescribed codeine	Qualitative research	Practicing pharmacists	Registered community pharmacist having experience with dispensing codeine.	None	Other: Email invitation and/or telephone communication	45	Focus groups	N/A	SBIRT were described as a useful system but complicated by lack of resources, including lack of referral structures and reimbursement.
18[11, 70]	To assess pharmacists' attitudes and motivation towards delivering SBI for prescription opioid abuse and identify factors associated with pharmacists who currently screen and discuss misuse with patients	Cross sectional study	Pharmacists in Utah and Texas	Email linked to practice license	None reported	Other: Email	739 (19% response rate)	Online survey	SBI resources would increase pharmacists' motivation to deliver SBI; pharmacists were interested in helping patients who misuse; and pharmacists possess sufficient opioid knowledge and confidence in practice to address prescription abuse. Chain setting pharmacists ([OR] 6.16, 95% [CI]1.16-32.72) and pharmacists interested in being directly involved in SBI research projects (OR 2.06, 95% CI1.35-3.15) were most likely to report current	Pharmacists are interested in helping those who misuse prescription opioids and believe pharmacies are appropriate settings for SBI services to be tested and delivered. Practice location and pharmacists' interest in addressing opioid issues are important factors for implementing SBIs.

									screening. Pharmacists who reported currently screening for misuse (OR4.27, 95% CI 2.83-6.45) and who reported wanting to help patients who misuse prescription opioids (OR3.03, 95% CI1.50-6.15) were most likely to currently discuss abuse.	
19[71]	To evaluate pharmacists' attitudes toward the Take Home Naloxone program and identify areas that could be improved to support pharmacists' involvement.	Cross sectional study	Clinical pharmacists	Clinical pharmacists from the Alberta College of Pharmacists registry	None	Other: Email	470	Online survey	A total of 76.8% and 79.8% of respondents strongly agreed or agreed that pharmacists should be screening patients and recommending naloxone respectively.	Pharmacists had positive attitudes toward screening patients to identify those at risk of opioid overdose, recommending naloxone kits and willingness to participate in the program. Factors that may facilitate increased participation in the program include addressing time issues and improving education about the program.
20[72, 73]	To evaluate a training to promote behavioral change by altering pharmacists' perceptions & practice toward opioid misuse	Cohort study	Community pharmacists	Pharmacists practicing in North Dakota	Not reported	Other: Email	43 (Study 1) and 63 (behavior outcome) (Study 2)	Survey	Significant changes ($p<.05$) in pharmacist perceptions were reported for opioid addiction being outside the control of the affected person, the role of family history in prescription drug abuse, the value of counseling to support patients at risk	The information presented in the training influenced pharmacists' attitudes and perceptions about the value of screening for opioid misuse or overdose risk and counseling patients about the benefits and risks of opioids. Survey results and opioid harm reduction interventions indicate the

	through the provision of content-related education.								of prescription opioid abuse, the value of screening tools, and the importance of viewing things from the patient's perspective. 97% of respondents recommended the training program, 77% indicated commitment to provide the SBI. Pharmacists registered to prescribe naloxone increased by 67% and reporting naloxone dispensing doubled from 23% to 46%.Pharmacist interventions included medication take back programs explained (88.4%), naloxone dispensing to high-risk patients (10.9%), and counseling(49%).	training resulted in sustained pharmacy practice behavior change.
21[74]	To elicit beliefs of community pharmacists regarding their willingness provide interventional counseling with suspected controlled	Qualitative research	Practicing retail pharmacists in Austin and Houston	Retail pharmacists who have used the PDMP and have their contact information listed in regional pharmacy organizations and colleges.	None	Other: Email and telephone calls	31 (4 groups)	Focus groups	The most prevalent behavioral belief was the disadvantage associated with patient confrontations. Pharmacists believed that engaging patients may cause loss of customers/business but may help patients receive appropriate counseling. Pharmacists identified regulatory agencies	Challenges faced by community pharmacists when considering counseling of patients who misuse prescription opioids need to be addressed to increase pharmacists' willingness to provide SBI.

	substance misuse identified from PDMP data								(e.g., pharmacy boards, law enforcement) and family/ friends of patients as groups of individuals who influence their willingness to counsel (normative beliefs). Time required for counseling was most commonly cited control belief.	
22[75]	To examine situations that prompt pharmacists to access a prescription drug monitoring program (PDMP) database (screening) and assess pharmacists' actions when abuse is suspected (brief interventions)	Cross sectional study	Texas community pharmacists	Licensed Texas community pharmacists practicing in the state as of September 1, 2011 randomly selected from Texas State Board of Pharmacy list	Pharmacists who listed their primary employment type as hospital, consultant, or other non-direct-patient-contact practice setting (e.g., mail service)	Mail	998	Mailed survey	Pharmacists were more supportive of a statutory requirement for prescribers (4.1± 1.2) than for pharmacists (3.2 ± 1.5), P <0.001. They reported that patients who prefer to pay cash (48.1%), mistakes or irregularities in prescriptions (68.1%) and early refill requests (66.3%) would also always trigger PDMP use. They were neutral in regard to notifying law enforcement (44.0%) and counseling patients about addiction (35.1%), majority agreed with either refusing to dispense the prescription (51.6%) or	Older pharmacists with a BSPharm degree may be more willing to provide counseling to patients with opioid addiction based on their work experience and additional CPE related to controlled substances after identifying misuse through PDMP.

									documenting the incident (79.1%).	
23[76]	To evaluate PDMP use in two states with different PMP accessibility and examine its associations with pharmacists' responses to suspected opioid misuse	Cross sectional study	Licensed pharmacists in Connecticut (CT) and Rhode Island (RI)	Pharmacists registered with the CT PDMP at the time of the survey, the CT Pharmacists Association's membership listserv, the Department of Consumer Protection's communication listserv and all RI pharmacists licensed to dispense medications with a registered e-mail address	None	Other: Email	294	Online survey	When suspecting opioid misuse, PDMP users were less likely than nonusers to discuss their concerns with the patient (AOR: 0.48 [95% CI 0.25-0.92]) but as likely to contact the provider (0.86 [0.21-3.47]), refer the patient back to the prescriber (1.50 [0.79-2.86]), and refuse to fill the prescription (0.63 [0.30-1.30]).	Current PDMP use with prevailing systems had limited influence on pharmacy practice.
24[77]	To examine attitudes and perceptions of pharmacy technicians in the provision of naloxone in a sample of Massachusetts pharmacies	Cross sectional study	Pharmacy technicians working in retail pharmacies in Massachusetts	Lead technician in sampled pharmacies	None	Other: Face-to-face	39	Survey	Technicians believed they could identify patient groups at risk of overdose in their practice, but high-risk municipalities' (HRM) technicians recognized the need for naloxone for more of their at-risk patients (81% in HRM vs. 33% in LRM believed>25% of patients need	Pharmacy technicians would benefit from overdose prevention training and are well positioned to recognize overdose risk and offer preventive interventions, such as naloxone.

									naloxone, P<0.01). A willingness to provide naloxone was high (>89%) in both groups.	
25[78]	To explore the feasibility and acceptability of a proposed pharmacy-based harm reduction intervention to reduce opioid overdose, HIV and hepatitis C called PharmNet	Cross sectional study	Indiana community pharmacists	Managing pharmacists from the list of Indiana community pharmacies obtained from Hayes Directories, Inc	Hospital, clinic-based, and compounding pharmacies and closed pharmacies	Mail	984 pharmacy managers	Surveys	83.3% believed PharmNet would benefit patients, and that staff could deliver the intervention with adequate training (70.0%). While 77.2% believed their pharmacy culture supported practice change, 57.5% of chain pharmacists believed their pharmacies would not have time for PharmNet. 73.3% believed screening is needed and pharmacies should offer new services to help reduce opioid overdose and addiction among their patients (79.5%). While 62.4% believed PharmNet was within pharmacy scope of practice, pharmacists reported that they had limited control over the implementation environment.	An implementation trial of a modified version of PharmNet is likely feasible; yet will be challenged by structural pressures particularly in chain pharmacies. Successful implementation will involve the development of resources and policy components to manage outer and inner setting characteristics and align the intervention to the implementation environment.
26[78]	To develop and evaluate a candidate	Qualitative research	Community pharmacists in	None	None	Other: Email	62 (discussion	Discussion groups and semi-	Key themes were that the algorithm should start with ensuring	Developed algorithm should be tested for

	guideline to help community pharmacists monitor and manage potential opioid prescription abuse.		Massachusetts, public health and pharmacy state officials, and a pharmacy distributor				groups) and 6 (interviews)	structured interviews	authenticity of the prescription, employ state prescription drug monitoring program (PDMP) as a primary screening tool, employ the additional abuse detection steps of clinical profile review and observation of the person picking up the prescription, involve protocols of sharing concerns with the patient, making contact with the prescriber, and/or return of the prescription if appropriate, and be easy to follow through color coding.	effectiveness and feasibility
Grey Literature										
27[80]	To explore pharmacists' roles and responsibilities regarding opioid use and identify strategies to address opioid abuse	Other: Conference Proceeding	N/A	N/A	N/A	N/A	N/A	Information presented at a conference convened by the American Pharmacists Association (Pharmacists' Role in Addressing Opioid Abuse, Addiction,	N/A	Although eliminating misuse, abuse, and diversion of opioids may not be possible, pharmacists' use of a number of tools and strategies would improve patient management and benefit public health.

								and Diversion;		
28[81]	To highlight both the evidence base available as well as strategies of clinical decision making for pharmacists	Educational Resource	N/A	N/A	N/A	N/A	N/A	Guideline developed based clinical practices	N/A	Guideline document intended to educate community pharmacists on interventions they can employ to provide safe and appropriate access to opioids while also protecting the public from the hazards of misuse and abuse
29[82, 83]	To implement the 30-month SBIRT practices in 14 community pharmacies in Allegheny County, Pennsylvania.	PowerPoint slides, Webpage	N/A	N/A	N/A	N/A	N/A	N/A	Ongoing project	Project Lifeline expected outcomes include: integrating SBIRT services into existing workflows at participating sites increasing positive health outcomes for patients, reducing SUD-related costs in Allegheny County, and advocating for reimbursement models for pharmacists providing SBIRT services in Pennsylvania.

Table 3: Quality Assessment

Ref ID	Validity	Validity rationale	Reliability	Reliability rationale	Applicability	Applicability rationale
Intervention Studies						
01[49]	Low	Data variables were limited.	Can't tell	No statistical analyses, power analysis, no confounders	High	Describes SBI
02[50]	Low	Study instruments not clear, no information on confounders, no information on validity of outcomes (pharmacist reports)	Can't tell	Only descriptive information included without statistical tests of significance	Low	Patients with opioid use disorders were also included. Pharmacist recommendations may not have been used.
03[51]	High	Methods and outcomes were clearly described	High	Large sample, statistically significant results	High	SBI development clearly described
04[52,53]	High	Blinded randomization, low attrition, valid and reliable instruments	High	Pilot trial (no power analysis), most results statistically significant	High	SBIRT model described in detail and used in community

						pharmacy settings. Larger RCT underway.
05[54]	Low	Instruments not validated, confounders and outcomes unclear	Can't tell	Significant statistics with uncertainty measures but small sample	Can't tell	Screening not described
06[55-57]	High	Variables, methods and outcomes clearly described	High	Statistically significant results, large sample	High	SBI clearly described
07[58,59]	High	Appropriate methods, valid measures, variables and outcomes clearly described	High	Power analysis, large sample, significant statistics	High	SBI clearly described and implemented
Case Series / Reports / QI Initiatives						
08[60]	High	Detailed description of the initiative with background and significance described	Can't tell	Statistics were not reported	High	Pharmacist-led team-based SBI
09[61]	High	Methods and outcomes clearly described	Low	No statistical results reported	High	Various SBI models described

10[62]	Low	Methods unclear, unaccounted confounders	Low	Statistics inappropriate, small samples	Can't tell	Unclear as results were not clinically significant
11[63]	High	Methods and outcomes clearly described	Low	No statistical analysis	High	Pharmacy-led SBi
12[64]	Can't tell	Methods clearly described. Potential confounders and outcomes unclear.	Can't tell	No statistics reported, significance unknown	High	SBI clearly described
13[65]	Can't tell	Data analysis not described in sufficient detail	Can't tell	Statistics were not reported	Low	Pharmacist did not have a large role in providing the SBI
14[66]	High	Methods, outcomes clearly described	Low	No statistical analysis	High	SBI clearly described
15[67]	Low	Variables, outcomes not described	Low	No statistical analysis	Low	Clinical significance unknown
Observational Studies						

16[68]	Low	Study methods inappropriate, no instruments or variables described, outcomes	Can't tell	Results were narrated without connection to data collected	High	SBI described
17[69]	Low	No guiding framework, data analysis not described in detail	Low	Findings were not confirmed, no context provided, saturation not mentioned	Can't tell	SBIRT were only briefly discussed
18[11,70]	High	Methods, measures, and outcomes clearly described	High	Significant statistics reported in large sample	High	Pharmacist perceptions and factors associated with SBI described
19[71]	Low	Instrument not tested for validity and reliability, confounders not evaluated	Low	No power analysis, effect size and statistical uncertainty unknown	Low	Screening method not specified
20[72,73]	Low	Instruments not validated, confounders not accounted for	Can't tell	Significant and appropriate statistics, no power analysis, effect size or measures of uncertainty included.	High	Pharmacist perceptions and practice related to SBI

21[74]	Can't tell	Guiding framework identified, context of participants provided, credibility and confirmability not discussed	High	Findings reported in context, data saturation discussed, data analysis described in detail	High	Transferability of findings to other Texas pharmacists is possible
22[75]	Can't tell	Methods and outcomes clearly described, random sampling used, questionnaire not validated and confounders not accounted for	High	Appropriate and significant statistics, large sample and standard deviations reported.	High	Perceptions and factors related to pharmacist-led PDMP use and counseling evaluated
23[76]	Can't tell	Methods, outcomes clearly described but questionnaire not validated and some confounders (practice setting) not accounted for	High	Appropriate and significant statistics with precisions indicators provided	Low	Not a specific SBI but pharmacist practices as they relate to PDMP use are described

24[77]	Low	Instrument not validated, confounders not accounted	Can't tell	Small sample but appropriate and significant statistics	Low	No specific SBI included
25[78]	High	Appropriate methods, variables and outcomes described clearly	High	Large sample, appropriate statistics	High	Pharmacist perceptions of SBI evaluated
26[79]	Low	Data collection and analysis not described, guiding framework not used, credibility or trustworthiness not discussed	Low	Findings not confirmed, no context provided, saturation not discussed	Low	No effectiveness data collected
Grey Literature						
27[80]	High	Information shared by well-known association, not for commercial purposes, based on data	High	References included, authors disclosed, publication date provided	Low	No specific SBI described

28[81]	High	Information shared by well-known association, not for commercial purposes, based on data	High	References included, authors disclosed	Low	No specific SBI described
29[82,83]	High	Information shared by well-known association, not for commercial purposes, based on data	High	Sponsor and authors disclosed, publication date provided	Can’t tell	Outcomes related to SBI are forthcoming

Summary of results

Intervention Research

Of the 29 records included in the review, only seven were intervention-based studies (Ref ID 01-07). Of these, two interventions included chart review by the pharmacist to screen and monitor opioid prescriptions to identify potentially inappropriate prescriptions. Chart review involved using a pharmacogenomics report (Ref ID 02) or screen of patient charts for naloxone eligibility (Ref ID 03). Similarly, another secondary data analysis of an intervention involved pharmacist screening for naloxone eligibility (Red ID 01). Additionally, three intervention studies used a cohort study design and reported positive outcomes related to pharmacist practices (Red ID 05- 07). Two of these interventions used naloxone as the brief intervention (Ref ID 05, 06) and the third used patient counseling, education, and naloxone if indicated (Ref ID 07). Lastly, one intervention study was a small-scale randomized control trial (Ref ID 04) using the Prescription Opioid Misuse Index as a screener and motivational interviewing, counseling, and naloxone navigation as brief interventions, with referral to treatment. It showed improvements in misuse, pain control, and depression scores.

Case Series / QI Initiatives

Eight studies were descriptive reports of initiatives conducted within particular health systems/pharmacies (Ref ID 08-15). These reports mainly used case series designs or cohort study designs. However, the main difference between these reports and the above interventions was the lack of focus on generalizability of findings. Therefore, they were classified as quality improvement rather than research. Initiatives in this category followed the alcohol SBI model, where naloxone dispensing was the brief intervention most often offered/studied. Interestingly,

almost all reports in this category involved clinical pharmacists rather than community pharmacists. This was mostly because of how integrated the clinical pharmacist was within the healthcare system, reducing common barriers associated with SBI such as access to clinical and patient information. Only one study was conducted in grocery store pharmacies (Ref ID 11) using a case-control design to identify naloxone-eligible patients, and it showed moderate success.

Observational Research

All other papers were descriptive observational studies that were mostly initial explorations on the topic (Ref ID 16-26). All studies were focused on assessing pharmacist attitudes and practices regarding their role opioid misuse or some type of SBI. Most studies used quantitative surveys (Ref ID 18-20, 22-25) but four studies used qualitative interviews or focus groups (Ref ID 16,17, 21,26). All studies reported generally positive attitudes regarding SBI but many reported practice challenges and implementation barriers. Interestingly, most observational research also evaluated chart review or PDMP as their screening method. Also, screening practices in the studies included were closely linked to naloxone dispensing. However, some did not specify a screening method (Ref ID 17-19). Only one paper described the SBI in detail and was a harm-reduction based SBIRT where ‘PainCas’ was a screening tool and brief interventions included syringe exchange, naloxone dispensing, motivational interviewing, and treatment recommendations and referrals (Ref ID 25).

Grey Literature

Three reports were included in the final synthesis of the grey literature search (Ref ID 27-29). Two were reports from professional pharmacy organizations: one summarized different type

of screening tools and interventions pharmacists can engage in (Ref ID 27), and the other described guidelines for opioid misuse pharmacy practice including SBI (Ref ID 28). The final report was a brief description of an ongoing statewide pharmacy-based SBI project (Ref ID 28).

Quality Assessment

Overall, many studies had low/mixed validity or reliability. Applicability of the studies to our review was often considered low because a specific SBI was not evaluated. Only five studies (Ref ID 03, 04, 06, 07, 18) were rated high on all three factors: validity, reliability, and applicability. These studies had clear descriptions of appropriate methods and outcomes and used standardized instruments (validity), had sufficient sample size and reported significant statistics (reliability), and had a clearly described SBI that could be used for our research (applicability). Although, results from the other studies can be used for future research, caution must be exercised during interpretation of their findings.

Patient-Centeredness

Most studies were not patient-centered. Among the four studies that incorporated some aspect of patient-centeredness as per Morgan and Yader's criteria, no study included all criteria. The pilot trial (Ref ID 04) attempted to take a holistic view by evaluating mental health and overall patient-reported health status, and provided patients with the option to choose naloxone and included individualized motivational interviewing, but did not empower patients. Another paper (Ref ID 07) described a relatively individualized model including screening and naloxone information. The authors of the case series regarding naloxone education described the intervention as intending to be holistic (Ref ID 12) and the pharmacogenomics report-based intervention was tailored for individual patient needs (Ref ID 02).

Apart from the four studies mentioned above which attempted to be holistic or individualized, none of the included studies had any aspects of patient-centered research. Also, none of the included studies explicitly described the research as patient-centered. Moreover, even though pharmacist views and preferences were included or analyzed in the observational studies, patient preferences were not solicited in the development or implementation of the interventions. This is especially concerning as research indicates that patients may not believe that pharmacists have a role in opioid safety initiatives[38] or may have fears regarding future consequences of requesting naloxone.[84]

D&I Science

Implementation science principles were addressed in only seven studies overall. Four of the intervention studies incorporated some D&I principles. One study indirectly measured feasibility among pharmacists to perform the intervention by noting that a significant number of pharmacists performed the intervention and by implementing the SBI within workflow (Ref ID 05) (principle: measure implementation outcomes). However, measuring implementation outcomes in this manner does not provide reliable results. It is possible that these outcomes are over-estimated and data on ways to improve these outcomes is lacking. One intervention study disseminated their training material widely to allow for easy adoption of their intervention (Ref ID 06) (principle: develop user-friendly research summaries). The pilot trial summarized all research conducted using CFIR and evaluated some initial implementation outcomes (Ref ID 04) (principle: used implementation framework and measure). Although they developed a context-relevant pilot measure to plan implementation of the SBI, it was not developed based on any implementation theory/framework, nor was it based upon qualitative findings. Previous literature about alcohol SBIs were used instead. The other intervention implemented the SBI within

workflow and used RE-AIM to measure implementation outcomes (Ref ID 07) (principle: used implementation framework).

Only one observational study addressed D&I science (Ref ID 25). They used the CFIR framework in the development of the questionnaire and piloted the context-specific measure (principle: used implementation framework and measure). However, it was unclear how implementation outcomes were associated with the evaluated CFIR constructs. Also, the SBI was geared towards harm reduction overall rather than being specific to prescription opioid misuse. Two reports from the grey literature search either included resources for implementation (Ref ID 28) (principle: develop user-friendly research summaries) or involved pharmacy stakeholders in development of the intervention (Ref ID 29) (principle: engage stakeholders).

Addressing gaps in existing research

It is extremely important to explore the patient's perceptions of the pharmacist in relation to opioid misuse screening for many reasons. As most misuse screenings are based on self-reported behaviors, patients' perceptions of pharmacists and their views on screening will directly affect the validity of their responses (social desirability bias). Their experiences with interacting with a pharmacist regarding opioid medications or other services may provide better insight into their relationship with the pharmacists and inform interventions. Also, the patient's views and opinions regarding the pharmacist and the services they can provide such as screening interventions contribute to the acceptability and effectiveness of such interventions.

From the included papers, it was apparent that pharmacy-based opioid misuse SBI was a relatively new topic in the field, with most papers published in the last five years. This was also

why most papers were descriptive or QI studies, with intervention studies being in the development or pilot testing stage. However, the findings suggest high potential for evidence-based interventions to be successful. Among the interventions, most followed the SBI model due to its prior use in alcohol screening and the relatively easy implementation. This model is also very appropriate for a fast-paced community pharmacy setting, where pharmacists only have time for a quick screening and brief intervention. Such a model can thus be implemented within the existing pharmacy work structure and not burden the pharmacist excessively. It is also important to note that lack of comprehensive services and tailoring of interventions are generally proposed as reasons for limitations in SBI effectiveness for alcohol/other substances.[14,85] These limitations may continue in SBI for opioid misuse as well. It is possible that the limited time spent on intervention would lead to limited patient engagement, thereby resulting in no effect. In contrast, one intervention was designed to be comprehensive including screening, individualized intervention (motivational interviewing), treatment referral, and continued monitoring (Ref ID 04). Results of the intervention show greater success, probably due to higher patient-centeredness. However, this intervention, unlike the typical SBI model, is extremely resource intensive and its feasibility and sustainability would need to be measured seperately.

A patient-centered approach was not utilized in any of the studies, although four studies had some aspect of patient-centeredness. This resulted in large knowledge gaps. For example, conclusions regarding patient comfort with asking for naloxone varied across studies, which could have been accounted for by incorporating patient opinions and needs when designing interventions. Questions regarding patient acceptability of the SBI versus comprehensive model could also have been answered if patient preferences were included. A hybrid model with patients answering questions on a tool for screening purposes and an individualized component

of brief or comprehensive intervention based on patient preferences could also be designed if a patient-centered approach was utilized. Designing and implementing interventions with only one stakeholder (pharmacist) and not engaging another (patient) would not lead to effective and sustainable interventions.

The studies also did not address implementation science principles, with most not considering implementation at all. Even addressing implementation outcomes such as feasibility and acceptability without direct measurement raises questions regarding the reliability of their findings. For example, an intervention is not necessarily acceptable even if some pharmacists or patients participate in it initially (Ref ID 05). Development of interventions without an implementation focus results in an intervention that remains only a research project rather than being translated into actual practice. To ensure successful translation of the developed SBI into pharmacy practice, researchers must pay heed to implementation science principles at the development stage itself.

Some limitations of this review may have affected the results. Mainly, the qualitative synthesis i.e. data extraction and the quality assessment of the included studies was conducted by only one reviewer. This may have led to some bias in the results. However, final data were reviewed by multiple researchers and rationale was provided for each assessment to reduce potential bias. This search included studies that described some sort of SBI (based on the SAMHSA definition) even if the research was not explicitly stated as SBI to capture a broader set of studies. This could cause some bias as reviewers may have excluded some studies that did not define their intervention as a SBI and did not appear to meet the SAMHSA criteria, such as multifaceted and long-duration (not brief) interventions.

Implications of the Review

Overall, the review suggested a strong need and potential advantages of a patient-centered and implementation science approach to designing pharmacy-based opioid misuse screening interventions. Future studies should include interventions designed based on needs assessment of patients and pharmacists. Interventions may need to be individualized and could be developed as primary, secondary, or tertiary prevention interventions based on the specific components included. This in turn will depend on patient needs and preferences as well as pharmacy work structures. Inclusion of implementation science principles in the development of these interventions will lead to greater impact on pharmacy practice, as such interventions have a greater chance of being translated and sustained within regular practice. Findings suggested that such a robust patient-centered intervention would be successful in this area.

CHAPTER 3

STUDY PURPOSE AND SIGNIFICANCE

Study Objectives

The overall objective of the project was to design a patient-centered opioid misuse screening and brief intervention for the community pharmacy setting. The rationale was that addressing patient and pharmacist views in designing the intervention prior to implementation would lead to the development of an intervention that is more acceptable to patients and more feasible to deliver, with greater chance of successful implementation. The overall objective was achieved by addressing the following specific aims:

1. Explore needs and barriers regarding a screening and brief intervention among pharmacists dispensing opioid prescriptions. We expected that needs such as training to deliver intervention and barriers such as managing time and keeping up with regular duties would be identified. (Qualitative Pharmacist)
2. Explore patient needs regarding opioid prescriptions and barriers to participating in a screening and brief intervention. We expected that needs such as information on opioids, private space for counseling and barriers such as delivery method of intervention (in-person or online) or comfort with pharmacists would be identified and would inform intervention development. (Qualitative Patient-Centered)
3. Use qualitative findings (from Aim 1) to create a quantitative survey implementation measure to evaluate setting, individual, and intervention characteristics relevant to pharmacists providing the SBI. Our working hypothesis was that pharmacy-specific

measures of factors affecting design and implementation of the intervention would be measured. (Mixed/Quantitative)

4. Develop a patient-centered opioid misuse screening and brief intervention by integrating findings from Aims 1&2 for community pharmacy settings. Our working hypothesis was that systematically mixing findings from both phases and including patient voices in the design would lead to an intervention that is considered acceptable by patients and feasible to deliver by pharmacists.

Significance and Innovation

While some pharmacy-based opioid misuse SBIs have been recently developed,[53,86] patient perspectives of these SBIs are limited. Issues regarding private space and method (in-person or online) of the intervention as well as comfort with a pharmacist providing such interventions need to be explored. The impact of patient needs on the acceptance of a pharmacist-led SBI is unknown. This research was innovative because it utilized a patient-centered approach. Patient-centered interventions that include individual patient preferences and values are holistic.[45] They respect patient's autonomy, and empower them to make decisions about their own care.[45] Such interventions should be designed across a continuum of patient-engagement levels that address the individual preferences for engagement in their own care.

Additionally, SBI are generally secondary prevention interventions i.e., identifying patients who are at risk but do not have a diagnosis of OUD. However, patient-centered interventions need to be tailored to a patient's needs. Therefore, our study objective is to develop a SBI that allows for tailoring and can address risk universally (primary prevention) and reduce harms associated with OUD (tertiary prevention). This is innovative because a more robust SBI

would be developed as a result of integrating patient needs and preferences as well as pharmacy work structures.

Some opioid misuse prevention interventions have used clinical pharmacists to provide patient-centered services. These include comprehensive pain inventories and functional status assessments, opioid dose escalation and de-escalation recommendations, management of adverse drug reactions, patient education, urine drug testing, pill counts, and prescription drug monitoring program (PDMP) queries.[61,87] These individualized and comprehensive patient-centered interventions that include screening, treatment, and monitoring have decreased opioid misuse and improved patient outcomes.[61] However, these interventions do not follow the SBI model and are not adapted for community-pharmacy settings.

Most recently developed opioid misuse SBIs (identified in the review) except one, did not include qualitative data collection methods beyond open-ended survey questions. These studies also reported the lack of in-depth and contextual information about pharmacist perspectives as a significant limitation. The qualitative data that was collected for development of one of the SBIs was a discussion group and not a rigorous qualitative study.[88] Conducting qualitative exploration as the first step to designing the SBI would help overcome this common drawback.

Although countless behavior-change prevention interventions have been designed, their translation into practice has been limited. This is mainly due to gaps in intervention design, inappropriate target settings, and research designs that neither include a representative sample of individuals involved nor address implementation outcomes.[89] Typically, researchers address dissemination and implementation only after effectiveness of interventions are proven. The ‘designing for dissemination’ principles identify key actions in the process of designing interventions and the subsequent products. Using these principles will lead to higher rates of

successful implementation and future dissemination.[44] These actions include engaging key stakeholders as early as possible, using implementation frameworks and dissemination constructs, pilot-testing and developing context-relevant measures, documenting implementation outcomes, and disseminating research summaries to all stakeholders.[44] Utilizing designing for dissemination and implementation principles at the development stage allows for more context-relevant intervention that addresses stakeholder needs and priorities.

This project designed the SBI by engaging both pharmacists and patients through qualitative interviews and used the Consolidated Framework for Implementation Research (CFIR) to inform data collection and analysis.[90] The project also developed a context-relevant implementation measure through mixed methods research. Interventions in this area have rarely used dissemination and implementation science principles, which limits the translation of research into actual practice. Thus, this research project was innovative because of the use of qualitative methods for exploring context, a comprehensive and general framework like the CFIR to design the study, instruments, and guide interpretation along with a mixed methods approach to develop a measure.

CHAPTER 4

METHODS

Theoretical and Conceptual Frameworks

Designing for Dissemination and Implementation

The study used designing for dissemination and implementation principles to guide study design and methods.[44] These principles are categorized into three domains: system changes, processes, and products. While system changes address how research should be funded, processes and products include principles that researchers can apply in research studies. As system change principles cannot be directly applied to the study, only principles from the processes and products domain were included. The framework also lists potential actions that can be undertaken by researchers corresponding to each principle.[44] These potential actions were adapted to be specific to the study. The principles under these two domains and the corresponding actions taken in the study are described in Table 4.

Table 4: Designing for dissemination principles and corresponding actions[44]

Principles	**Sample Actions**	**Actions Undertaken**
Processes Domain		
Involve stakeholders as early in the process as possible	Engage as advisors and collaborators Engage in the research process	• Included patients and pharmacists as participants in the study before and during design of the intervention.

Engage key stakeholders (receptors) for research through audience research	Identify gaps in research, relevance of methods, messages Ensure stakeholders represent potential adopter organizations	• Identified gap: Lack of patient-centered research • Ensured stakeholders (community pharmacists, owners, managers) represent potential adopter organizations (community pharmacies)
Identify frameworks or theories for dissemination efforts	Review existing frameworks for applicable constructs Pilot test measures for assessing model constructs among key stakeholders	• Reviewed existing frameworks and selected CFIR (details below) • Created CFIR construct-specific implementation measure for pharmacists • Developed a context-relevant intervention
Products Domain		
Identify the appropriate message	For interventions, document evidence of effectiveness, cost of implementation, and cost-effectiveness	• Documented evidence of potential effectiveness, acceptability, and feasibility of SBI
Develop summaries of research in user-friendly, nonacademic	Document evidence of ease of use so that	• Developed a research summary for non-scientists included as Chapter 8

formats (audience tailoring)	interventions can be disseminated	

Consolidated Framework for Implementation Research (CFIR)

The CFIR was developed by identifying various theories that facilitated translation of research findings into practice and then combining their constructs into a comprehensive model for implementation.[90] The framework provides a means of systematic implementation of interventions and analysis of findings. There are five main CFIR domains (Fig 2): Intervention Characteristics (key attributes that influence Implementation), Outer Setting (economic, social and political context), Inner Setting (structural and cultural characteristics of the place of implementation), Individual Characteristics (persons involved in the intervention), and Process (stage of implementation).

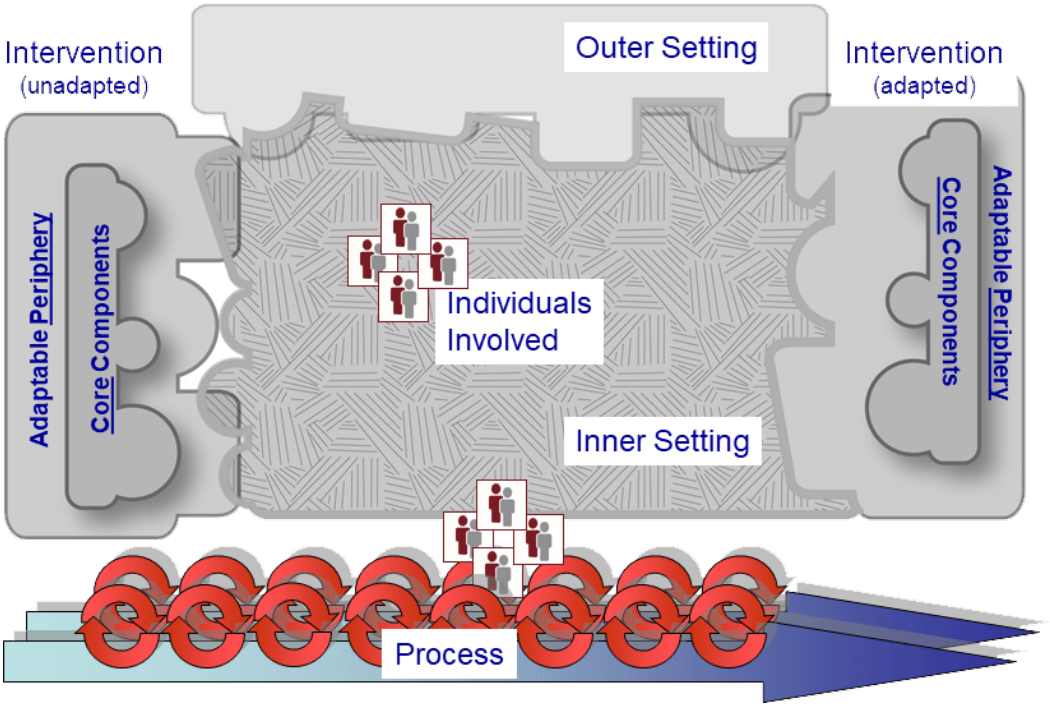


Fig 2: CFIR Diagram

All CFIR domains have individual constructs that affect the implementation of the intervention (Table 5). Not all constructs under the CFIR domains are appropriate for intervention design, and some are implementation specific. The constructs that can be evaluated and appropriate for this research study have been bolded in the table, an approach similar to a recent pharmacy-based opioid harm reduction intervention development study.[78]

Table 5: CFIR Constructs (with bolded constructs included in the study)

Innovation Attributes	Inner Setting	Outer Setting	Characteristics of Individuals	Processes
Source	**Structural characteristics**	**Patient needs and resources**	**Knowledge & beliefs**	**Planning**
Evidence strength and quality	**Network/ Communication**	Peer pressure	**Self-Efficacy**	**Engaging**
Relative advantage	**Culture**	Cosmopolitism	Stage of change	Implementing
Intervention: **Adaptability** Trialability **Complexity** Design quality & packaging **Cost**	Implementation Climate **Change Tension** **Compatibility** **Relative Priority** **Organizational incentives** **Goals & feedback**	External policies and incentives	Personal attributes: Ambiguity tolerance **Motivation** Values Competence Capacity Learning style Innovativeness	Evaluating

	Learning climate			
	Readiness for implementation		Individual identification with organization	

Since its introduction, there have been several adaptations of the CFIR model. One such relevant adaptation by Safaeinilli and colleagues is for the evaluation of a patient-centered intervention.[91] The adaptation focuses on a patient-centered transformation of the CFIR by tailoring the definition of four constructs (goals and feedback, champion, reflecting and evaluating, and patient needs and resources) and transforming the patient needs construct into a sixth domain. However, the constructs of the new patient-centered domain were not defined, and the transformed definitions were intervention specific. Therefore, it does not directly aid development of our intervention any more than the original CFIR. Apart from the CFIR, other commonly used comprehensive implementation frameworks include the Exploration, Preparation, Implementation, and Sustainment (EPIS)[92] and the RE-AIM[93,94] frameworks. However, while RE-AIM is useful to understand implementation outcomes, the constructs are not appropriate for designing interventions before implementation. The EPIS framework is similar to CFIR in organization and domains but does not have any patient-centered constructs nor individual characteristics constructs in the exploration and preparation stages. Thus, the CFIR was the most comprehensive and appropriate framework to use in this study.

The constructs from the framework were used to guide study design, development of interview guides and data analysis. The CFIR interview guide[41] was also used to develop specific interview questions and the accompanying codebook template was used for initial deductive

coding of interview data. The CFIR domains were used to organize the developed survey items. Finally, the CFIR constructs were used to help integrate quantitative items and qualitative results, serving as a link/bridge between the two. Specific details regarding these methods are included in the data collection and analysis sections below.

Study Design

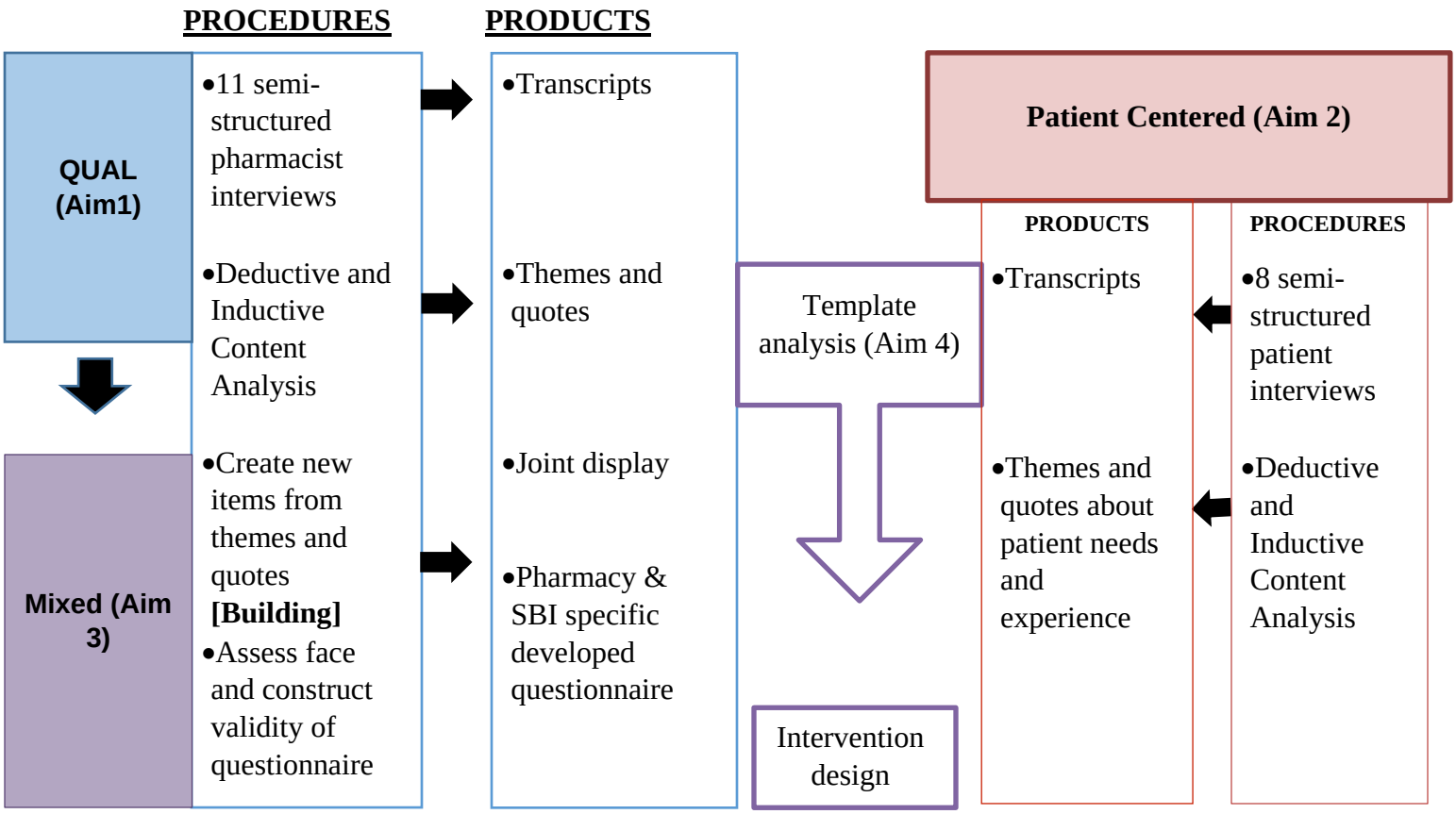
Although this study was not a mixed methods study as there was no quantitative data collection, a mixed methods approach was utilized to build a quantitative instrument from qualitative data (Fig 3). The study design was similar to exploratory sequential mixed methods studies, where we first explored pharmacist perceptions and needs qualitatively followed by development of a quantitative questionnaire for pharmacists. At the methods level, integration mainly occurred using the building approach, wherein themes and quotes from the qualitative phase were used to build survey items. Finally, pharmacist themes and quotes as well as the developed quantitative questionnaire were integrated together and presented as a joint display.

As the study involves a patient-centered approach, semi-structured interviews were conducted among patients exploring their experiences, needs, and barriers to participation in the pharmacy-based SBI. Interviews were designed to help inform the intervention design by focusing on patient perceptions of the SBI. Finally, qualitative results from the interviews were analyzed with findings from pharmacist interviews using a template approach.[95]

Utilizing a mixed methods approach in this study was essential for two reasons. First, one of the actions identified in the Designing for Dissemination principles is developing pilot, context-specific implementation measures. Using the initial qualitative findings to develop the

implementation measure and testing it for initial face and construct validity ensured that the pilot measure is relevant to pharmacists and specific to the SBI. Second, most of opioid misuse SBI research used quantitative methods only. Lack of in-depth and contextual information about pharmacist perspectives regarding SBIs can lead to ineffective interventions. The mixed methods approach allowed for qualitative exploration as the first step to designing the SBI.

Fig 3: Procedural Diagram of the Development of a Patient-centered Opioid Misuse SBI Using a Building Approach



Study Sample

Rationale

This study required two separate qualitative samples; (1) community pharmacists and the (2) patients. For the pharmacist sample, all community pharmacists practicing in Wisconsin were eligible. Restrictions on type of pharmacy (small/independent versus large pharmacy chain) were not needed because the intervention was not being designed or implemented for a particular pharmacy setting in this study. Moreover, variance in practice characteristics in the sample was beneficial to gain richer qualitative data. For example, pharmacists practicing in independent or specialty pharmacies would have different experiences with dispensing opioid prescriptions and spend more time interacting with patients as compared to pharmacists practicing in larger chain pharmacies. It was important to capture these differences in our explorative qualitative research. Although, the interview guide remained consistent, probing questions depending on the different responses were included.

For the patient sample, interviews were conducted with patients who were prescribed opioids because the intervention was targeted towards these patients. Some prevention interventions are designed to be more secondary or tertiary prevention, where patients who are at risk of developing or have developed OUD are targeted. Considering the SAMHSA definition of SBIRT, that requires screening to be universal, all patients with opioid prescriptions would need to be screened. Therefore, all patients who were prescribed opioids for chronic non-cancer pain can be targeted for the intervention and were accordingly included in the study sample. Some patients have been diagnosed with an OUD and can still be on opioid medications for their chronic pain. These patients were excluded from the sample because the SBI does not target patients who are already diagnosed with OUD. Finally, some patients typically do not use in-

person pharmacy services for their opioid medications. Although their pharmacy experience would be limited, it was important to explore their perceptions about opioid medications and the pharmacy-based intervention, especially for making interpretations regarding the modifications required in the SBI in future research. These interviews would also lead to insights about potential limitations of the proposed intervention as well as potential modification such as telehealth-based or digital intervention that would have to be considered in future research.

Sample size and criteria

Generally, 10-25 participants are considered sufficient for theory/model based qualitative studies using content analysis approaches.[96,97] Initially, both pharmacist and patient interview samples were planned to include 15 participants each. However, the final sample size was reduced due to higher information power of the completed interviews. The higher information power was gained by sample specificity (purposive sampling rather than convenience), using an applied conceptual framework (CFIR), the strong quality of dialogue (lengthy, in-depth interviews), and the exploratory nature of analysis (identifying patterns/themes rather than in-depth phenomenological description).[97] Thus, interviews were conducted until data saturation was achieved, i.e. no new dimensions regarding the topic emerged. A purposive sample of English-speaking community pharmacists practicing in Wisconsin were included in the sample. Exclusion criteria were practicing in a non-retail setting or not licensed to practice in Wisconsin. For patient interviews, a purposive sample of adult, English speaking patients who have been prescribed an opioid medication at least once for acute or chronic non-cancer pain was used. Patients diagnosed with an OUD, receiving opioids for cancer-related pain, or unable to participate in the interview (hospitalized, in hospice care, suffering from debilitating pain) were excluded from the sample.

Data Collection

Recruitment

For recruiting pharmacists, an advertisement in the Pharmacy Practice Enhancement and Action Research Link (PearlRx) of Wisconsin newsletter describing the study opportunity and contact information of the researchers was used. PearlRx is a statewide pharmacist practice-based research network of 763 members (559 actively practicing Wisconsin pharmacists, of which 35% are community pharmacists). As these newsletters are sent to all members via email, a screening mechanism to exclude pharmacists practicing in non-retail settings was necessary. The email was accompanied by a link to a Qualtrics form with screening questions to identify retail pharmacists who were actively practicing in Wisconsin. Contact information including name, phone number, and email address (if available) was also collected through the Qualtrics form. A reminder email with the same advertisement was sent three weeks after the first email. An example of recruitment announcement is provided in Appendix 4. Pharmacists were also recruited using an informal list curated by study team for other SUD studies. All emails sent to pharmacists included an information sheet (Appendix 5) that described the study in detail. All contact information was stored securely in a Box folder.

For patients, recruitment initially occurred through select UW Health, SSM Health pain clinics and primary care providers. Pharmacists who completed the interviews and expressed interest in the study topics were also asked to help with patient recruitment. A study flyer was developed describing interview procedures and other study information (Appendix 6) and sent to healthcare professionals to share with eligible patients. As all the patients who were initially recruited had chronic pain, the UW Emergency Department Research Coordinator (EDRC) program was utilized to recruit patients with acute pain conditions. Patients were given the

option to contact study team themselves or allow the healthcare professional/EDRC staff to share patients' contact information with the study team. Contact information of eligible and interested patients was shared with the study team using Cisco Jabber software. Eligible and interested patients were contacted, inviting them to participate in the study and schedule the interview using Jabber as well.

Procedures

For both pharmacists and patients, all semi-structured interviews (except one) were conducted virtually using WebEx or via the telephone (using Jabber). One patient interview was conducted face-to-face in a private room. WebEx is UW certified as secure for video-calling for research purposes. Jabber is also considered secure to make telephone calls remotely using the app. Verbal informed consent was solicited prior to beginning the interview. The patient interviews were 30 min long and pharmacist interviews were 60 min long and all interviews were audio-recorded. Recordings were professionally transcribed or auto-generated transcripts from WebEx were used for further data analysis. Recordings were stored only in the UW Box folders accessed by the transcriptionist and study team only. Recordings were deleted at the end of the study, and only de-identified transcripts were stored and analyzed. Patients completing the WebEx interview received a $30 Amazon e-gift card. If email wasn't available or a face-to-face interview was conducted, the $30 incentive was mailed/given as cash. Pharmacists received $50 incentive as Amazon e-gift cards for their participation.

The interview guide for the two sets of interviews were different but developed using the CFIR guide. The patient interviews focused on patient experiences in pharmacy and needs regarding their opioid medications in addition to the more SBI-specific questions. Pharmacist interviews focused on their roles in OUD prevention and individual characteristics, pharmacy

culture in general and specific to SBI (inner setting), and their perceptions of the SBI (intervention characteristics). Additional questions regarding education and practice settings were also added to the pharmacist interview guide. The interview guide was piloted in the first couple of interviews and probing questions were added as appropriate. Following the SBI knowledge question, if pharmacists reported not being familiar with the model, a brief description of the SBI model based on the SAMHSA definition was given to them. Similarly, patients were prompted with examples of different types of interventions that pharmacists could potentially provide within the SBI model to generate richer discussions. The sample interview questions linked to the CFIR constructs for both pharmacists and patients are provided in Table 6. The full interview guide (including all probing questions and descriptions) for patients and pharmacists is provided in Appendix 7.

Table 6: Interview Questions for Pharmacists and Patients

CFIR Domain	**Constructs**	**Pharmacist Questions[#]**	**Patient Questions[#]**
Innovation Attributes	Relative advantage	How does the SBI compare to other similar existing programs in your pharmacy?	What other pharmacy-based programs for opioid medicines do you know about? How does this compare?
	Adaptability	What kinds of changes do you think you will need to make to the SBI so it will work effectively in your pharmacy?	What kinds of changes would you prefer in the program so it will work effectively for you?
	Complexity	How complicated is it to provide the SBI? How can it be made simpler?	What barriers do you think will stop patients from participating in the program? How complex is this program?
	Cost	What costs will be incurred to implement the SBI? How do costs compare to benefits?	What are some possible ways this program may be beneficial? What disadvantages do you see in participation?

Inner Setting	Structural characteristics	What kinds of infrastructure changes will be needed to accommodate the intervention?	How should the program be conducted in your pharmacy, for you to comfortably participate in the program?
	Network/ Communication	Can you describe your working relationships with your colleagues? With managers/leaders? How do you typically find out about new information? When you need to solve a problem, what do you do? Who are your "go-to" people?	When you have questions about your opioid medicines, what steps do you take to seek out answers? Have you ever talked with your pharmacist about opioid medications? If yes, what has your experience been in communicating with your pharmacist about opioid medicines? If not, what inhibits your willingness to talk with your pharmacist?
	Culture	How would you describe the culture of your setting? To what extent are new ideas embraced	N/A

		and used to make improvements in your organization?	
	Change Tension	Is there a strong need for this intervention? How essential is this intervention to meet the needs of the patients?	N/A
	Compatibility	How well does the intervention fit with existing work processes and practices in your setting?	How do you feel about this program being conducted in your local community pharmacy?
	Organizational incentives	What incentives would you need to provide the intervention?	N/A
	Goals & feedback	How does the SBI align with your organization goals?	N/A
Outer Setting	Patient needs and resources	How well does the SBI meet the needs of patients?	What do you need to help you take your opioid medicine safely? How well would this program meet your needs?

Characteristics of Individuals	Knowledge & beliefs	What do you know about SBIs? How do you feel about SBI for opioid misuse implemented in your pharmacy?	What do you know about taking opioid medicines safely? How do you feel about pharmacists talking to you about opioid medicines?
	Self-Efficacy	How confident are you that you will be able to provide the SBI?	How confident are you in taking your opioid medicines correctly? How can pharmacists improve your confidence?
	Motivation	What would motivate you to provide the SBI?	If such a program is developed, would you be interested in participating? Why?

Order of the interview questions was changed to maintain flow in the final interview guide.

Data Analysis

Qualitative (Aims 1, 2)

Both pharmacist and patient interview transcripts were analyzed using deductive and inductive content analysis. Initially, deductive analysis based on the CFIR constructs was used followed by an inductive approach using descriptive and open coding to identify other relevant themes not covered by CFIR. Two coders independently coded each interview transcript and discussed their coding in detail. Any conflicts in the coding were resolved at this stage. Finally, all categories were abstracted into themes that were then matched to the CFIR constructs. Some themes were completed unrelated to the CFIR constructs and were kept separate.

Mixed (Aim 3)

Mixed method integration occurred at the methods level in this study. The first was the building approach to integration where the qualitative themes and quotes from the pharmacist interviews were used to develop quantitative items. This was achieved by creating a joint display for visualizing and organizing the data. First the CFIR constructs and qualitative themes were listed in two columns and then matched together. Themes from deductive analysis were initially matched as it was a straightforward process. Most themes from the inductive analysis were then matched with the quantitative constructs. If a theme could potentially match with multiple constructs, the best match was chosen for clarity. This decision was based on the context of the quotes and themes. For example, if pharmacists discussed using existing structures as not needing structural changes rather than compatibility of the intervention, the ‘using existing structures’ theme was matched to the ‘structural characteristics’ construct. Without the best match approach, constructs with multiple themes would become over-represented in the questionnaire. After matching as shown below (Table 7), salient and clear quotes were chosen

for each matched theme. Questionnaire items were developed using the language from the chosen quotes and themes.

Table 7: Example of matching data sources in mixed method integration:

Qualitative Sources	Example Qualitative Themes	Connect with lines	Example Quantitative Constructs	Quantitative Sources
Pharmacist Interviews	Provides opportunity for clinical services Using existing structures Need training		Relative advantage Adaptability Complexity Cost Structural characteristics Culture Change Tension Compatibility Knowledge & beliefs Self-Efficacy Motivation	Developed Survey Questionnaire

Note: Only some example themes and constructs are shown here. This matching process was carried out for all themes and constructs (not shown). Best match is shown in red.

At the reporting and interpretation level, integration occurred using a side-by-side joint display as well as narrative contiguous text. CFIR domains, constructs, matching themes, selected quotes, and developed items with response scales were presented as a joint display.

Quantitative (Aim 3)

The developed questionnaire items were assessed for face validity by two experts with practice and SUD experience. Face validity evaluation involved checking for clarity, appropriateness, and completeness. Specific questions asking for expert opinion on these factors were created (Appendix 8). Their responses identified issues with the items and response scales

which were then addressed to improve face validity of the questionnaire. Results of this process with examples were reported.

The joint display was assessed for initial construct validity by three experts including a mixed methods expert and an implementation science expert (both with pharmacy experience), and a psychometrician. Construct validity testing included evaluating the joint display for complementarity between qualitative themes/quotes and quantitative items as well as the applicability of the developed questionnaire as an implementation measure for future research. The psychometrician evaluated the joint display for correspondence with the CFIR construct definitions, over and under-representation of constructs, and overall uniformity of the full questionnaire and response scales. All issues identified and corresponding solutions to improve construct validity with examples were reported.

Template Analysis (Aim 4)

Following content analysis of the interview data from the two groups, a template approach was utilized to bring the themes, sub-themes, and categories from the patient and pharmacist interviews together to create a template of common themes. The template was initially created based on the patient interviews first and then pharmacist data was added. Then, salient quotes from the two groups corresponding to the template themes were included in a matrix. This matrix was used to make comparisons and meta-inferences regarding pharmacists and patient perceptions of the SBI as well as report findings. Opposing views across of the same themes across the two groups were also presented in the matrix. MAXQDA software was used for all qualitative analysis.

All data collection and analysis procedures are reported in the implementation matrix below for easy review:

Table 8: Implementation Matrix of Study Phases, Aims, Procedures and Outcomes in the Development of SBI

Study Phase	**Study Aims**	**CFIR Domains**	**Data Collection Procedures**	**Data Analysis Procedures**	**Outcomes**	**Point of Integration**
Patient-Centered	Explore patient experiences with opioid medications and needs/barriers of participating in SBI (Aim2)	Patient Needs and Resources (Innovation Attributes, Inner Setting, Individual Characteristics)	Purposive sampling of English speaking adult patients living in Wisconsin, who are prescribed opioid medications. 8 semi-structured telephone/video/face-to-face interviews	Use MAXQDA software Deductive and Inductive Content analysis of interview transcripts with descriptive and invivo coding Template analysis with pharmacist themes	Themes of patient experiences, needs, knowledge and beliefs regarding opioids, barriers to participation, and perceptions of SBI	Interview questions developed based on CFIR constructs Themes inform SBI design
Qualitative	Explore pharmacist needs and barriers of participating in SBI (Aim1)	Inner Settings, Innovation Attributes, Outer Setting, Individual Characteristics	A purposive sample of, English-speaking community pharmacists practicing in Wisconsin. 11 semi-structured telephone/video interviews	Use MAXQDA software Deductive and Inductive Content analysis of interview transcripts with descriptive and invivo coding	Themes of prescribing experiences, needs, knowledge and beliefs regarding opioids, barriers to participation, self-efficacy and perceptions of compatibility with pharmacy	Interview questions developed based on CFIR constructs Themes inform SBI design
Mixed/ Quant	Develop pharmacist questionnaire about SBI perceptions and evaluate initial validity (Aim3)	Inner Settings, Innovation Attributes, Outer Setting, Individual Characteristics	Use pharmacist quotes to develop survey items under each theme. Match to CFIR constructs	Evaluate face and initial construct validity (expert review)	Joint display of CFIR constructs, themes, quotes and corresponding survey items	Themes from Aim 1 inform quantitative measurements **[Building integration]**
	Develop a patient-centered opioid misuse SBI for pharmacy setting (Aim4)		N/A	Spiral analysis of themes, quotes, survey domains, items with theoretical constructs	SBI design	Integrate all qualitative findings from Aims 1&2 together

Rigor

Methodological rigor in this study was addressed in the following ways:

1. Qualitative rigor was achieved by establishing credibility and confirmability through purposeful sampling, using CFIR to guide data collection and analysis (theoretical triangulation), achieving data saturation, using multiple coders for analysis (analyst triangulation), template analysis with patient and pharmacist data (triangulation of data sources), integration with quantitative data to build complementarity (methods triangulation), and reporting in-depth qualitative data separate from mixed method data.
2. Integration legitimation: Multiple approaches to systematic integration of qualitative and quantitative data at the methods level (building) and reporting level (joint display) as described above were used.
3. Sample integration legitimation: Appropriate purposive sampling procedures involving pharmacists in diverse settings and roles and patients with different opioid and pharmacy experience were used.
4. Sequential legitimation: The quantitative phase was directly built on the qualitative findings.

CHAPTER 5

RESULTS

Qualitative Findings

Aim1: Pharmacist Interviews

Sample Characteristics

Eleven semi-structured interviews were completed virtually with community pharmacists. The participant group comprised of pharmacy managers, pharmacy owners, full-time pharmacists, and part-time or rotating pharmacists, all actively practicing in Wisconsin. Practice settings included large chain pharmacies, smaller co-owned pharmacies, independent family-owned pharmacies, specialty pharmacies, and community pharmacies associated with clinical systems. Most pharmacies were located in suburban settings with some in rural or urban areas. Both male and female pharmacists were interviewed and all but one had a PharmD degree (vs a Bachelor's degree in Pharmacy). Number of years worked as a pharmacist ranged from 3 years to over 25 years. Overall, the participants represented a diverse and varied sample in terms of, practice locations and settings, roles, and years of experience.

Themes from Content Analysis

Salient themes from the deductive analysis have been categorized using CFIR domains and constructs and described below. Themes from inductive analysis have also been matched to CFIR constructs wherever possible (for questionnaire development) and included below.

A) Inner Setting Domain

(Constructs: Culture, Network, Communication, Change Tension, Structural Characteristics, Compatibility, Organizational Incentives, Goals & Feedback)

This domain consists of themes that are specific to the SBI as well as themes that are generally describing the pharmacy setting. The general themes were important to explore current practices and nature of the pharmacy setting, as they relate to future implementation of the SBI. The specific themes were also closely linked to the intervention characteristics domain (discussed later).

Theme: Culture of pharmacy and openness to new initiatives

Most pharmacists had positive comments about their workplace culture. They generally described a progressive culture and an organization that was open to new ideas and initiatives. Although most pharmacists described the culture as collaborative, one pharmacist mentioned a more top-down approach, with newer employees not being involved in creating change. One pharmacist also noted that despite having a good working culture, the current pandemic situation led to a busy and high-pressure environment which created a lot of stress and burnout among employees. However, that pharmacist also believed that their work environment would improve when the pandemic would be under better control.

"I would say it [new initiatives] can be a case-by-case basis where we have to implement something new, depending on a patient that we're working with. But we try to use whatever feedback we get to ensure that other patients get the same care or same level of care that they might need. And again, we use our communication and collaborative environment to make that happen." – RPh 04

"The culture of pharmacy, it's an independent pharmacy so it's one where there's more of a sense of ownership that permeates the organization and not one where you're accountable to

something, or someone that several layers of administration above you. We do work side by side with ownership." – RPh 10

The pharmacists described a positive working culture that was open to new ideas and implemented change often. Although some pharmacists discussed negative aspects of their work culture, majority reported working in a collaborative and empowered environment.

Theme: Strong network and good communication

Pharmacists described having a strong network with their colleagues and good working relationships. This network was generally described as collaborative with both supervisors or leadership and with colleagues and subordinates. Communication channels were varied, ranging from meetings and emails to educational sessions and feedback loops. Pharmacists typically used their immediate supervisors for problem-solving but also had avenues to communicate with people in leadership roles.

"We have a good working relationship, like I say. We all respect each other, we get along really well, there's no drama, there's no gossip – talking behind people's backs. There's nothing like that. It's actually one of the nicest places in that regard." – RPh 03

"I would say most of the direction comes more from the system versus just things that are solely implemented at our pharmacy, but we also do have quarterly meetings with our pharmacist core team where we have a discussion kind of after work, typically an hour to two hours, talk about what's been going well in the pharmacy, what new process changes have come down from the system, and how do we implement those." – RPh 05

Theme: Mixed perceptions about the need for the SBI (Change Tension)

While many pharmacists believed there was a strong need for the SBI, some also said there wasn't sufficient need for change (change tension) to overcome barriers. Pharmacists who described positive work cultures typically believed that the SBI would be a welcome change and create a system for services that they were already providing to some extent. However, the few pharmacists who did not describe their work environment positively also stated that there wasn't high change tension because of already busy work schedules or not having a supportive network of supervisors. One pharmacist reported not having sufficient patients who would benefit from the SBI as reason for lack of a strong need.

"I think, especially kind of in the faster retail world, having some sort of standardized process for that so that [SBI] it doesn't leave as much to your, judgment." – RPh 09

"Yeah, I can tell you right now that it [change] would not be embraced because we're already tired. Whether you want the new stuff coming down there's always things that are being added." – RPh 07

Overall, most pharmacists reported a strong need for the SBI, but some mentioned not having high need for immediate change in their pharmacy.

Theme: Using existing structures for SBI implementation

Most pharmacists did not perceive a need for structural changes for optimum implementation of the SBI. However, similar to the theme of compatibility above, pharmacists discussed the exact process of SBI implementation specific to their own setting. For example,

many pharmacists discussed the need to create a system where SBI services and intervention results are documented. While pharmacists who already had electronic systems discussed using it for documentation, others discussed written hard copy protocols for pharmacists to follow and standardized forms for documentation. Some pharmacists mentioned requiring private space for optimum patient counseling, but recognized that it may not be practical or suggested making simple changes such as enhancing the waiting area to resemble a doctor's office and offer more privacy.

"I think it will fit in our flow just fine. I don't think I would need any infrastructure changes. I have a very good software program, I have a [software name], which allows me to take notes, keep notes able to pull notes up very readily. So, if we needed to document anything within their profile, it would be easily done. We're starting to work with E-care plans. So this would play nicely into doing E care plans also." – RPh 11

"We do have private spaces, but it's difficult. It turns out to be more of a slightly larger closet, which just seems a little too far to try and pull somebody in there to have that conversation. Definitely some structural changes would be nice, if possible, but I don't see that being a practical option." – RPh 01

Pharmacists generally did not perceive the need for structural changes to implement the SBI and using existing structures wherever possible. Some discussed adapting the process of providing the SBI to fit with the structural characteristics of the pharmacy and needing private space to provide patient counseling (brief intervention) if possible.

Theme: SBI is compatible with pharmacy

Pharmacists from all type of settings believed the SBI was compatible with their pharmacy setting. This was mainly due to the similarity of the SBI with other initiatives that have been implemented at their pharmacies. It is important to note that the although the SBI model was considered compatible across all pharmacies, the actual components and process of providing the SBI differed based on the existing work processes. For example, in smaller independent and specialty pharmacies, participants discussed patient-centered counseling as the brief intervention while fast-paced large chain pharmacies discussed naloxone as the most appropriate brief intervention. Pharmacists also discussed how the SBI would build on existing initiatives to improve their effectiveness.

"Yeah, I think it's very, very similar to what we're doing. And definitely the bases are built very similar to what we're doing, and are built on our beliefs. So, it's just individualized patient care and making sure that things are appropriate for them, that they're going to benefit the patient. So, it's the fundamentals [of the SBI] are built on the same fundamentals we already have." – RPh 09

"I think [large chain pharmacy] is already doing their part as far as offering naloxone… they're doing this for free. So, they're trying to do their job and trying to kind of stem any kind of misuse of opioids. Could they probably be doing a little bit of a better job as far as educating pharmacist, for example, what you're trying to do [through SBI]? Yeah, I think there's an opportunity there." – RPh 08

Pharmacists believed the SBI was compatible with their pharmacy setting because of its similarity with other initiatives previously implemented in their pharmacy. However, the exact

components of the SBI and the process or flow of providing the SBI differed significantly based on setting type.

Theme: Patient interaction and reimbursement as incentives for providing the SBI

This theme describes the organizational incentives required for providing the SBI and was closely linked to the individual motivators (discussed below). Most pharmacists said that they did not need incentives beyond an increased clinical role and patient interaction through the SBI. Some discussed various models of reimbursement such as incorporating the SBI as a 'Comprehensive Medication Review (CMR)' service or using models such as the 'cognitive billing' through the Medicaid fee for service plans. Some pharmacists also discussed incorporating the SBI service as part of quality ratings or other metrics offered by insurance plans. However, one pharmacist mentioned reimbursement using insurance plans could lead to health disparities by missing patients who are uninsured.

"*For my particular pharmacists, because I have a small team, I don't really think that I would need incentives. I think just having them understand the company's goals and then setting that expectation, and meeting those. I think they're incentivized just for wanting to do a good job and practice to the top of their license.*" – RPh 10

"*…it would just be nice to have a little better relationship with some of them [patients] where they're not always so on edge. So that would be rewarding for me.*" – RPh 02

"*Doing it [SBI] in addition to a CMR, would be great, but then you're going to be missing the patients who don't have means to pay for a CMR or have an insurance payer.*" – RPh 06

"I think there's definitely a mechanism for the standardization, maybe like a star rating for plans that would possibly use us to ensure safety." – RPh 07

Overall most pharmacists discussed not needing monetary incentives to provide the SBI and some deliberated on different reimbursement models.

Theme: Fit with organization goals

Almost all pharmacists reported that the SBI aligns with their organizational goals. Pharmacists recognized different aspects of the SBI as fitting with their respective organizational goals such as prevention, patient-centered care, specific focus on OUD initiatives, or improving patient outcomes. However, one pharmacist mentioned that there is revenue loss at the core of the SBI, mainly in terms of not filling inappropriate opioid prescriptions, which goes against the company's profit goals. Other pharmacists did not see this as an issue because other brief interventions such as dispensing naloxone or providing OUD medications if needed would offset the costs of an unfilled opioid prescription.

"Yeah, because again, [national chain pharmacy] tries to put, patient care at the center. So, anything that we can show is improving our patients' experience at the pharmacy and just their health outcomes, I think, is worthwhile and compatible with [national chain pharmacy]." – RPh 02

"[Small chain of partially-owned pharmacies] is more of a functional medicine type so, prevention is always forefront. So, if this [SBI] is a tool that will prevent misuse I think that it would align with their goals nicely." – RPh 06

Pharmacists believed that the SBI aligned with organizational goals based on different aspects of the intervention.

B) Individual Characteristics Domain

(Constructs: Knowledge, Beliefs, Motivation, Self-Efficacy)

This domain consists of themes describing individual characteristics among pharmacists as they directly relate to the SBI. Often individual characteristics were affected by external factors such organization policy or societal norms. Although these relationships have been discussed, they are primarily in relation to individual characteristics and categorized as such.

Theme: Lack of Knowledge and Education/Training regarding SBIs

Pharmacists in general had never heard of SBIs before. However, when given a brief explanation of the model, some pharmacists felt that some aspect of screening or brief interventions were covered as part of their routine practice. Pharmacists reported not receiving any education or training related to SBI. Only one pharmacist reported receiving a practice training of motivational interviewing regarding smoking cessation as part of their PharmD curriculum. However, all pharmacists had good knowledge regarding opioid safety issues and were familiar with identifying inappropriate prescriptions, naloxone dispensing and counseling patients.

"I have not heard about it[SBI]." - RPh 03

"I have a lot of experience with, like, fake prescriptions, or improper doctor-to-patient relationships, and things like that… we do kind of screen and kind of keep doing the same things for our practice, and I kind of rely on the experience I had in some of my other channels in the past [previous retail pharmacy experience]."- RPh 09

Overall, pharmacists did not have knowledge of the SBI model but had quite a bit of familiarity with individual aspects of SBI and related services.

Theme: Beliefs about SBI, Pharmacist Roles in OUD prevention, and Stigma

Most pharmacists had positive beliefs about the SBI. They believed the SBI would be helpful in increasing opioid safety and help improve outcomes for patients. They also discussed the SBI helping increasing patient interaction and giving them the ability to provide more clinical services than usual. This tied into their perceived role as pharmacists in opioid misuse and OUD prevention. They discussed having a gatekeeper role but also wanted a more clinical role in OUD prevention and treatment. Although pharmacists discussed challenges of time and getting buy-in from stakeholders, they were optimistic of the SBI being an effective tool, if implemented to fit within their workflow. However, some pharmacists also discussed being skeptical of the opioid prescriptions and even disclosed being biased towards patients picking up their opioid prescriptions, indicating presence of stigmatizing attitudes towards patients.

"This [SBI] sounds interesting and we're trying to get more interactive with our patients, backgrounds and histories and I think this [SBI] is going to give us the ability to do more of that. I'm excited about it." – RPh 11

"I would welcome it. I think I would expect the same kind of challenges of time and buy in, but this is something that we've really been doing in our pharmacy to some degree for a while."– RPh 10

"I was just a little leery of stories that are similar, and I hate to bring any bias into the situations that I'm dealing with patients, but in the back of my mind, it is a safety issue that that has to come first." – RPh 06

Most pharmacists had positive beliefs about the usefulness of SBI for patients as well as their own practice. However, some pharmacists were wary of challenges such as time and described negative attitudes towards patients.

Theme: Motivation to provide SBI and motivators

Pharmacists were highly motivated to provide the SBI and discussed many reasons behind their motivation. Primarily, preventing OUD and misuse behaviors and improving patient outcomes by providing the best care possible, were the most important motivators, according to pharmacists. They also discussed the opportunity to provide more clinical services through the SBI being an important factor in motivating them. The SBI also provided an opportunity to connect with patients, which is typically not possible for many community pharmacists, and was an important motivator. Finally, some pharmacists discussed requiring reimbursement for their services to motivate pharmacists to provide the SBI and sustain the intervention. As expected, these motivators were also discussed as organizational incentives that would be needed to provide the SBI.

"I think a lot of it is going to just be self-motivating… we get into this field because we do want to effect change and we do want to provide patients with the best care we can." – RPh 10

I've always kind of been motivated to do this [OUD prevention], because I know the opioid epidemic and stuff like that is a little out of hand. But I think it's more just to have that connection with the patients and wanting see them survive, I guess. I do care." – RPh 01

"I think that pharmacists could probably do a lot more than what we do right now, in terms of the prescription misuse. So, I think this [SBI] is a very worthy and good idea, and I'm excited to see what happens and what comes from it." – RPh 05

"…money always motivates short term." – RPh 07

Pharmacists were motivated to provide the SBI due to various reasons. Improving care for patients was the most common and biggest motivator, according to pharmacists.

Theme: Self-efficacy and reasons behind their confidence

Pharmacists reported feeling very confident in their ability to provide SBI. Three main factors were important in making them feel confident – prior experience or practice with SBI, compatibility with setting or current practice, and years of work experience as a pharmacist. Experience with similar initiatives as part of routine practice or familiarity with OUD prevention interventions helped pharmacists feel confident. Their self-efficacy was also improved when they believed the SBI would be compatible with their practice setting and barriers to implementation were addressed. They also believed that pharmacists' self-efficacy would increase with more

practice with providing the SBI, until it becomes routine. Finally, pharmacists with many years of practice experience discussed feeling confident because of it.

"Oh, incredibly confident. We've been doing it [services similar to SBI] for years. That easy access – we're kind of like the point person in healthcare, so people do have that conversation, for sure." – RPh 01

"I'd say fairly confident. I have a pretty good relationship with my patients, so I feel like I would be able to talk with them, with empathy and understanding and that they would understand where I'm coming from, and that it's not accusing them of anything, but it's a matter of safety. And as a pharmacist, I'm looking at drug safety with all kinds of medication and opioids are just one of those that have some risk" – RPh 03

"Well, I think a lot of it [self-efficacy] just comes from experience a lot of it comes from having communication skills." – RPh 07

Overall, self-efficacy to provide the SBI was quite high among pharmacists. Pharmacists trusted their past experiences when discussing confidence in their own abilities to provide the SBI.

C) Innovation Attributes Domain

(Constructs: Complexity, Adaptability, Cost, Relative Advantage)

This domain included themes focused on the characteristics of the SBI. The individual components of the SBI and the process of providing the SBI differed among pharmacists. These specific categories have been used in the template analysis (described later). The themes discussed here are those that were consistent across all participants.

Theme: SBI not complicated (in terms of disruptiveness or duration)

Pharmacists believed the SBI was easy to implement and not complicated. They did not perceive it to be disruptive to their workflow, if care was taken to design the SBI implementation protocol specifically for their setting. All but one pharmacists also did not think the SBI was time-intensive because of the brief nature of the screening (<5 minutes) and intervention (10 minutes). Some pharmacists also suggested using technicians or having the patient fill out the screening on their own to reduce time burden.

"I don't think it would be very disruptive to workflow. My technicians do all the counting, the data entry. I'm basically checking prescriptions that allows me more time to talk to patients. So, I don't take too much time to talk to patients, but that's part of my thing is that I ask them how their day is I ask them so many other things other than pharmacy related questions. So, yeah, it could be worked in without any problems." – RPh 11

"I think if you can integrate it digitally, I think that would probably be the easiest approach where it could somehow be saved, like, in a notes or a comment field that could be part of like a patient chart if you will. So you could go back and look to see what's happened before. And at the point of care, when you're actually counseling, you have limited amount of time. So I mean ideally, yeah, it can be done." – RPh 07

Most pharmacists did not think that the SBI was complicated to implement within their pharmacy.

Theme: Adaptability of the SBI

As described previously, all pharmacists discussed adaptation of the main SBI model in terms of the individual components to be included and the process of providing the intervention,

based on their own pharmacy settings and workflow. Adaptations ranged from minor changes such as creating a standardized protocol for the SBI to larger changes such as incorporating providers into the intervention protocol as stakeholders or creating digital version of the SBI. Adaptability was also linked to the trialability of the SBI, where pharmacists expected needing adaptation of the standard SBI model but required a trial or using Plan-Do-Study-Act (PDSA) cycles before finalizing adaptations.

"I guess consistency across pharmacists. I could follow one protocol, and the next time do something completely different and allow a prescription, and the pharmacist after that might refuse it." – RPh 01

"I think, having communication with providers to help them understand, especially with the landscape opioids… I feel like there needs to be a better, hand-off of getting patients into treatment for opioid misuse, and counseling, and education, and therapy." – RPh 09

"It's hard to tell [what exact adaptations are needed], because I don't know exactly what it looks like. I can see that it would look different at different pharmacies." – RPh 03

The SBI was considered to be highly adaptable by pharmacists for their individual settings. A wide range of adaptations were discussed.

Theme: Benefits of the SBI outweigh costs

All pharmacists perceived the intervention to require minimal costs and mostly included printing costs for screening forms or intervention handouts. Most did not perceive the time needed as a significant cost because the SBI model is designed to be brief. Some also suggested adaptations (see above) to reduce time involved. However, a couple of pharmacists mentioned that there could be higher costs involved if pharmacists refused to fill potentially inappropriate

prescriptions (thereby losing money) or provided other brief interventions that took longer than 15 minutes. All pharmacists believed the benefits outweighed the costs significantly.

"Definitely low cost [and] higher - potential for high reward. Yeah. I just, it's hard to see your patients… when you know there's opioid misuse. It's hard to let it continue." – RPh 03

"I could definitely see it increasing a little bit more time, as far as the pharmacist's time. But I think that that could be augmented with some… a pre-checklist or something like that. Maybe we augment it with technician help, where they're kind of getting some of the data, or if we need to call a doctor. I don't think that the cost would be that that high for us." – RPh 08

Pharmacists considered the costs to be minimal in a monetary sense. Time was a tangential cost but pharmacists discussed ways to reduce it. All pharmacists believed that the benefits outweighed the costs.

Theme: Opportunity for more clinical role: Relative advantage of the SBI

Many pharmacists did not provide prevention interventions specific to OUD that involved any patient interaction. For example, although all pharmacists in Wisconsin have the ability to dispense naloxone through standing orders, most pharmacists did not offer it to patients routinely. Some pharmacists also mentioned that they only counsel patients or even interact directly with them when a new prescription is being filled. Pharmacists saw the opportunity for more clinical services and patient interaction as the biggest advantage of the SBI over other interventions. Pharmacists from smaller independent pharmacies that had the opportunity to counsel patients regularly and provide more clinical services saw the SBI as a great addition to existing services or replacement of previously implemented interventions that were not

sustained. None of the pharmacists were offering any kind of screening for opioid misuse as part of practice other than using the PDMP.

"We used to actually have an opioid sheet. But, I've got to tell you, I have not seen that thing in years. And then, all of a sudden, those packets kind of came out –this is a safe way to dispose of your medication. And since then, I don't necessarily know that we have an effective tool that I can think of to talk to patients about opioid use. Or if there were, it's buried somewhere pharmacists would have a hard time trying to find something like that." – RPh 08

"Other than accessing PDMP I really don't have any type of program right now… As a [Pharmacy chain] Corporation, we're trying to be more proactive in healthcare, as opposed to being reactive which traditional healthcare is. We're talking about anxiety, pain. As opposed to treating them with pain medications, we're trying to get them to sleep more to realize they need to sleep more. So I think this will fit in with what we're trying to accomplish." – RPh 11

Pharmacists believed the improvement in their clinical role through the SBI as compared to other interventions or existing services was the biggest relative advantage of the SBI.

D) Outer Setting Domain

(Construct: Patient needs)

This domain consisted of only the patient needs theme as other constructs such as peer pressure and policies were not relevant to this exploratory study. However, some pharmacists discussed themes in relation to the current pandemic situation. As that is an external factor, it was categorized under the outer setting domain. However, a COVID-19 specific theme was not created because pharmacists generally talked about the pandemic affecting their current

workflow making it difficult to implement any new interventions. This was not specific to the SBI and therefore was not abstracted into a theme.

Theme: SBI meets patient needs

All pharmacists believed that the SBI met the needs of the patients to a certain extent. Pharmacists based this belief on previous experiences with patients specific to opioid prescriptions as well as other initiatives implemented in the pharmacy. Pharmacists identified the education and increase in knowledge regarding opioid medication safety among patients as a result of the SBI would be the biggest factor in meeting their needs. Additionally, pharmacists discussed using patient-centered counseling methods to better connect with patients and meet their needs. Many pharmacists also posited that the SBI would meet patient needs that are unrecognized by the patients themselves, as patients may not have knowledge regarding opioid safety practices. Some pharmacists noted that a few of their patients may be unreceptive to the SBI, at least until it becomes part of routine practice or they perceive direct benefit from it.

"[National chain pharmacy] does a call list that when it looks like a patient picked up a new prescription, and when we call on those, it's just a courtesy call to see how they're doing on their new medication. And those are always really well-received, so I do think [with the SBI] there could be some patients probably would be like: "Why are you wasting my time?" But I think some would appreciate that you were concerned and reaching out about it [opioid medications]." – RPh 02

"It [SBI] may need meet their needs more than they think it will. I mean, obviously there's a lot of people that take narcotics on a regular basis that don't think there is a problem where maybe there is a problem." – RPh 11

"My philosophy as far as counseling patients is maybe not as strict as some other pharmacists that I've seen before, but I really truly believe in a much more collaborative type of interaction right there, because I really want to know what their thoughts are about that [SBI]. And then, if it tends to be more, I don't want to do that [naloxone]– well, that's fine. That still gives me the opportunity. I asked their permission to do so, but at least it still gives me the opportunity to offer new information as far as why it might be a good idea." – RPh 08

Overall, pharmacists believed that the SBI would meet patient needs to an extent, but that patients themselves may not recognize that need.

Aim 2: Patient Interviews

Sample Characteristics

Eight semi-structured interviews were completed virtually, over the phone, or face-to-face with patients taking opioid medications for non-cancer related pain. The participant group comprised of patients with acute or chronic pain living in Wisconsin. Most participants used in-person pharmacy services, but some also used mail order or drive through pharmacy for their opioid medications. Most patients lived in suburban settings with some in rural or urban areas. Both male and female patients were interviewed and all except two participants were over 40 years of age. Information about race or other demographics were not collected, but most patients were white. Overall, the participants represented a varied sample in terms of pain chronicity and experience with pharmacy services.

Themes

Although, deductive analysis was initially conducted, the CFIR constructs did not appear to fit the data well. Therefore, most categories and resulting themes were formed inductively.

Some of the deductive themes were used in the template analysis (reported later). The following four themes are the most salient findings from the patient interviews.

Theme: Experience with opioid medications and opioid-related care

Patients who were taking opioids for chronic pain had been first prescribed opioids over five years ago at minimum. Patients with acute pain were prescribed opioids for a short-term after having surgery or due to an accident in the past year. Most patients did not report having major side effects from opioids. The biggest concern for patients was having trouble getting access to medications. Many patients attributed this difficulty to restrictions on opioid prescriptions. Many patients also discussed being worried about access to medications because their prescriber was attempting to taper their prescriptions. Some patients did not trust their provider and described a tenuous relationship. Negative experiences and stigma from healthcare professionals were common.

"I've been on it [opioid] for about ten years… The only side effects I really get from it [opioid] is constipation, which is easily treated with prunes or high-fiber foods." – Pt 01

"I haven't had trouble until now because my primary doctor is out of town but she has been providing me prescriptions. But [she is] now trying to wean me off of it right now, from the morphine. I have been taking extended release and long lasting release but immediate release which I take short acting which is 6 hours...she wants me to be off of it. But I had surgery and I'm recovering from that and I haven't yet... I need it more." – Pt 02

"It sucks that they keep trying to decrease the medication I'm on. [Prescriber] just says something about the pain medication causes you to have more pain than you're really in. I don't

think it does. I mean, I can see it if you're on a larger dose, but I'm on a lower dose than that. And I just don't see it causing that kind of problem." – Pt 04

"There was one time when I was at a local pharmacy… And he [pharmacist] treated me like I was kind of like a drug addict. And so I just quit going to him… he just, he looked at me, and he's like, "Boy, this is a lot of medicine and for someone so young. And really, do you really need all of this?" And it was very discomforting." – Pt 06

Overall, patients described having many years of experience with opioid medications but also negative experiences with healthcare professionals and accessing opioids. While most healthcare professionals were using their clinical judgement to reduce opioid prescriptions, patients did not trust them. Some patients also described being actively stigmatized by healthcare professionals.

Theme: Knowledge and beliefs about opioid safety and the SBI

All patients were somewhat aware of the safety concerns with opioid medications. However, most patients received very little information from healthcare professionals. Issues regarding about opioid safety were learned from external sources such as media, news outlets, rather than validated information from accredited and reliable sources. All patients mentioned being told to 'take as intended' and 'not to take more than needed' as part of medication counseling for opioids, beyond the usual information regarding minor side-effects. Most patients were not counseled regarding safe storage, disposal, potential for tolerance development, major side-effects including respiratory depression, risk of misuse, or contra-indicated substances and medications such as alcohol or benzodiazepines. A few of the patients mentioned being provided

information about naloxone but only one patient reported having naloxone at their home. They had no knowledge of any other opioid safety or OUD prevention interventions.

There was a strong belief among patients that there was no risk of opioid misuse or developing an OUD for them. Although they had knowledge that opioid misuse was common, they believed it was only intentional abuse behaviors among other people. There was a common tendency to distance themselves from anyone who misused opioids or had an OUD. Some patients even used stigmatizing language to describe people who had an OUD. These negative beliefs also impacted their own personal choices regarding opioid safety, such as refusing naloxone or keeping a large supply of unused opioids, as patients did not believe they were at personal risk. Most patients believed they did not need any more information about opioid safety. However, most patients were comfortable with pharmacists providing them information about opioid safety as part of the SBI and were willing to participate in it if it was offered once or twice a year. One patient was not interested and some said they would only want it to be opt-in type of intervention and not compulsory.

"I take it as needed my pill is 50 milligrams and I take 25 milligrams at a time… When I first started taking them in 2012, the doctor talked to me about side effects of the Tramadol… Well, like all medicines, you take it [opioids] within the realm of what it's prescribed to you and, you know, if you need more, then you call your doctor, or if you have any questions, you call your doctor." – Pt 05

"I think that the opioid epidemic or whatever they want to call it, they make such a fuss about it. But I believe that it has a lot to do with the recreational drugs that people take, the alcohol intake. Where, myself, I don't fit into that. So you can give me, 500 pills and say, this is you've got for the next 5 years, and I'd probably still have 450 of them left. My brain doesn't

work like an addict… I had back surgery eight months ago, and I was prescribed… it seemed like they gave me like 70 hydrocodone, and I still have 50 left." – Pt 07

Overall, lack of knowledge regarding opioid safety and negative beliefs regarding opioid misuse led to gaps in opioid care among patients. Unfortunately, mistrust of professionals and lack of patient-centered counseling regarding opioid safety meant that patients were not aware of these issues. Patients were acceptable of pharmacy-based SBI but did not believe they needed it.

Theme: SBI and opioid care needs

Apart from better pain control, patients did not feel they had any unmet needs regarding opioid prescriptions. However, when asked about what other patients taking opioid medications would need, participants were generally more forthcoming. A variety of needs were identified ranging from counseling regarding non-opioid medications or pain management alternatives, more education and information about recognizing tolerance and dependence, how to handle emergency situations such as accidental overdose, contra-indicated substances, consequences of intentional misuse including legal issues, and in general more patient-centered counseling about opioids. Most patients were welcoming of pharmacists addressing these needs.

"I'd be lying to you if I didn't joke with people and say: Hey, you know, I've got this prescription. Now, how much money can I make on the street? I would never do that. Not in a million years would I do that. But other people might, and they need to know what the issues could be." – Pt 08

"…maybe more education on the effects of… I don't know if there's such a thing as being more addicted to something when you're already on, drinking alcohol and recreational drugs. But maybe a little more information on that [would be helpful]." – Pt 07

"if they're [patients on opioids] really, truly in pain and they need this prescription, I think that they would be more than willing to do it and to try to get a better understanding of what the pain medication is going to do." – Pt 03

"I think that, that [SBI] would really be helpful for people if the pharmacist did get involved when you did pick up your prescription…you have to talk to the pharmacist about something… I think that would be the first step in being proactive is talking with the pharmacist. And maybe an opioid patient would feel more comfortable talking to the pharmacist rather than their general practitioner." – Pt 05

Patients tended to be defensive about their own needs, probably because of previous negative experiences (described above). However, when asked about other patients who are taking opioid medications, patients described various needs that could be met by the pharmacist through the SBI.

Theme: SBI implementation barriers and solutions

Patients described the biggest barrier to implementation would be the stigma attached to substance abuse. Patients said that people participating in the SBI would feel 'grilled' and get 'certain looks' because there was no privacy at the pharmacy. Some also mentioned that the lack of privacy may lead to dishonest responses to the screening questions from patients, especially those who are misusing opioids. Time was another common barrier both from their own perspective as well as the pharmacist's. Two participants mentioned that the pharmacist-led SBI may be seen as 'interfering' and patients may not like 'being told what to do.'

Despite these barriers, patients also described acceptable solutions to overcome the barriers and comfortably participate in the SBI. For example, patients suggested that both

privacy and time concerns could be addressed by providing the SBI telephonically. This would entail the pharmacist completing the SBI before or after the patient has filled their opioid prescription but allows the patient the privacy and comfort of their own home to answer questions. However, a couple of patients mentioned they would prefer face-to-face conversations as they are more personal, and it would be hard to pay attention over the phone. They also thought phone calls would easily be missed. Some patients suggested using a digital app, which they compared to their experiences with MyChart. They believed using an app would give them what they most need – knowledge regarding opioid medication safety in an easily accessible format. Patient-centered counseling using motivational interviewing strategies that address the patient's needs at the stage of change they are currently in was suggested as way to avoid the perception of interference. Patients wanted autonomy in making decisions or changing behavior, which they suggested should be emphasized in the brief intervention.

"I think it's just the whole feeling of like you're a drug seeker. You just, it's just been classed, been over-classified [referring to scheduling of opioids as controlled substances] and [I've] been on opiates for so long, and now you just need more meds, because you've become so used to it. And, yeah, I wouldn't feel comfortable." – Pt 06

"I don't know if you've been in a retail pharmacy lately, but they're zoos. I mean, you've got people lined up dropping off, prescriptions, picking up prescriptions, getting vaccinations. I mean, it's a circus. So, I don't know how much more you can expect from these people who are doing their very, very best to be professionals. It's difficult in a retail setting." – Pt 08

"Well, I just think, for instance, you go in, and you talk to your pharmacist first time you get an opioid or whatever. And let's say you have to get a refill on that. Maybe a pharmacist

could send a text out and say, you know, your refill is due in four days, and at that time, have a little skit that tells you about the opioid before you accept it." – Pt 07

"Just ensuring people that they're [pharmacists] there for information, pretty much information only and that they're not, they're not telling them exactly that they have to change anything that they're doing, just being there for more knowledge." – Pt 04

Despite discussing several barriers to participating in the SBI related to stigma, time, and pharmacist roles, patients also suggested innovative solutions to improve patient acceptability of the SBI.

Mixed Method and Quantitative Findings

Aim 3: Quantitative questionnaire

The questionnaire was developed based on the themes and quotes from pharmacist interviews (Aim 1). The final questionnaire consisted of 36 items. The CFIR domains, constructs, qualitative themes, quotes, developed quantitative items, and their corresponding response scale are presented together as a side-by-side joint display in Table 9.

Table 9: Joint Display of Conceptual Framework, Qualitative Themes and Quotes, and Quantitative Questionnaire Items

CFIR* Constructs	**Themes**	**Quotes**	**Questionnaire Items**	**5-point Likert Response Scale**
Domain: Characteristics of Individuals				
Knowledge	Lack of Knowledge of SBI	*"I have not heard of the term SBI before."* - RPh 04 *"I really don't know much about it [SBI] so I don't have a lot to bring into it from, my prior knowledge, I guess."* -RPh 06	1. How aware are you of screening and brief interventions?	Not aware - Somewhat aware - Moderately aware – Mostly aware- Extremely aware
			2. How would you rate your current knowledge regarding SBIs for opioid misuse?	Poor- Fair- Adequate- Good- Excellent
	Lack of education and training regarding screening for opioid misuse	*"I guess, I feel like we kind of did some in school, where, like, I feel like we did one with smoking cessation that you were just supposed to address. Like: do you smoke? If you do: would you be interested in learning more about quitting? Basically, like, pretty open-ended, I guess. Yeah, just to kind of get an idea for what your patients are thinking about, but not really specifically with opioids. I don't think we ever did anything."*-RPh 02	3. Please rate the <u>education</u> you have received regarding screening for the following: a. substance misuse b. opioid misuse 4. Please rate the <u>training</u> you have received regarding screening for the following: a. substance misuse b. opioid misuse	Poor- Fair- Adequate- Good- Excellent
	Familiarity with brief interventions	*"We kind of already do it. I mean, like a general sense, whenever someone drops off a narcotic prescription, we're usually talking through everything, and we have standing orders Narcan, so we always offer it. Not a lot of people want to take it, because it's a Narcan prescription. But we have the ability to give it to them."* -RPh 01	5. How often do you provide the following services for patients when they pick up opioid prescriptions? a. Dispense Narcan (naloxone) to patients	Never- Rarely- Sometimes-Often- Always

		"We'll even go to the effect that if you're finding that you're needing more of it [opioid] to basically treat the same type of issue [patient has developed tolerance], at that point we invite them [patients] to start talking to us or to start talking to their doctors. And I think we really do a really good job with that." –RPh 08	who may benefit from it b. Counsel patients regarding opioid safety issues (such as storage, disposal) c. Counsel patients regarding opioid misuse d. Contact prescribers for safe opioid prescribing	
Beliefs	Beliefs about SBI in general	*"I would think it would be helpful. I'm always interested in protecting the patients and having them have a good experience in my pharmacy. So I think they would view it hopefully, as a new program that we are rolling out to, help them to be more safe."* –RPh 11 *"I think everyone would be also willing to do this [SBI] "* – RPh 10	6. Please rate the helpfulness of the SBI in improving patient outcomes. 7. Please rate the helpfulness of the SBI in improving opioid safety.	Not helpful-Somewhat helpful-Moderately helpful-Very helpful-Extremely helpful
	Perceived Role	*"I mean, I think there's definitely a watchdog aspect to make sure that people aren't refilling controlled substances too early, that they're not getting controlled substances filled by more than one provider, things like that. So, you know, kind of just watching over people, making sure that their use is appropriate."* -RPh 03 *"I think this [SBI] is fascinating. I love the idea of improvements and using our abilities to the highest of our*	8. My role as a pharmacist includes watching for opioid-misuse. 9. The SBI gives me an opportunity to use my clinical skills more than usual.	Strongly agree – Strongly disagree

		license [through the SBI]…we got to get away from reimbursements from [just] dispensing stuff." -RPh 06		
	Negative and Stigmatizing Attitudes	*"I think my coworkers are skeptical sometimes, of those situation… especially with like opioids or, like, other C2's. But I think overall, like, yeah, I guess skeptical is kind of a big word I would use with my coworkers and the people who are picking up their prescriptions."* -RPh 02 *"I'm sorry but I have to bring some bias to some of this because I want to be aware of the entire situation and have that gut feelings saying, "Hey is this somebody who's maybe abusing? Are they telling me the whole story? Am I being, you know, having the wool pulled over my eyes that kind of thing?"* -RPh 06	10. Most pharmacists are skeptical of patients misusing opioids when they pick up opioid prescriptions. 11. Most pharmacists are negatively biased against patients picking up opioid prescriptions.	Strongly agree – Strongly disagree
Motivation	Highly motivated to provide the SBI	*"I mean, this interests me just because there have been so many issues with opioid abuse and misuse that I think… just helping to prevent issues is motivation enough."* -RPh 03	12. How motivated are you to provide the SBI in your pharmacy?	Not motivated – Somewhat motivated- Moderately motivated- Very motivated- Extremely motivated
	Motivators:		13. Please rate how important each of the following factors are in increasing your motivation to provide the SBI.	

	Improved Patient Care and Outcomes	*"I think a lot of it is going to just be self-motivating because we get into this field to at least pharmacies I work with, we get into this field because we do want to effect change and we do want to provide patients with the best care we can."* – RPh 10	a. Improved patient care and outcomes as a result of the SBI	Not important- Somewhat important- Moderately important- Very important- Extremely Important
	Increased Clinical practice	*"I think their motivation would come from being, you know, and practicing to the top of their license and making good educated decisions based on what they would do in their own practice."* –RPh 09	b. Opportunity to provide more clinical services	
	Improved connection with patients	*"I think it's more just to have that connection with the patients and wanting see them survive, I guess. I do care."* – RPh 01	c. Opportunity to connect with patients	
	Reimbursement	*"And then if there was, any type of reimbursement available for this like a CMR that would be ideal. The time being spent and taken to do a wonderful thing but the pharmacist should be reimbursed."* -RPh 06	d. Reimbursement for providing the SBI	
Self-Efficacy	High confidence	*"I would say fairly confident that it's something that we would be able to implement on our pharmacy."* –RPh 05	14. How confident are you in providing the SBI at your pharmacy?	Not confident- Somewhat confident- Moderately confident-Very confident-Extremely confident
	Reasons behind self-efficacy:		15. Please rate the importance of the following factors in making you confident to implement the SBI.	

	Many years of practice experience	*"I'm confident I have been doing this [practicing] for many years, so I don't really have too many concerns."* –RPh 07	a. Opportunity to address your concerns through practice	Not important- Somewhat important- Moderately important- Very important- Extremely Important
	Compatibility with practice/setting	*"Yeah, I'm highly confident, I think just because at our practice, we just have more time to spend with the patient and ask them questions. So, we can really get to know them on an individual basis. You know, I can take 15-20 minutes to talk to a patient, and if they're not giving me the answers, or they're kind of scooting around questions and things like that, we can kind of see more of the red flags, and things like that"* –RPh 09	b. Compatibility of SBI with your setting/workflow	
	Experience with similar interventions/ initiatives	*"I would feel very confident, because a lot of the times we do these things [brief interventions] anyway. So, um, doing it systematically would be better and, I think… we can do that, no problem."* –RPh 04	c. Prior experience with similar interventions	
Domain: Inner Setting				
Structural characteristics	Using existing structures	*"I would probably, I write a lot of notes on prescription leaflets on the information sheet for the patient. Either just for me to talk to them about, or for my tech [pharmacy technician] to pass on."* –RPh 01 *"I don't think any infrastructure changes [are needed]. I mean, we have a good work flow system, a good pickup area. We have a private consultation room that we can use in case somebody needs more privacy to talk about it. We use a lot of, reminder cards, reminder tags in our baskets, so, to have a quick little, maybe quarter sheet tag that has some of those prompts on it to begin that discussion."* –RPh 03	16. We can use existing work processes to implement the SBI at our pharmacy. 17. We need physical infrastructure changes to implement the SBI at our pharmacy.	Strongly agree – Strongly disagree

Network/ Communication	Good working relationships	*"Yeah, I would say we [pharmacy colleagues] have a good working relationship. We definitely try to raise each other up."* –RPh 04	18. Please rate the working relationships with your pharmacy colleagues.	Poor- Fair- Adequate- Good- Excellent
	Strong communication	*"We have a lot of message boards that basically tell us about new procedures. We have a district meeting every other Thursday, so anything new that's coming through will also be explained there, with opportunities, of course, to answer questions...There's always feedback sessions every year. And you basically bubble up ideas."* –RPh 08	19. Please rate the communication networks with your pharmacy supervisors.	Poor- Fair- Adequate- Good- Excellent
			20. I can easily learn about new initiatives in my pharmacy. 21. I can provide feedback about new initiatives undertaken at our pharmacy.	Strongly agree – Strongly disagree
Culture	Open to new initiatives	*"I would say the biggest culture is progressive. We're constantly looking at the market of pharmacy and seeing the needs of the area and how we can adapt to make a difference." –RPh 09* *"I guess specifically with [Pharmacy Chain], they're definitely trying to always use new ideas and new cultural mindsets. I think my pharmacy as well, for being where we are, my co-workers specifically are definitely pretty open to trying new ideas."* –RPh 02	22. The culture of our pharmacy is progressive. 23. Our pharmacy organization is close-minded about new initiatives.	Strongly agree – Strongly disagree
Change Tension	Strong need for SBI	*"I think that the need is high and I think it would be very welcomed to have in our pharmacy."* –RPh 10	24. A strong need for the SBI exists at our pharmacy.	Strongly agree – Strongly disagree
Compatibility	Similar to other initiatives	*"I think it'd be very easy to implement both from a workflow standpoint, because we've done this before with the good faith dispensing process that we currently have."* –RPh 07	25. The SBI is similar to other initiatives implemented at our pharmacy.	Strongly agree – Strongly disagree

Organizational incentives	Relationship with patients	*"Anything that gives them [pharmacists] more time to spend with their patients."* –RPh 01 *"People are happy to work more clinically and do more than just verifying and dispensing prescriptions, so I don't think there would necessarily be incentives at my pharmacy that we would need in order to provide this [SBI]."* –RPh 05	26. Incentives beyond increased clinical care time with patients would be necessary to provide the SBI.	Strongly agree – Strongly disagree
	Reimbursement	*"Reimbursement almost exclusively. When you start talking about community pharmacies, business models always come up. So, if there's a way to, you know, do the screening and be reimbursed for it or do an intervention and reimburse for it. That's what we'd like to see."* –RPh 04	27. How important is reimbursement as an incentive for providing the SBI?	Not important- Extremely important
			28. How much incentive is adequate to provide the SBI?	Free response
Goals & feedback	Fit with Organization Goals	*"I think it aligns very well. [Pharmacy] is very proactive. They promote patient care. They really want their pharmacists talking with patients, they're promoting using clinical services, so I think it fits in very nicely with our goals."* –RPh 03	29. How well does the SBI align with your pharmacy organization's goals?	Not at all aligned- Somewhat aligned- Moderately aligned- Very aligned- Extremely aligned
Domain: Outer Setting				
Patient needs and resources	Meets patient needs	*"I think for a lot of our patients that this would be really welcome and a needed type of more thorough and consistent interaction. We do have a lot of patients who are on chronic pain meds. We do a lot of patients who have low health literacy, and with our injection program, we have a lot of patients who are already in opioid dependence, and this would be the kind of tool that would establish from their perspective another resource that they could utilize."* –RPh 10	30. How well does the SBI meet the needs of your patients? 31. The SBI can act as a resource for patients to obtain thorough and consistent pharmacist interaction.	Not at all- Extremely well Strongly agree- Strongly disagree

Domain: Innovation Attributes				
Cost	Minimal costs	*"Minimal [costs]…it'll probably be some paper that we print out with the questions and the reminder on it, so very minimal."* –RPh 05 *"Probably none. Almost no [costs]. The biggest thing [cost], would maybe just be the printing of the surveys or the intervention tools to actually hand out to patients and give to them. So – pennies, if that."* –RPh 05	32. How would you describe the costs involved in implementing the SBI?	Insignificant-Minor-Moderate-Major-Severe
	Benefits outweigh costs	*"I think that benefits definitely outweigh the costs."* –RPh 09 *"Oh, the benefits are tremendous. If we can save one person from going to the emergency room for an opioid overdose. I mean, that cost in itself is tremendous. Just that one emergency room visits. So the benefits are much, much more important than that one cost of going to the ER."* – RPh 04	33. Costs to implement the SBI outweigh its benefits.	Strongly agree-Strongly disagree
Complexity	Not complicated or disruptive	*"I don't think it's complicated at all. I mean, we're used to asking questions and kind of getting a dialog started so, you know, this is just… we're doing that and it's just a different topic."* –RPh 03 *"Yeah, I don't think it would be super disruptive or difficult to provide this. Especially, like I said, if the patient may be able to fill it out on their own, that would be a very, very easy, easy thing to do. If our technician has to come in and help the patient read, they've always been happy to do that in the past"* –RPh 05	34. How complicated is providing the SBI at your pharmacy?	Not complicated-Somewhat complicated-Moderately complicated-Very complicated-Extremely complicated

	Not time intensive	*"I don't think it would be necessarily time consuming. It would be time consuming if you had to chart or put stuff in the notes, if they're lengthy. If they're short and concise and they're easy like bullet points or a couple of things then it's doable."* –RPh 11	35. Providing the SBI would be time-consuming.	Strongly agree-Strongly disagree
Relative Advantage	SBI offers opportunity for patient education	*"When I look at the training for [existing intervention], it's really more trying to identify fraudulent prescriptions. I mean, several 'what to look out for'. So, it's more… a policing action, versus actually having a conversation about that [misuse]."* –RPh 08	36. The SBI offers more opportunity for individualized patient care as compared to other opioid safety interventions implemented at our pharmacy.	Strongly agree-Strongly disagree

*Consolidated Framework for Implementation Research (CFIR) Note: A brief description of the proposed SBI (including exact components) will be provided at the beginning of the questionnaire. Pharmacists will be told that the term SBI in the questions refer to the proposed model described above.

Initial Validity Testing

The final questionnaire formatted for future research applications is included in Appendix 9. Table 10 and 11 include results of the face and initial construct validity conducted by expert review. The tables include the exact factors assessed, the issues that were identified in the question, and the solutions used for addressing the issues. Each factor is accompanied by an item that exemplifies the identified issue. The corresponding change that was made to the item or the action to be taken for future research (i.e., content validity using cognitive interviews) is also included.

Table 10: Results of Face Validity Testing

Factor Assessed	Issues Identified	Solution	Example Item	Change/Action
Questionnaire achieves its purpose	Achieves purpose as pre-implementation measure but needs stakeholder confirmation	Content validity testing with cognitive interviews will be carried out in future research	How often do you provide the following services for patients when they pick up opioid prescriptions?	Evaluate if services listed are appropriate brief interventions in future cognitive interviews
Clarity of items	Some items have wording from the quote but may be unclear to many responders	Change wording to retain meaning of the quote but improve clarity	"I think there's definitely a watchdog aspect…" – Q- There is a watchdog aspect to my role…	My role as a pharmacist includes watching for opioid-misuse.
Clarity and appropriateness of response options	Some of the response options are unclear	Changed response options to be specific or replaced with standard agreement scales	Relative advantage of SBI over other interventions- (Much worse - much better scale)	Reverse coded item and agreement scale

Completeness of questionnaire	Questionnaire is complete but one additional item was suggested	Cognitive interviews will be used to evaluate if additional item is relevant	Need for structural changes is evaluated but what changes are needed is not asked	If participants state that structural changes will be needed, they will be probed further and their response will be used to create additional items

Table 11: Results of Initial Construct Validity Testing

Factor Assessed	Issues Identified	Solution	Example of Issue	Change made/ Action to be taken
Match between items and construct definitions	Some items do not fit the construct perfectly	Move items to more appropriate constructs	I would be willing to provide the SBI at my pharmacy.	Moved item from beliefs to motivation construct
Match between items and qualitative themes and quotes	Some quotes do not seem related to the item	Add context to quotes to show match better	Quote about brief interventions: "We'll even go to the effect that if you're finding that you're needing more of it to basically treat the same type of issue…"	"We'll even go to the effect that if you're finding that you're needing more of it [opioid] to basically treat the same type of issue [patient has developed tolerance]"
Consistency of items within constructs and domains	Both question and statement formats have been used	Changed item format wherever possible. Ordered	Inner Setting domain has both question and statement formatted items	Final questionnaire has items grouped based on

		items to group items with same format together		format consistency rather than CFIR domains
Complete representation of constructs	Some constructs need more items for completeness	Added items as needed	Organizational incentive incomplete without asking about how much reimbursement is needed	Added item 'How much incentive is adequate to provide the SBI?'
Construct over and under representation	Some constructs are represented by multiple items when not capturing new information	Removed redundant items	Two workflow fit related items included in structural characteristics (inner setting domain) and complexity (intervention characteristics domain)	Removed one of the items from the 'complexity construct' related to disruptiveness of the SBI to workflow
Appropriateness of response options to assess construct	Some response options are vague and not specific to constructs	Changed response options or made note	Please rate the costs involved in implementing the SBI: Insignificant-	Add dollar amounts to response options based on pharmacist perceptions

		to evaluate further in cognitive interviews	Minor-Moderate-Major-Severe	evaluated in future cognitive interviews
Structure of questionnaire	General items and items specific to SBI are mixed together	Re-order items to include general items first	Items related to pharmacy culture and networks are not specific to SBI	General items included first followed by SBI definition and then SBI specific items

Template Analysis Findings (Aim 4)

The findings from the template analysis are reported below. The same template of themes was used in analyzing patient and pharmacist interviews. Some themes occur as constructs of the CFIR model, but most themes in the template were formed inductively. After using the template across groups, findings were compared across groups and interpreted for its implications to future implementation of the SBI. All these results have been presented in Table 12.

Table 12: Template Themes, Representative Quotes, Explanation, and Application for the SBI

Themes	**Patient Quotes**	**Pharmacist Quotes**	**Explanation**	**SBI Application**
Knowledge and education about opioid safety	*"[All I was told about opioid safety is] that you should do what the bottle says, and not overuse it."* – Pt 02	*"…ascertaining from the patient whether or not they're getting this opioid for the very first time, because that presents the greatest opportunity for us to talk about the issue and everything with dependency or misuse."* – RPh 08	Patients did not have much knowledge of opioid safety. Pharmacists agreed that patient counseling also provides opportunity to discuss misuse.	Brief intervention must include patient education on opioid safety by pharmacist/ using tools/ applications.
Beliefs about the SBI	*"I'm good with it [SBI]. I think my pharmacy is amazing. I prefer to know about the medications I'm taking. I mean, you're only helping yourself when they give you this information… my pharmacist does that [counseling]already. He's very knowledgeable, he says if, if this [fentanyl]patch is working for you and you can go longer without your pills, then maybe we could cut down on the pills… he's already giving this information."* –Pt 03 *"I think most people would think it [SBI] would be fine. But then some people would feel like it's interfering.*	*"I'm pretty confident that we are at the very least get some momentum and set the groundwork for [the SBI], what could evolve into this standard of practice."* – RPh 10 *"I don't want to be coming across like I'm accusing this person of being an abuser of medication. I don't seem to have a problem with it [counseling], because I think a lot of it, we do a lot of the homework and prep work ahead of time. In other words, as far as: hey, this is our policy about filling these [opioid] prescriptions… [SBI needs] training more on making pharmacists feel comfortable that they*	Both patients and pharmacists believed the SBI could be helpful in providing patient education regrading opioid safety and misuse. While patients would like more information about their prescription, they did not want to be told what to do or the pharmacist to 'interfere'. Pharmacists would like training in improving their comfort with providing counseling on such a sensitive subject and making it into	SBI must be patient-centered and provide information without using accusatory or labeling language which will require pharmacist training and introducing the SBI into routine practice.

	So maybe for those patients, it would be helpful to tell them that this is just information only." – Pt 04	*can discuss that issue with patients. I think that's it."* – RPh 08	their routine practice or policy for opioid medications.	
Stigma	*"It feels like every time you get an opioid medication, you're being looked at like you're an abuser, or like does this person really need it?"* – Pt 01	*"I'm sorry but I have to bring some bias to some of this because I want to be aware of the entire situation and have that gut feelings saying, "Hey is this somebody who's maybe abusing? Are they telling me the whole story?"* – RPh 06	While only some pharmacists admitted to being biased towards patients picking up opioid prescriptions, most patients discussed feeling stigmatized by healthcare professionals, which is a barrier to SBI participation.	Patient centered education, Anti-bias training to address stigma against OUD
Patient - pharmacist relationship	*"…at some point, you would think the doctor could realize [recognize misuse]. Because I know my doctor takes steps. I didn't start out on 10 milligrams oxycodone. I didn't start out on a fentanyl patch, I started out on the lowest dose of what he could prescribe. But as I got older, and I got you know, a lot more things wrong and pain…a lot of doctors are very good at telling that, seeing in a patient, whether they really need them[opioids] or they don't. That's what doctors get trained on. I truly think that it would be more up to the doctor in the 1st place, because he's the 1 who's going to prescribe it."* – Pt 03	*"We have a few patients; they'll get five-day prescriptions for hydrocodone. And it'll be from a couple of different doctors sometimes it'll be one every six hours. Sometimes it'll be one every four, sometimes it'll be one every eight, and it's kind of odd to me. So, I do try to delve into, like: "Hey, has your pain [increased]… are you still [in pain] … what's still going on that you still need these three-day courses every… couple times a month they'll get a couple of days of it. And I don't really get anywhere because I, I am afraid of them jumping to conclusions."* – RPh 02	Patients used informal sources such as the internet for questions about their medications. They also had conversations with prescribers about their medications but most never discussed it with their pharmacists and did not view pharmacists as providers of clinical services. While many pharmacists attempted to intervene when they suspected misuse, most were not comfortable with it and did not view it as part of their practice scope.	SBI must be marketed as a clinical service; advertise the SBI and clinical role of pharmacist using posters and brochures, prompting patients to ask questions.

	"I research it [opioid medications] online, or I'll ask my general practitioner." – Pt 05			
Self-efficacy due to experience	*"I've taken them [opioids] for years and that I, without them, I can't function. And I feel comfortable because my doctor explains anything that I have questions about."* – Pt 06 *"I'm doing well, and I don't need it [SBI] because I've already asked all the questions."* – Pt 04	*"I'd say fairly confident [in providing the SBI]. I have a pretty good relationship with my patients, so I feel like I would be able to talk with them, with empathy and understanding and that they would understand where I'm coming from, and that it's not accusing them of anything, but it's a matter of safety."* – RPh 03 *"Oh, incredibly confident. We've been doing it for years. That easy access – we're kind of like the point person in healthcare, so people do have that conversation, for sure."* – RPh 01	Patients had confidence in their ability to take opioids safely because they have been taking it for many years. Hence, they believed the SBI would be more useful for new patients. Pharmacists believed the SBI would be useful for both new and experienced patients and thought the existing relationship with their experienced patients would help in SBI implementation.	SBI must be adapted differently for new and experienced patients (tailored SBI). Experienced patients may be hesitant to participate in the SBI because they do not perceive the need for it.
Screening component	*"I think an interactive tablet might be good. A form, obviously, you can certainly do that. But a form might, given all the germs and everything like that, form might actually be better than a tablet."* – Pt 01 *"I think both would work. What would I prefer? Probably talking to the pharmacist."* – Pt 04	*"I think the ideal screening would start with some of the things that were already just doing by default, checking the PDMP, calculating the morphine equivalence for everything, we're looking for diagnosis codes for what an opioid is being prescribed. We are assessing the risk of the other medications that they're on, that would increase the risk for patients such as concurrent benzos.*	Patients discussed answering screening questions on a tablet, form, or app for privacy or wanting a face-to-face conversation with pharmacists. Pharmacists wanted the screening to be in addition to services already offered. They also discussed needing technician help to initiate the screening through a form or	Online, phone, and in-person formats of screening will have to be tested to compare effectiveness, test feasibility and to also meet patient

		That'd be part of our, just initial information gathering prior to any kind of screen." – RPh 10 *"I think you would have to involve the entire pharmacy. So, that technicians would maybe be able to initiate the whole process, they'd recognize this is a controlled substance, and we have not talked with this patient before and then it would probably travel with the prescription as it's going through the processes of being entered and filled and checked. And then everything is laid out for the pharmacist, that's going to be counseling and the only way I can really see it is happening at pick up. Or do it by phone, maybe that would be effective."* – RPh 06	tablet. Some suggested doing the screening over the phone to make it more efficient and save pharmacist time.	preferences. Standardized screening tools can be used if they are brief (< 5mins) and easy to answer.
Brief Intervention - Naloxone	*"I think that the doctors are starting to, give counter measures so if people would accidentally OD they could help themselves at home with Narcan. And I think that's good and that maybe people understand and know how to use that."* – Pt 06 *"I'm afraid that if people could get narcan to carry with them...it's giving them a reason to take more, because they could use that*	*"making it maybe a little bit easier to dispense [Narcan] sometimes. So, having a script to kind of explain what it is, possibly, having a script to say why we're dispensing it."* – RPh 05 *"Everyone seems to understand the concept of an Epi-pen. So, we usually explain the Narcan is like an Epi-pen for an overdose."* – RPh 01	Patients and pharmacists discussed naloxone as a potential brief intervention. Many patients did not think they needed it because they believed it was only for people who intentionally misused opioids.	Naloxone can be a brief intervention but a script for pharmacists that discusses it as an antidote for a potential side-effect of the opioid rather than patient's

	[naloxone] and it'll bring them back. I think that could go either way." – Pt 03			intentional misuse behavior will be needed.
Brief Intervention - Counseling	*"Just ensuring people that they're [pharmacists] there for information, pretty much information only and that they're not telling them exactly that they have to change anything that they're doing, just being there for more knowledge and then leaving it up to them if they're going to change. Because when people have more knowledge, they're more willing to change things about what they're doing than just to be told, well, you should be doing it this way."* – Pt 04 *"I think before you can accept or decline the prescription that you have to read through the information, which maybe people will, maybe people won't. But at least you get, have a little box that says I acknowledge something."* – Pt 07	*"We have a handout that we give to our patients. I think in an ideal circumstance, we would use it [SBI] as an educational opportunity as well to show patients how an opioid will actually work in the system for chronic use where there seems to be this sinusoidal wave that shows more and more diminishing return on investment, where the effects of analgesia do seem to diminish the more chronically this is used as the body develops tolerance and sometimes just have that paradoxical effect of taking more leading to the pain being worse. Along with that, as far as the abuse potential goes with that euphoria and needing to take more to get back up to just a baseline level of not feeling that pain."* – RPh 10	Patients were enthusiastic about the SBI if it improved their knowledge of opioid medication safety. They suggested both face-to-face conversations or online digital app-based education options for the SBI. Either way patients stressed the need for autonomy in the design of the SBI. Pharmacists also suggested that counseling could be used as brief interventions to improve patient knowledge. Handouts could be used to help with counseling and reduce the time needed.	Counseling as a brief intervention offers ample opportunity for patient education but the counseling offered must be patient – centered. The digital format of the SBI could provide this education through an app, if preferred by the patient.
Brief Intervention –	*"I don't know if currently there is a system or a program or procedures in place where pharmacists can have*	*"The obvious choice will be to let the patient know why you have reservations and then let them know*	Patients were comfortable with their pharmacist contacting prescribers	Pharmacists can contact prescribers as

Contacting prescribers	*actual conversations with doctors. I don't know if that's a regular thing, if they regularly do. But I think that's not a bad thing if somebody feels that, oh, this stuff is just too strong, I don't need this much. Or on the other side, wow, it's really, it's not doing enough, because there might be a different, you know, medication or a higher dose or something along those lines that might be better for that patient. I think that that kind of conversation should be happening."* – Pt 01	*what you're doing - contacting the doctor. Maybe the doctor's not aware. I've had a couple instances where I've had mostly with our ER doctors where they will prescribe pretty strong pain reliever, it's really potent medications in people who probably may or may not need them or the doses. So, they may or may not be aware of the history or other drugs that the person is taking. So if you see something, that's not appropriate you'd want to contact the provider and discuss whether you should proceed, or whether they should try something different."* – RPh 07	regarding opioid medications. However, they wanted to be involved in that process and be aware of the conversation. Pharmacists also suggested that contacting prescribers regarding inappropriate opioid prescriptions must be done but with the patient's approval.	part of the brief intervention as long as patients are involved in the process.
Implementation Needs	*"I think asking somebody, offering the benefit of what the program does, and then ask them, would you like to participate? I think that's probably the best way to do it."* – Pt 01 *"My thought would be, face to face is the best. I think it forces the patients to communicate, to think about, it because you have someone in your immediate presence as opposed to filling out a form, or even on a phone call where you can let your mind*	*"That's my biggest problem right now. The question is making the professional judgment of when I should do this or when I should not."* – RPh 08 *"…there would have to be an education piece for pharmacists there. I don't think I'm alone in saying that that I would be out of my comfort level."* – RPh 06 *"I think, having just communication with providers to help them understand, especially with the*	Patients wanted education in a format that offered autonomy and privacy. They also wanted the prescriber to be involved. Pharmacists discussed needing a protocol (instead of relying on judgement) and training to provide the SBI. They also discussed prescriber education and involving prescribers as stakeholders in SBI implementation to get their buy-in.	The SBI must be designed to have multiple formats (face-to-face) and online to offer patients an individualized service. Prescribers must be involved in implementation

	wander. So, I think face-to-face is the better way to do it [SBI].” – Pt 08 *“it seems like the world is going to cell phones and computers, so just somehow get information out on there. … And when they’re looking something up online, maybe a little skit can pop up, a little box beside it”* – Pt 07 *“First of all, though, I think the doctor and the pharmacists both need to have a discussion with this person. And more so if that it's [misuse] what they're doing and if they keep doing it, then, you know there's going to be consequences.”* – Pt 03	*landscape opioids, I feel like there's the providers that just don't care at all about it and are just like, “Well, my patient’s in pain. I need them on as many pain meds as they can. Who are you to question me?” And then you have the providers that are like: “Well, I'm being judged now, so my patient's going to get nothing, and they're left with no meds.” And then those patients end up, you know, using drugs on the street or heroin or things like that.”* – RPh 09		as stakeholders. Educational material and training for pharmacists must also include a protocol for providing the SBI.
Implementation challenges – Time, Roles & Stigma/ Privacy	*“I think there's a certain amount of embarrassment that “I don't know what's going on,” or “I didn't listen to the prescribing doctor.” Um, so I think that's something that has to be taken into consideration. Time is an issue. Where do you find the time?”* – Pt 08 *“I like to have a relationship between my doctor and myself rather than the pharmacist. And it seems like when you go to the pharmacy,*	*“I think some of the challenges we're going to face one is going to be time pressure. Two is going to be feeling like, perhaps you're not educated to really ask these questions and make the interventions. And I think three is going to be a certain fear that you're going to be perceived as somebody who is now the accuser of the patient.”* – RPh 10	Both patients and pharmacists identified time required as the primary challenge for SBI. Some patients did not perceive that pharmacists’ role to provide the SBI and pharmacists had similar concerns regarding their ability or scope of practice. Patients did not want to be labeled or have conversations without privacy and	Using digital formats may provide more privacy and save time. Appropriate patient-centered SBI training for pharmacists and marketing it as a clinical service will

	there's always five people standing in line, where I don't know if people would be real comfortable answering questions, when there's five people standing there listening to you." – Pt 07		pharmacists did not want to perceived as accusatory.	help improve pharmacist roles and reduce stigma.

CHAPTER 6

DISCUSSION

Summary

Overall, this study resulted in identifying pharmacist and patient perceptions and needs regarding an opioid misuse screening and brief intervention for the community pharmacy setting. Pharmacist interviews helped establish their views as a stakeholder in providing the SBI and implementing it in their own setting. We also identified potential barriers to participation and explored possible solutions. This study was the first in-depth qualitative exploration of patient needs and perceptions regarding opioid medication safety, misuse behaviors, and pharmacy-based OUD prevention. Patient interviews were helpful in designing a patient-centered SBI and offering novel ideas for SBI implementation such as using digital technologies. As part of our focus on D&I science in designing the SBI, we successfully used the building approach to mixed methods integration to develop an implementation measure specific to the SBI and the pharmacy setting. This measure, once standardized, can be used in future implementation studies of the SBI. All pertinent findings from the four aims (qualitative pharmacist, qualitative patient, mixed, and quantitative) have been discussed in detail below.

Aim 1 (Pharmacist Themes)

The first aim of the study was to explore pharmacist perceptions, needs, and barriers to providing the SBI in their pharmacy. Questions and themes were organized based on CFIR domains. Each domain is discussed below.

Inner Setting

Pharmacists described general factors regarding their pharmacy setting that were important facilitators for effective implementation of the SBI. Most pharmacists described positive working cultures and having strong network and communication with their pharmacy colleagues and supervisors. These constructs have been included in the CFIR based on the complexity theory that relationships between individuals maybe more important than individual attributes and can directly impact implementation of healthcare initiatives within organizations.[90] Also, less tangible aspects of the organization such as culture and climate are often harder to measure but could be key to success or failure of initiatives.[90] Therefore, having positive perceptions of culture and network in pharmacies can help improve the implementation of the SBI in the future. Existing communication channels within pharmacies could also be used to disseminate information about the SBI and provide avenues for linking potential adopter organizations in the future.

In addition to general themes of culture and network within pharmacies, pharmacists had specific perceptions regarding the implementation of the SBI as it relates to the implementation climate. One factor that could act as a barrier to future implementation of the SBI was the mixed perceptions about the need for the SBI. Although all pharmacists believed it would be beneficial to patients, some pharmacists suggested that there was a stronger need to reduce pharmacist workloads, rather than add to it. Involving technicians and using digital technologies in SBI implementation may help address this barrier. However, impact of digital interventions on healthcare professionals' workload and efficiency is still an emerging topic of research, and requires more evidence.[98,99]

Other specific themes regarding implementation were the degree of compatibility between the SBI and pharmacy, incentives for providing the SBI, and the fit of the SBI model with their organization goals. Pharmacists generally had positive perceptions of compatibility and fit with goals, which could be important facilitators of future SBI implementation. Pharmacists were in support of different types of brief interventions depending on their compatibility with their own pharmacy workflow. This indicates that the SBI model is consistently compatible across pharmacies but the specific aspects of the SBI and its implementation format will need to be adapted for different pharmacies to ensure maximum compatibility. Interestingly, this positive perception regarding compatibility and fit was shared among pharmacists at different levels of the pharmacy structure i.e. pharmacists in provider and leadership/management roles. It will therefore be very important to emphasize these facilitators when communicating information about the SBI to adopter organizations. While pharmacists mentioned improved patient outcomes as the primary incentive to provide the SBI, many also discussed reimbursement options, especially if the SBI shows good evidence for effectiveness and positive results for feasibility and acceptability. Reimbursement for providing the SBI would also directly increase the sustainability of the intervention and dissemination across different pharmacies, depending on the state regulations regarding pharmacist reimbursement.[100]

Although the CFIR definition of structural characteristics is broad and includes the social architecture, age, age and size of the organization, pharmacists discussed structural characteristics mostly in terms of infrastructure needs. Most stated that no infrastructure changes would be needed. However, it is important to note that not all pharmacies had the same infrastructure resources. For example, many pharmacies did not have an efficient private space for consultation. While some suggested making minor changes to the existing layout, others

suggested providing handouts to reduce the amount of information that is shared verbally, thereby reducing risk to privacy. This indicates that pharmacists preferred adaptation of the SBI model to their pharmacy rather than making changes to their pharmacy structure, which also speaks to pharmacist perceptions of the high degree of the adaptability of the SBI.

Individual Characteristics

Four salient themes regarding individual characteristics were found in this study: knowledge, beliefs, motivation, and self-efficacy. Although knowledge and beliefs are considered as one single construct in CFIR, our study categorized them as separate themes. With regards to motivation, pharmacists generally talked about different motivators to provide the SBI. We also found that pharmacists had high confidence in their ability to provide the SBI and the theme included various reasons behind their high self-efficacy.

Knowledge as a CFIR construct includes familiarity with the intervention and the skills necessary to provide the intervention.[90] We found that pharmacists were not familiar with the SBI model but were familiar with some components that can act as brief interventions such as naloxone or screening using prescription drug monitoring programs (PDMP). Evidence regarding knowledge and familiarity of naloxone among pharmacists has been mixed.[101,102] However, the increasing use of the standing order for naloxone in the past few years in Wisconsin could explain our positive findings. Research indicates that PDMP use especially among pharmacists has been limited.[32,103] It is possible that the high familiarity and frequent use of PDMP as a screening tool by the pharmacists in the sample is a reflection of their practice setting policy rather than individual motivation. Many pharmacists reported that PDMP was checked by technicians at their pharmacy rather than the pharmacist, further illustrating the need to fit the SBI into the workflow rather than focusing only on individual characteristics. Finally,

despite their familiarity with some aspect of the SBI, none of the pharmacists reported having received any formal education or training regarding SBIs for substance misuse. Considering the opioid overdose epidemic has been worsening in the past few years, it was surprising that pharmacists did not receive any continuing education that involved SBIs. However, research indicates that substance use specific education in pharmacy schools in the US on average is lower than American Association of Colleges of Pharmacy (AACP) recommended levels.[104] This is a barrier to future implementation of the SBI that must be addressed through specific training-based implementation strategies.

Positive beliefs about the SBI stemmed from pharmacist views that the SBI could help improve patient outcomes, increase patient interaction, and increase their clinical role in OUD prevention and treatment. Positive beliefs regarding the SBI were closely tied to their perceptions of their own role as mostly gatekeepers and last line of defense against opioid safety concerns, rather than healthcare professionals who can provide clinical services. These perceptions regarding their scope of practice can act as a barrier to increase their clinical role,[105] especially in OUD prevention through the SBI.

Pharmacists believed that typical barriers to improve their clinical roles include lack of time, clinical information, and buy-in, which could be addressed by implementing the SBI into their workflow. These findings are similar to what has been reported and discussed by Cochran et al in their study of Utah and Texas pharmacists.[11] However, a barrier that was not accounted in their research and by pharmacists in our sample was presence of negative and stigmatizing attitudes towards patients taking opioid medications. Although few pharmacists openly discussed stigma and bias, many pharmacists were afraid of offending patients or labeling them as ‘addicts’. Our previous research suggests that there could be a relationship between higher

stigma towards patients with SUD among pharmacists and considering screening as important.[41] This indicated that these pharmacists could be motivated to screen for misuse solely as a punitive measure, rather than an avenue to offer clinical services to those who need it. To avoid this, pharmacists must be trained to provide patient-centered counseling and the SBI must be packaged as a prevention and harm reduction effort and not cause patient harm.

As mentioned previously, pharmacists were motivated to provide the SBI primarily to improve opioid safety and patient outcomes. An opportunity to interact more with patients and improve their clinical role in OUD prevention were other important motivators. These motivators were also linked to organizational incentives that pharmacists would need to provide the SBI. These motivators can be emphasized during future implementation of the SBI to facilitate greater reach and adoption of the SBI in pharmacies. It is also unlikely that these motivators would be sufficient to translate the SBI into regular practice and sustain it over time. Reimbursement for providing the SBI, which some pharmacists mentioned as a motivator could become a highly important factor in sustaining the SBI. Apart from these motivators, providing resources and fitting the SBI into the workflow of the pharmacy could also motivate the pharmacist to provide the SBI, especially in fast-paced retail settings.[70]

Pharmacists were highly confident in their ability to provide the SBI despite a lack of training and knowledge of the model. This was mainly because pharmacists had experience with many individual components of the SBI or had offered similar interventions at their pharmacy. This indicates that providing an opportunity for practicing the SBI or conducting a trial SBI, especially for pharmacists who do not have experience with such services will help improve their self-efficacy. It is important to build on their self-efficacy because pharmacists with higher confidence in their ability to provide the SBI are more likely to commit to the SBI even when

other barriers are present.[90] More years of practice experience were also linked to higher self-efficacy, which could be because of increased knowledge gained over the years.[41]

Innovation Attributes

Themes regarding the SBI included pharmacists' perceptions of its complexity, adaptability, costs, and relative advantage. Complexity is defined broadly in the CFIR where the construct is reflected by the duration, scope, radicalness, disruptiveness, centrality, intricacy, and number of steps involved for providing the intervention.[90] When asked about the SBI, pharmacists mostly discussed duration, disruptiveness, and number of steps involved. Most pharmacists believed the SBI was not too complicated. They also believed the duration of the SBI could be shortened by using technicians or digital methods for the screening. The ease of SBI implementation can also be increased by reducing changes to central work processes i.e. using SBI components that are already provided as services within that pharmacy and integrating the SBI into their workflow.

To ensure that the innovation is not disruptive but tailored to the settings and workflow, we need a highly adaptable intervention. It was interesting to find that all the pharmacists in the sample not only believed that the SBI was adaptable, but also suggested different adaptations to fit the SBI within their setting and workflow. Considering this was an exploratory study where the exact components of the SBI were not described prior to the study, the pharmacists had more freedom in suggesting adaptations and proposing best versions of the SBI. However, it is important to note that any intervention has core components that cannot be altered to maintain its effectiveness. Often, the distinction between the core elements and the 'adaptable periphery' can only be identified after dissemination in different contexts.[90] Allowing for flexibility for the implementation sites to make adaptations must be balanced with ensuring intervention

standardization and consistency across settings. As pharmacy-based SBI implementation is a novel research area, more evidence will be needed to achieve this balance and identify the core elements of the SBI, before its potential adaptability can be specifically evaluated.

Finally, costs of the SBI and its implementation were not high according to pharmacists. Costs typically involve investment, supply, and opportunity costs for implementation.[90] Pharmacists believed that investment cost was not high as most pharmacies were providing similar services as part of their regular practice. The brief nature of the SBI also reduced time investment in their opinion. They believed supply costs were also minimal and mostly included printing handouts or forms. These perceptions may change if the brief intervention requires more time than anticipated or if pharmacists find the pre-implementation training and preparation required for the SBI onerous. Pharmacists also believed that the opportunity cost was not high because the benefits associated with the SBI were much higher than costs and there was no existing SBI-like intervention in their pharmacy. This was related to the 'relative advantage' theme, wherein pharmacists perceived the opportunity for more patient interaction and clinical services through the SBI than current interventions. Pharmacists who practiced in a setting that already had opportunity for clinical services saw the SBI as way to standardize those services across pharmacists in their setting and make it a sustained part of routine practice.

Aim 2 (Patient Themes)

Inductive content analysis of the patient interviews led to four main themes: patient experience with opioids, knowledge, and beliefs about opioid safety, SBI and opioid care needs, and implementation barriers of the SBI.

Patient experience with opioid medications spanned many years and was complex. Patients with chronic pain described issues with access to their medications, which had apparently worsened in the last few years. This is probably due to stricter opioid prescribing guidelines released by the CDC in 2016.[4] However, evidence of this relationship is yet to be evaluated. A 2011 study reported that there was 7.43mg per capita need for morphine equivalent and 420.7mg per capita consumed in the United States.[106] Even a drastic reduction in opioid prescribing should still meet adequate levels of opioids based on this calculation. At the same time there have been increasing concerns and anecdotal data from patients and prescribers that unbalanced opioid policies have resulted in negative patient outcomes and decreased access to opioids.[107] Either way, we found that balancing opioid safety and patient needs led to tenuous relationships between patients and healthcare professionals. The lack of trust in healthcare professionals and presence of stigma causes increased tensions in these interactions and does not promote optimal pain care.[108] These barriers can be exacerbated by prevention interventions that focus solely on reducing opioid prescribing and are not patient-centered.[109]

Despite their long-term experience taking opioids, there was a severe lack of knowledge regarding opioid safety among patients. This seemed to be primarily because of missed opportunities to counsel patients regarding their medications. Patients reported only talking to their prescribers or using internet sources of information. This lack of knowledge regarding opioid safety can lead to increased risk of negative outcomes such as an accidental opioid overdose. Research indicates that this lack of knowledge of opioid safety, especially related to overdose risks and naloxone, is very common among patients with chronic pain.[110,111] Moreover, patients taking prescribed opioid medications may have lower knowledge regarding opioid safety than people who use illicit drugs, most likely because most harm reduction efforts are targeted

towards people who use illicit drugs.[112] These findings indicate the need for the SBI to focus on patient education first and foremost, even if patients are not misusing opioids.

In addition to the lack of patient knowledge, negative beliefs regarding opioid safety were also very common. A tendency to distance themselves from people who use illicit drugs or patients who misuse prescribed opioids was common, mainly due to the stigma associated with substance use disorders. This led to gaps in opioid care because patients practiced risky behaviors such as storing large quantities of opioids and refusing naloxone. Research suggests that negative beliefs, such as believing that an opioid addiction risk is personally irrelevant, are associated with higher risk of opioid misuse.[113] However, patients were comfortable with pharmacists providing information about opioid safety as part of the SBI. This indicates that the SBI must also address negative beliefs through patient education, to improve opioid safety outcomes.

The lack of patient awareness of their gaps in knowledge and presence of negative beliefs meant that patients did not perceive any unmet needs regarding opioid safety and care. However, patients discussed needs of the general patient population who use opioids. According to the patients, specific needs that could be met by the SBI included: recognizing tolerance, dependence, consequences of intentional and unintended misuse, managing an accidental overdose, contra-indicated substances. Additional topics that could be useful here as suggested by the gaps in knowledge (discussed above) include risk of addiction or accidental overdose especially in patients who are older, are co-prescribed other medications, or have co-morbid conditions. These needs could be met as part of the patient-centered counseling (brief intervention) in the SBI or digital health interventions. Recently, a web-based digital intervention

that meets some of these needs has shown increase in patient knowledge and was rated as highly acceptable by patients.[114] Such interventions will need to be adapted to fit into the SBI model.

Finally, when discussing practical aspects of implementing the SBI, patients discussed various challenges in implementation. These challenges mainly included stigma or 'being labeled as a drug-seeker / misuser', privacy, time needed for the SBI, and their perceptions of pharmacist roles as a medication expert but not a clinician. All these challenges would be barriers to patient acceptability of the intervention. However, patients also suggested solution to these problems, mostly using a different format of delivery. Most patients preferred that the SBI be delivered telephonically or using digital health technologies. Some patients did mention that they would prefer face-to-face conversations rather than other formats. It would also be important to test the SBI in various formats and compare effectiveness and patient acceptability data. In the current literature, the only digital component of the pharmacist-delivered SBI is the screening tool loaded on a tablet that the patient can answer questions on.[52] Digital health interventions in pharmacy practice is an emerging area of research that can aid the pharmacist in providing more clinical services without increasing work burden and improve patient outcomes.[115,116] Our findings indicate that a digital format of the SBI would not only be useful for pharmacists but also preferred by most patients.

Aim 3 (Implementation Measure)

Using the building approach to mixed method data integration, we developed a quantitative implementation measure using the qualitative pharmacist interviews from Aim 1. A 36-item questionnaire was developed, and initial face and construct validity of the questionnaire was evaluated. The item development process was presented as a joint display of qualitative and

quantitative data (integration at the reporting level). Issues raised during initial validity testing and corresponding actions taken to improve face and construct validity were also reported. The following section discusses the findings from the integration and validity testing.

Integration

The building approach to mixed methods integration is most commonly utilized in exploratory sequential mixed methods studies, where the quantitative questionnaire/intervention is built upon the previous qualitative findings. In our study, we began by matching themes from the deductive and inductive content analysis to the CFIR constructs and then developed questionnaire items using the themes and salient quotes. This allowed the questionnaire to be formed based on the CFIR structure. However, not all CFIR constructs were included in our study design, which also meant that there are no items in the questionnaire corresponding to those excluded constructs. Although unlikely, it is possible that the excluded CFIR constructs are important for evaluating pharmacist perceptions of SBI implementation. If future studies indicate this, then additional items may need to be created (see face validity results for completeness of questionnaire).

Using the building approach to data integration also helped increase the content validity of the questionnaire. As these questionnaire items are built directly on pharmacist views and their exact quotes, the questionnaire will be a better reflection of the target population's views than using only existing literature to develop items. This also helps with increasing the credibility of the qualitative findings because the data from the quantitative questionnaire can be used to evaluate complementarity between the two methods (methods triangulation).

Validity Testing

The questionnaire was assessed for face validity and initial construct validity through expert review. Face validity testing involved evaluating the questionnaire for serving its purpose, clarity of questions and responses, and completeness of the questionnaire. Most issues identified in face validity testing were minor and easily solved with changing wording or response options. However, future cognitive interviews will be used to evaluate if changes made to the questionnaire are sufficient to ensure clarity, appropriateness, and completeness of the questionnaire.

Initial construct validity testing of the questionnaire focused on the congruence between the items and the qualitative themes as well as the CFIR constructs. We also assessed the structure of the questionnaire, appropriateness of the items and response to measure constructs, construct representation (over and under), and overall consistency of items within the same constructs and domains. Both simple and more complicated steps were used to address these issues. The simple steps included restructuring and reorganizing the questionnaire items, removing items, and adding context to qualitative quotes. More complicated steps included changing item and response formats and adding new items as well as steps to be taken during future cognitive interviews. Although cognitive interviews are conducted mainly for content validity testing, some of the changes made to increase construct validity of the questionnaire need further evidence from the target responder population i.e., pharmacists.

Aim 4 (Template Analysis)

This aim was focused on identifying SBI components and implementation needs by comparing themes across pharmacist and patient groups. We used the template analysis method to analyze data from pharmacists and patient interviews and identify the implications for the SBI.

For the purpose of this discussion, the themes of the template analysis have been categorized as follows:

Individual and Interpersonal Characteristics

Five themes form this domain: knowledge, beliefs, self-efficacy, stigma, and the patient pharmacist relationship. As discussed previously, lack of patient knowledge regarding opioid safety was an important theme from the patient interviews. Although pharmacists were not aware of this gap in knowledge among patients, they saw the SBI as an opportunity to provide patient education regarding opioid medications, safety practices, and potential risks. All patients were also comfortable receiving more information about their medications from pharmacists and were motivated to participate in the SBI to get more education. Therefore, the educational piece of the brief intervention must be provided to patients regardless of misuse behaviors. It can thus act as a primary prevention intervention for patients who do not require any more intensive services. It will also be necessary to adapt the education provided for patients with acute pain and only short-term opioid prescriptions, by focusing more on safety topics such as storage and disposal. This would also expand the reach of the SBI to all patients taking opioid medications, rather than focusing only on those who are at risk of misuse. Since most opioid safety initiatives are not designed to be primary (i.e. universal) prevention,[112] the SBI can fill the gap in a patient population that is often overlooked.

In addition to the need for education in general, both patient and pharmacist groups believed that the SBI could be a useful tool to provide patient-centered counseling for patients who are at risk of misuse and patients needing more education about opioid safety. This would however require a thorough training of pharmacists before implementation, as many were not comfortable discussing sensitive subjects such as misuse. Pharmacists would also need to focus

on patient autonomy and provide individualized care, which may be a challenge in fast-paced retail settings. One patient in our sample discussed their experience with a pharmacist successfully providing patient-centered counseling regarding naloxone using non-labeling language. The pharmacist also respected patient autonomy by giving them the opportunity to choose whether or not to fill their naloxone prescription. *"I thought the conversation [with pharmacist] went really well, and how it was approached was, it's [naloxone] not necessarily for myself. It was more for somebody that maybe got into it [opioid stored at home] that didn't know what it was, like a little kid. And I thought that was a good way to ease into it that it wasn't like, "Oh, we think you are going to be the one to overdose," but it could be some small child, and you saved their life."- Pt 06* However, digital or phone-based formats of the SBI may be needed to provide this counseling so that it fits within the workflow of large chain pharmacies.

Moreover, most patients described being labeled or stigmatized by healthcare professionals including pharmacists and facing bias when accessing opioid medications. Although few pharmacists openly discussed bias towards patients with opioid prescriptions, many had concerns about coming across as stigmatizing. Research indicates that pharmacists commonly distance themselves from patients who misuse opioids and hesitate to form therapeutic relationships with them.[117] Stigma would act as a barrier to participation in the SBI for both groups because patients are wary of feeling interrogated or labeled as misusers, and pharmacists are wary of making patients uncomfortable or simply do not want to connect with patients who are at risk of misuse. Therefore, it is extremely important to ensure that the SBI does not cause further patient harm. Pharmacists would also require anti-bias training and

patient-centered education. Such trainings have been shown to increase pharmacist knowledge about opioid misuse and decrease stigma.[73]

Many patients described having high self-efficacy in taking their opioid medications safely and effectively. Interestingly, these self-efficacy beliefs led to a barrier to SBI participation. Patients did not perceive a need for the SBI for themselves since they believed they were not at risk for misuse, and they had been taking opioids for many years. Such beliefs have been reported in the literature previously, where patients taking opioids chronically have lesser concerns related to opioid addiction.[118] However, pharmacists suggested that they might find it easier to provide the SBI to patients on long-term opioids because of their strong relationships. Therefore, patients who have been taking opioids for a long time may not be motivated to participate in the SBI, unless care is taken to validate their self-efficacy first. For example, patient counseling for patients with long-term opioid prescriptions can focus on long-term consequences of opioids such as developing tolerance and not simply emphasizing the need for adherence to the regimen. Topics such as naloxone can be discussed with pharmacists emphasizing that it is a precautionary measure for factors outside of the patient's control.

Finally, the patient-pharmacist relationship was non-existent for most patients. While all patients agreed that pharmacists were medication experts and they were comfortable with the pharmacist providing opioid related information, very few had the experience of receiving patient-centered counseling regarding opioid safety initiatives. Pharmacists also described overall good relationships with their patients but mentioned being uncomfortable with providing counseling and felt it was out of scope of their practice. These findings are similar to what has been studied previously.[119] Most patients only discussed their medications with their prescribers and some even believed pharmacists would be seen as 'interfering' in their care. Therefore, there

is a need to revise the professional role of the pharmacist into a more clinical one, as it relates to this SBI. Packaging the SBI as a clinical service, advertising the program in the pharmacy as a value-added service for all patients taking opioid medications, and highlighting the role of the medication expert in ensuring patient safety will help improve the patient-pharmacist interaction.

SBI Components

Screening and brief intervention are the two main components of the SBI model but the brief intervention can have multiple components based on the screening results. Both patients and pharmacists were comfortable with a short screening tool. Pharmacists wanted to fit the screening within their workflow in addition to tools such as the PDMP, which they already used as part of routine practice. To save time, self-reported screening tools that patients can answer on their own or with the help of technicians were preferred by pharmacists, which is similar to what has been studied previously.[52] The actual screening questions could be based on the standardized screening tools that have been used for this purpose such as the Prescription Opioid Misuse Index,[52,53] the Opioid Risk Tool,[55-57] or the Routine Opioid Outcome Monitoring tool.[58,59] Patients had mixed preferences about the mode for screening including face-to-face conversation with the pharmacist, phone conversation, filling a form, using a tablet, or completing the screening via an application, with digital methods being mostly preferred for privacy reasons. However, effectiveness of the different formats and implementation outcomes such as patient acceptability and pharmacist feasibility will have to be explored in the future.

Three main brief interventions were discussed in the pharmacist and patient interviews. Naloxone provision was a commonly proposed brief intervention, but many patients were hesitant to accept it and some even had negative attitudes towards other patients taking it. Pharmacists also mentioned that despite their efforts, most of their patients refused naloxone. A

recent SBI has found some success in increasing naloxone uptake.[55,86] To combat these barriers, a patient-centered script for pharmacists that stresses on the need for naloxone for patients who are at risk of an accidental overdose because of factors beyond their control, will be needed. Such resources have been developed by pharmacy organizations that can be easily incorporated within the SBI model.[120]

Patient-centered counseling was another commonly discussed brief intervention by both groups. Counseling regarding opioid safety and risks of misuse also offers the best opportunity to give patients what they most need – education. However, as discussed before, patients stressed the need for autonomy and individualized counseling. Pharmacists mentioned needing tools such as handouts or scripts/talking points for helping them structure the conversation. Recently, effectiveness of an opioid safety handout for counseling was evaluated with mixed results.[121] Although 60% of the pharmacist sample believed the handout would be useful, pharmacists with more work experience and those who already counseled patients about opioid safety were significantly more likely to use the handout.[121] This indicates that both training of pharmacists and sustaining the intervention with their workflow will be required for effectiveness. Finally, in busy large-chain pharmacies or those without private space, alternate formats of counseling such as telephone-based, telehealth, or digital applications would be more feasible to implement. Using existing applications that already enable patients with medication adherence and pharmacist interaction can be used to deliver the patient centered counseling.[122,123]

Lastly, both patients and pharmacists wanted opioid prescribers to be involved as potential stakeholders in the intervention. Patients believed that prescribers were ultimately responsible for what they prescribe and to identify patients at risk of misuse. Pharmacists wanted prescriber input and support so that they could be sure that any concerns they raised were heard

and addressed. Patients were also comfortable with the pharmacist contacting prescribers of their concerns, as long as patients were informed beforehand. However, research indicates that prescriber-pharmacist relationships and communication are often tense, ineffective, and barriers to improving pharmacist roles in OUD prevention and treatment.[124,125] Therefore, before implementation of the SBI, stakeholder engagement with prescribers will be needed to ensure their support of the SBI and to avoid such barriers.

SBI Implementation

Two main themes are included in the template regarding SBI implementation – needs and challenges. Patients mainly wanted the SBI in a format that offered privacy as well as respect for autonomy. The need for privacy could be met by offering the SBI in a private space where available, calling patients over the phone, integrating the SBI into telehealth services, or using digital health technologies. However, patient preferences for the exact format varied in our sample and these preferences would need to be considered when implementing the SBI. Pharmacists also believed in using existing structures such as private consulting room wherever available or fitting the SBI into existing work processes such as pharmacist-led phone calls, comprehensive medication reviews, etc. rather than incorporating structural changes. Pharmacists also needed a protocol for standardization of the SBI and training to be able to efficiently provide the SBI. It is possible that standardization of the SBI protocol can lead to reduced opportunity for individualization for patient preferences. Pilot testing of different formats to assess effectiveness and patient acceptability in future studies may help achieve the balance between these contrasting needs.

Three main implementation challenges were discussed by both groups – time, stigma, and pharmacist roles. Patients were sensitive to long wait times, and pharmacists did not have the

time to provide an intervention longer than 15 minutes. Alternate formats for the SBI and using technicians may help make reduce time may address this problem. Alternate formats could also provide privacy to help address the issue of stigma that patients face, in addition to patient-centered anti-bias training for pharmacists before implementing the SBI. Pharmacist role limitations as perceived by both patients and pharmacists themselves was another challenge. Marketing the SBI as a clinical service for medication safety provided by pharmacists, involving prescribers as stakeholders, and increasing pharmacists' self-efficacy in providing clinical services will help address these implementation challenges.[38]

Limitations

This study has some limitations that must be noted. Firstly, this was not a full-fledged mixed methods study because not quantitative data was collected, even though a mixed methods approach was used. Ideally, the quantitative questionnaire would also be psychometrically tested within the same study to truly evaluate complementarity between qualitative and quantitative data. However, instrument standardization can still be achieved in future quantitative studies.

Secondly, patient interview were conducted with a sample diverse in terms of pain chronicity, pharmacy experience, and gender but most of the patients identified their race/ethnicity as white, had insurance, and lived in suburban regions. As health disparities regarding opioids and OUD treatment are common in racial minority groups, underinsured, and more rural populations, involving patients from these groups could lead to different themes. Therefore, findings from the patient interviews cannot be transferred to all patients using opioids. Similarly, pharmacists were sampled from lists formed based on interest in participating in research. Pharmacists in our sample could also be highly interested in improving care for OUD

which may have affected our themes. Although we have attempted to increase credibility of our findings by showing disagreement among pharmacists and highlighting contrasting aspects of themes, care must be taken when transferring our findings to the general pharmacist population.

Although pharmacists serving many different roles such as pharmacy managers and owners, practicing in a variety of settings were recruited in our sample, we did not include pharmacy technicians, as they are not licensed practitioners. However, involving technicians in our study could have shed light on their role in OUD prevention, especially because pharmacists considered technicians pivotal to providing the SBI. Opioid prescribers and OUD treatment providers are other stakeholders who will need to be involved in future research, prior to implementation of the SBI.

Finally, our study focused only on the screening and brief intervention portion of the SBIRT model. Referral to treatment is an important component that was not explored thoroughly in our study. Although some pharmacists mentioned needing resources for referral, creating a warm hand-off for the patient, and increasing access medications for OUD, this was not a major theme. However, future research should explore this further by engaging treatment providers and connecting them with pharmacists within the same study.

Future Research

Based on the results of the study and some of its limitations, four different future research areas emerged. The developed quantitative questionnaire needs further testing for content validity. Cognitive interviews with pharmacists, practicing in Wisconsin and/or other states will establish content validity, prior to psychometric analysis. The questionnaire can then be evaluated for reliability and validity using a survey of pharmacists. In addition to the

psychometric data, findings from the survey can be used to inform future implementation of the SBI.

Another area of research that would address our study limitations is exploring perceptions of patients from racial and ethnic minority groups, belonging to underinsured populations and residing in rural areas regarding the SBI. This will require more community-engaged efforts and participatory-based approaches/designs to ensure the SBI is acceptable for a diverse patient population. More data on the themes that emerged from this study can be collected such as the different formats of the SBI. Engaging other stakeholders such as technicians, opioid prescribers such as primary care providers, pain specialists, etc. as well as OUD treatment providers will help make the SBI or SBIRT acceptable to a wider audience.

An important and unexpected finding from our interviews was the focus on telehealth services and digital methods of implementing the SBI. Considering the support from both groups (patients and pharmacists) for such formats, these should be explored in further research. Digital and telehealth-based services could be used to make the SBI more sustainable, especially considering the impact of the COVID-19 pandemic on health care.

Finally, this study was exploratory in nature but was conducted with future implementation of the SBI as the overarching goal. The next step of the exploratory work conducted so far would be to pilot test the SBI in community pharmacy settings. A pilot or small scale Hybrid type-1 trial can be used to evaluate effectiveness of the SBI and initial implementation outcomes such as feasibility and acceptability.

CHAPTER 7

CONCLUSION

This study developed a patient-centered opioid misuse screening and brief intervention for community pharmacy settings. Our scoping review of the current literature on pharmacy-based SBI identified several gaps including lack of patient involvement in study design, lack of focus on implementation of SBI, and gaps in contextual data through rigorous qualitative research. Our study addressed these gaps by conducting qualitative interviews with both patients and pharmacy stakeholders to identify needs and barriers to participate in the SBI. We also used a mixed methods approach to develop and evaluate an intervention and setting specific implementation measure. Finally, we used a template analysis approach to compare and contrast findings from different stakeholder groups and interpret the data for designing and implementing the SBI. We have also focused on implementation of the SBI by using designing for dissemination and implementation principles and the CFIR to design the study measures and interpret findings. We identified several important needs among pharmacists and patients regrading opioids and OUD prevention that can be addressed by the SBI. We also identified barriers to participation in both groups as well as solutions to address these challenges. Our exploratory findings have direct implications on future research where the SBI can be piloted within community pharmacy settings. Our quantitative measure can be standardized and used to inform SBI implementation in future research.

CHAPTER 8

SUMMARY FOR A GENERAL AUDIENCE

I have written this chapter to explain my research to a broad, non-scientific audience. All scientific research is done with the goal of being useful to many people. As a health researcher, my goal is to not only improve the health of the patients, but also center their needs in all that I do. I also focus on putting my research into actual practice and creating change through my work. These goals are impossible without communicating my findings with the public. Thanks to the Wisconsin Initiative for Science Literacy at UW-Madison for providing this platform, and for sponsoring and supporting the creation of this chapter. I also appreciate the efforts of Dr. Bassam Shakhashiri in leading this initiative and Elizabeth Reynolds for editing this chapter.

BALANCING OPIOID SAFETY AND PAIN MANAGEMENT: HOW CAN PHARMACISTS HELP?

Before the COVID-19 pandemic, researchers, clinicians, and public health officials in the United States were focused on another epidemic – the opioid overdose epidemic. While most of the research was concentrated on patients with opioid use disorders, I chose to focus on another group of patients - those who take opioids regularly and do not have opioid use disorders, but may be at risk of developing them. To explain why studying this patient group is important, I will first discuss opioid risks and give you a brief history on attempts made to reduce opioid risks for these patients. I will then describe how my dissertation project fits into the work that has been done already and what I found. My hope is that with this chapter, you will gain insights into this understudied patient population's needs and how my research attempts to help them.

Opioid risks and chronic pain

More than 142 million opioid prescriptions are dispensed every year in the United States. Opioids are a type of pain medication that help improve the quality of life for many patients who suffer from pain from a variety of sources, including after an operation, from a new injury, or a chronic condition. However, opioids have some inherent safety risks that need to be considered when being prescribed by doctors, dispensed by pharmacists, and taken by patients. These medications can be safe if used at an appropriate and prescribed dose and frequency, the patient is monitored for side effects, and care is taken to avoid mixing the medications with other substances such as alcohol. However, even on their own, long term use of opioids can lead patients to developing tolerance, meaning the same dose of medication becomes less effective. Some patients who become tolerant are at risk of eventually becoming dependent on their medications, and when that dependence takes over their lives or leads them to harming

themselves or someone else, they may even develop an opioid use disorder. If the patient develops an opioid use disorder, they need additional treatment to manage it well and avoid emergency situations such as an opioid overdose. Therefore, at every step of the process, opioids must be handled carefully, to ensure safe and appropriate pain relief without causing undue harm.

While the use of opioids for pain in the United States is over two hundred years old, and regulation of opioids to promote safety is over 100 years old, our understanding of their effect on patients continues to grow. It was not until the late 1990's that the medical community began to understand that opioids, even when prescribed and taken correctly, can still lead to tolerance and dependence. However, by then, patients who had been prescribed opioids for long-term treatment without careful monitoring had not only developed tolerance, dependence, and even opioid use disorders, but were also dying at unprecedented rates due to opioid overdoses. Overdose deaths have continued to increase in the past twenty years. In 2020, over 100,000 Americans died due to a drug overdose, most of them involving an opioid.

Restricting opioid prescriptions: Effective solution to the overdose epidemic?

In response to the opioid overdose epidemic, the Centers for Disease Control and Prevention (CDC) has taken some measures to limit the potential risks of opioids. This included creating prescription monitoring programs: state level systems that healthcare professionals use to check a patient's history with controlled substances, including opioids. The CDC also made state-level recommendations about the maximum dose of opioids per day that should be prescribed. However, these steps have not been sufficient and have opened the doors to new issues. For example, these new regulations and a culture that was more aware of potential harms of opioids put prescribers of opioids in a difficult place. If their prescriptions were too high, their

patients overdosed, or they were accused of being a “pill mill” (an office that provides excessive prescriptions for controlled substances), they could lose their practice, their license, or even face legal consequences. However, without access to opioids, or if forced to stop their medications suddenly, patients were at risk for uncontrolled pain, poor quality of life, and even severe withdrawal symptoms, which can be disabling. Many prescribers, perceiving a difficult choice with their livelihood and their patient’s safety in the balance, opted to limit their opioid prescribing, sometimes more drastically than even recommended by the CDC. Some prescribers simply stopped their patients’ opioid prescriptions, giving them little notice to find alternative pain treatment or another prescriber. Many of these patients could have benefitted from slower adjustments of their medications, or referral to resources or treatment if their healthcare providers felt they were at risk of tolerance, dependence, or an opioid use disorder. Prescribers were not the only ones who acted in what they saw as the patients’ best interests while trying to protect themselves. Some pharmacists refused to fill prescriptions at the pharmacy counter for patients who had “red flags” in the prescription monitoring programs.

In cases where patients were already dependent on their opioid medications, they were left with an impossible choice: do they withstand their pain and withdrawal symptoms without an end in sight, or keep looking for opioids? These patients, already vulnerable due to their pain and their dependence, were at risk of seeking out illicit sources of opioids. The situation was worse for patients from underserved groups such as Black and American Indian patients, and patients without insurance. Healthcare professional bias, media portrayal of the overdose epidemic, legal systems, and double stigma towards patients with opioid use disorders who were from marginalized groups meant that these patients had lower access to opioid medications and lower access to treatment for opioid use disorders, than non-Hispanic white patients from

affluent neighborhoods. These disparities in healthcare access continue to this day. I chose to use a patient-centered lens to conduct my research to avoid worsening these disparities.

How do we balance opioid safety and patient needs?

Everyone in this situation, from the prescribers to the pharmacists to the patients, is looking for a balance of symptom control and safety; it is clear that neither prescription without limits, which can eventually lead to an opioid use disorder and overdoses, nor abruptly stopping or reducing medications, which lead patients to uncontrolled pain and withdrawal, is the answer.

My dissertation project sought to explore this problem from the perspective of pharmacists and patients. I conducted interviews with pharmacists and patients who were taking opioids to understand their perspectives and experiences related to opioid medications. Consider the scenario below (Fig 1). On the left, a pharmacist from my study describes his experience seeing opioid prescriptions written for patients whose pain remains uncontrolled while their opioid dosage keeps increasing. Higher doses of opioids in patients who may also be at risk for misuse because of uncontrolled pain, increases the chance of an accidental overdose death. On the right, a patient I interviewed who has been taking opioid medications for the past ten years describes her experiences of stigma from being labeled a drug abuser and having the legitimacy of her need for opioids questioned. Both sides have their own perspectives, leading to a constant tension without reaching a balance of opioid safety and acceptable pain control. So, how can we

achieve this balance?

Fig 1: Quotes from pharmacist and patient study interviews

Clearly, this is a difficult balance to achieve. From my interviews, I found that while patients may be at risk for opioid-related harm, they may not fully understand this, even if they have been taking medications for years. Remember, the medical community did not fully realize even responsible opioid use could lead to tolerance and dependence until the late 1990's. Patients interpret the provider and pharmacist concern about a potential risk as being abrupt and inappropriate, stigmatizing, or not made in their best interests. Pharmacists have the training to identify inappropriate prescriptions, but don't necessarily have any tools to intervene other than refusing to fill the prescription. There is a need to develop a prevention program that addresses opioid misuse and safety in a way that is acceptable to patients and pharmacists. Instead of only checking for red flags of opioid misuse, such as the amount prescribed, there also needs to be a

'next step' or intervention so that patients who are found to be at risk for possible misuse are given appropriate resources by pharmacists, or their treatment plan is appropriately adjusted.

Screening and brief interventions: Are they an acceptable solution?

Screening and brief interventions (SBI) are a prevention strategy commonly used for identifying substance misuse behaviors and providing brief counseling to address that behavior and reduce misuse. SBI were initially developed for risky alcohol use and have been implemented in various clinical settings such as primary care offices, emergency care, and other non-substance use treatment facilities. They are also often designed as clinical interventions for prescribers, usually to be done in a clinical setting. However, pharmacists are much more accessible to patients than providers, and see patients outside of scheduled office visits. You don't need an appointment or even insurance to see a pharmacist. In rural areas, pharmacists are often the only healthcare professional for several miles. Pharmacists also have the training to identify inappropriate medications, and counsel patients regarding prescriptions. But the lack of focus on improving pharmacists' roles in clinical services has meant that the pharmacist is limited to only dispensing or refusing to dispense medications.

What do we know about pharmacy-based SBI?

My dissertation aimed to develop a SBI for opioid misuse to be delivered by pharmacists that was acceptable for patients. The first step was to conduct a scoping review of the literature on this topic. A scoping review is a systematic way of creating a search strategy from multiple databases of published studies and other reports. My search resulted in over 2500 studies and reports, which were screened and reviewed until 29 final reports were qualitatively analyzed. The results of the analysis informed the development of the SBI.

I found that research on pharmacist-led SBI for opioid misuse is very new (all studies conducted after 2016). Most of the research involved pharmacists surveys, and only 7 developed an SBI. Those programs involved a standardized screening tool, and resulted in pharmacists providing naloxone, commonly referred to as Narcan, an opioid overdose antidote. While such programs have been developed previously, they have not been centered on patient needs. As patients have not been involved in the development of SBI, uptake of such programs has not been high, and patients often refused the recommended naloxone. Additionally, even after rigorous design and development, few pharmacy-based interventions have actually translated into change in day-to-day practice. This was because the research was not focused on implementation and the practical realities of the setting, but was done in controlled clinical trials. Therefore, my scoping review highlighted a need for an intervention that improves opioid safety, is acceptable and useful to patients, allows the pharmacist to provide clinical services that they have been trained to provide, and can be implemented efficiently.

Addressing limitations of existing SBI research

In this dissertation, I addressed this gap by interviewing pharmacists and patients about what they find acceptable and feasible when it comes to such an intervention. I also identified barriers they might have with participating in this type of intervention and appropriate solutions to address those issues. Using this information, I have designed a program that includes screening for opioid misuse and a brief intervention that can be implemented in local community pharmacies in the future. The developed program includes screening using a standardized tool and offers the pharmacist a quick (<5min) way of assessing how the patient is taking their opioid medication and if they are at risk for misuse. The brief intervention (<15mins) then allows the pharmacist to intervene based on what the patient needs without causing patient harm. There are

several options for the brief intervention: this intervention will be simply providing opioid education to patients if they are not at risk, or contacting the prescriber if the prescription is inappropriate for the patient. My intervention will also include naloxone for at risk patients, but unlike previously developed programs, my program will describe naloxone in a non-stigmatizing way. For example, pharmacists will refer to it as a drug that can reverse an overdose and will compare it to an Epi-pen for allergies, and will clarify that it can be useful for patients who may be taking a high dose of opioids or are at risk of misuse. The program will also describe naloxone as helpful for patients who are older, take other medications that can lower breathing rates, live with children or teenagers who may accidently overdose, or have breathing issues like asthma. Finally, my brief intervention will involve the pharmacist referring the patient to additional treatment services if they are found to be at risk of developing an opioid use disorder. The entire SBI program has been designed from the ground up based on patient-reported needs and interests when it comes to their opioid medications.

Additionally, my dissertation also focused on what was practically possible to do and how best to implement the SBI in actual pharmacy practice. I used implementation science principles, which analyze the factors of a system that make change easier or harder, at the designing stage of this intervention to develop something that can be integrated within regular pharmacy workflow. I studied factors related to the pharmacy setting, the intervention, and pharmacists themselves to make the SBI more implementable. Pharmacists described not needing changes within the pharmacy itself, planned to use existing resources and workflow, and felt the intervention was compatible with their setting. They also believed that the SBI could be adapted for their setting, was not complicated to deliver, and had higher benefits than costs. Pharmacists had positive beliefs about the effectiveness of the SBI, and were highly motivated to

provide it within their pharmacies. Finally, the project also highlighted the implementation strategies that will be needed prior to testing the intervention, such as pharmacist training, and modifications specific to the pharmacy (such as phone-based or digital interventions for busy pharmacies). As part of the project, I also developed a tool to survey pharmacists in the future regarding the now developed intervention and its future implementation in their pharmacies. This tool will help evaluate how useful our intervention will be to larger groups of pharmacists in more diverse settings, and will serve as a way to test readiness for the SBI in new regions. This project has led to new findings about what the important factors are in a pharmacy setting and among pharmacists themselves that will help with sustaining the SBI as a clinical service offered by pharmacists in the long-term.

At the end of this study, I have systemically evaluated gaps in existing research, and developed a new way for pharmacists to screen for possible risk of harm from opioid medications and to briefly intervene to improve safety. This intervention is designed in a way that is more acceptable to patients, and can be efficiently implemented and tested. It is my hope that this project leads to a widespread patient-acceptable program for opioid safety within community pharmacies across the United States.

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APPENDIX 1

GREY LITREATURE SOURCES

1. Grey Literature Report
2. Open Grey
3. GreyNet
4. ProQuest
5. NIH Publications list
6. WorldCat
7. Kaiser Family Foundation
8. Robert Wood Johnson Foundation
9. Mathematica Policy Research
10. Clinicaltrials.gov
11. NIH rePORTER
12. NIDA
13. SAMHSA
14. CDC
15. CPF
16. APhA
17. CPNP
18. PCORI
19. Google
20. Google alerts for substance use disorder + pharmacist

APPENDIX 2

SEARCH STRATEGY

PubMed

1260 Results

997 results with English & human filters. 931 from 2000-2021

("Pharmacists"[MeSH] OR pharmacist*[tw] OR pharmacy[tw] OR pharmacies[tw])

AND ("opioid-related disorders"[mesh] OR ((opioid*[tw] OR opiate*[tw] OR heroin[tw] OR morphine[tw] OR opium[tw] OR "analgesics, opioid"[mesh] OR "methadone"[mesh] OR biodone[tw] OR Dolophine[tw] OR Metadol[tw] OR Metasedin[tw] OR Symoron[tw] OR Methadone[tw] OR Hydrochloride[tw] OR Methadose[tw] OR Methex[tw] OR Phenadone[tw] OR Physeptone[tw] OR Phymet[tw] OR Pinadone[tw] OR Amidone[tw] OR Methaddict[tw] OR Codeine[tw] OR Fentanyl[tw] OR Actiq[tw] OR Duragesic[tw] OR Fentora[tw] OR Abstral[tw] OR Onsolis[tw] OR Hydrocodone[tw] OR "Hysingla ER"[tw] OR "Zohydro ER"[tw] OR Lorcet[tw] OR Lortab[tw] OR Norco[tw] OR Vicodin[tw] OR Hydromorphone[tw] OR Dilaudid[tw] OR Exalgo[tw] OR Meperidine[tw] OR Demerol[tw] OR Dolophine[tw] OR Morphine[tw] OR Kadian[tw] OR "MS contin"[tw] OR Morphabond[tw] OR Oxycodone[tw] OR OxyContin[tw] OR Oxaydo[tw] OR Percocet[tw] OR Roxicet[tw] OR Tramadol[tw] OR Ultram[tw] OR Heroin[tw]) AND (disorder*[tw] OR addict*[tw] OR dependen*[tw] OR misus*[tw] OR abus*[tw] OR overdos*[tw] OR "substance-related disorders"[mesh] OR "drug overdose"[mesh] OR "prescription drug misuse"[mesh])))

AND ("prevention and control"[sh] OR prophyla*[tw] OR prevent*[tw] OR "drug therapy"[sh] OR pharmacotherap*[tw] OR "medication therapy management"[mesh] OR ((drug[tw] OR drugs[tw] OR pharmacolog*[tw] OR medication*[tw]) AND (therap*[tw] OR treatment*[tw])) OR "substance abuse detection"[mesh] OR "mass screening"[mesh] OR screening*[tw] OR detect*[tw] OR test*[tw] OR "Red flags"[tw] OR "risk factors"[mesh] OR risk[tw] OR risks[tw] OR "health correlat*"[tw]

OR

Attitude[mesh:noexp] OR attitude*[tw] OR “Attitude of Health Personnel”[mesh:noexp] OR opinion*[tw] OR stereotyping[mesh] OR stigma*[tw] OR belief*[tw] OR “social stigma”[mesh] OR stereotyp*[tw]

OR

“Patient Satisfaction”[MeSH] OR satisfaction[tw] OR “Patient Preference”[MeSH] OR preference*[tw]

OR

“Patient-Centered Care”[MeSH] OR “Patient-Centered”[tw] OR “patient centered” OR “patient-focused”[tw] OR “patient focused”[tw])

Scopus

697 Results Excluding Medline (ENG 633)

Title, Abstract, Keywords

Note: To use this search click the Advanced Search link in Scopus, and then enter your search into the search bar.

(TITLE-ABS-KEY((pharmacist* OR pharmacy OR pharmacies)

AND ("opioid-related disorders" OR ((opioid* OR opiate* OR heroin OR morphine OR opium OR "analgesics, opioid" OR "methadone" OR biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Hydrochloride OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict OR Codeine OR Fentanyl OR Actiq OR Duragesic OR Fentora OR Abstral OR Onsolis OR Hydrocodone OR "Hysingla ER" OR "Zohydro ER" OR Lorcet OR Lortab OR Norco OR Vicodin OR Hydromorphone OR Dilaudid OR Exalgo OR Meperidine OR Demerol OR Dolophine OR Morphine OR Kadian OR "MS contin" OR Morphabond OR Oxycodone OR OxyContin OR Oxaydo OR Percocet OR Roxicet OR Tramadol OR Ultram OR Heroin) AND (disorder* OR addict* OR dependen* OR misus* OR abus* OR overdos* OR "substance-related disorders" OR "drug overdose" OR "prescription drug misuse")))

AND ("prevention and control" OR prophyla* OR prevent* OR "drug therapy" OR pharmacotherap* OR "medication therapy management" OR ((drug OR drugs OR pharmacolog* OR medication*) AND (therap* OR treatment*)) OR "substance abuse detection" OR "mass screening" OR screening* OR detect* OR test* OR "Red flags" OR "risk factors" OR risk OR risks OR "health correlat*"

OR

Attitude OR attitude* OR opinion* OR stereotyping OR stigma* OR belief* OR “social stigma” OR stereotyp*

OR

satisfaction OR “Patient Preference” OR preference*

OR

“Patient-Centered” OR “patient centered” OR “patient-focused” OR “patient focused”)))

AND NOT INDEX(medline)

PsycINFO

361 Results (346 from 2000-2021) (342-english)

Title, Abstract, Subject Headings, Keywords

((SU(pharmacists OR pharmacy) OR TI(pharmacist* OR pharmacy OR pharmacies))

AND (SU("opioid use disorder") OR

((SU(opiates) OR TI(opioid* OR opiate* OR heroin OR morphine OR opium OR biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Hydrochloride OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict OR Codeine OR Fentanyl OR Actiq OR Duragesic OR Fentora OR Abstral OR Onsolis OR Hydrocodone OR "Hysingla ER" OR "Zohydro ER" OR Lorcet OR Lortab OR Norco OR Vicodin OR Hydromorphone OR Dilaudid OR Exalgo OR Meperidine OR Demerol OR Dolophine OR Morphine OR Kadian OR "MS contin" OR Morphabond OR Oxycodone OR OxyContin OR Oxaydo OR Percocet OR Roxicet OR Tramadol OR Ultram OR Heroin)) AND (SU("substance use disorder") OR TI(disorder* OR addict* OR dependen* OR misus* OR abus* OR overdos*))))

AND (TI("prevention and control" OR prophyla* OR prevent* OR "drug therapy" OR pharmacotherap* OR screening* OR detect* OR test* OR "Red flags" OR risk OR risks OR "health correlat*" OR attitude* OR opinion* OR stigma* OR belief* OR stereotyp* OR satisfaction OR preference* OR "Patient-Centered" OR "patient centered" OR "patient-focused" OR "patient focused") OR

SU("drug therapy" OR "drug usage screening" OR prevention OR "social perception" OR attitudes) OR (TI(drug OR drugs OR pharmacolog* OR medication*) AND TI(therap* OR treatment*))))

OR

((SU(pharmacists OR pharmacy) OR AB(pharmacist* OR pharmacy OR pharmacies))

AND (SU("opioid use disorder") OR

((SU(opiates) OR AB(opioid* OR opiate* OR heroin OR morphine OR opium OR biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Hydrochloride OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict OR Codeine OR Fentanyl OR Actiq OR Duragesic OR Fentora OR Abstral OR Onsolis OR Hydrocodone OR "Hysingla ER" OR "Zohydro ER" OR Lorcet OR Lortab OR Norco OR Vicodin OR Hydromorphone OR Dilaudid OR Exalgo OR Meperidine OR Demerol OR Dolophine OR Morphine OR Kadian OR "MS contin" OR Morphabond OR Oxycodone OR OxyContin OR Oxaydo OR Percocet OR Roxicet OR Tramadol OR Ultram OR Heroin)) AND (SU("substance use disorder") OR AB(disorder* OR addict* OR dependen* OR misus* OR abus* OR overdos*))))

AND (AB("prevention and control" OR prophyla* OR prevent* OR "drug therapy" OR pharmacotherap* OR screening* OR detect* OR test* OR "Red flags" OR risk OR risks OR "health correlat*" OR attitude* OR opinion* OR stigma* OR belief* OR stereotyp* OR satisfaction OR preference* OR "Patient-Centered" OR "patient centered" OR "patient-focused" OR "patient focused") OR

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((SU(opiates) OR KW(opioid* OR opiate* OR heroin OR morphine OR opium OR biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Hydrochloride OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict OR Codeine OR Fentanyl OR Actiq OR Duragesic OR Fentora OR Abstral OR Onsolis OR Hydrocodone OR "Hysingla ER" OR "Zohydro ER" OR Lorcet OR Lortab OR Norco OR Vicodin OR Hydromorphone OR Dilaudid OR Exalgo OR Meperidine OR Demerol OR Dolophine OR Morphine OR Kadian OR "MS contin" OR Morphabond OR Oxycodone OR OxyContin OR Oxaydo OR Percocet OR Roxicet OR Tramadol OR Ultram OR Heroin)) AND (SU("substance use disorder") OR KW(disorder* OR addict* OR dependen* OR misus* OR abus* OR overdos*))))

AND (KW("prevention and control" OR prophyla* OR prevent* OR "drug therapy" OR pharmacotherap* OR screening* OR detect* OR test* OR "Red flags" OR risk OR risks OR "health correlat*" OR attitude* OR opinion* OR stigma* OR belief* OR stereotyp* OR satisfaction OR preference* OR "Patient-Centered" OR "patient centered" OR "patient-focused" OR "patient focused") OR

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CINAHL

234 Results (Medline excluded) (2000-230) (eng 225)

Title, Abstract, Subject Headings

For exclude Medline: Enter search into Advanced Search Bar, scroll down, click to select Exclude Medline Records.

((SU(pharmacists OR “pharmacy service”) OR TI(pharmacist* OR pharmacy OR pharmacies))

AND ((TI(opioid* OR opiate* OR heroin OR morphine OR opium OR biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Hydrochloride OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict OR Codeine OR Fentanyl OR Actiq OR Duragesic OR Fentora OR Abstral OR Onsolis OR Hydrocodone OR "Hysingla ER" OR "Zohydro ER" OR Lorcet OR Lortab OR Norco OR Vicodin OR Hydromorphone OR Dilaudid OR Exalgo OR Meperidine OR Demerol OR Dolophine OR Morphine OR Kadian OR "MS contin" OR Morphabond OR Oxycodone OR OxyContin OR Oxaydo OR Percocet OR Roxicet OR Tramadol OR Ultram OR Heroin) AND (SU(“substance use disorder”) OR TI(disorder* OR addict* OR dependen* OR misus* OR abus* OR overdos*))))

AND (TI("prevention and control" OR prophyla* OR prevent* OR "drug therapy" OR pharmacotherap* OR screening* OR detect* OR test* OR "Red flags" OR risk OR risks OR "health correlat*" OR attitude* OR opinion* OR stigma* OR belief* OR stereotyp* OR satisfaction OR preference* OR “Patient-Centered” OR “patient centered” OR “patient-focused” OR “patient focused”) OR

SU(“drug therapy” OR “drug abuse detection”) OR (TI(drug OR drugs OR pharmacolog* OR medication*) AND TI(therap* OR treatment*))))

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AND ((AB(opioid* OR opiate* OR heroin OR morphine OR opium OR biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Hydrochloride OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict OR Codeine OR Fentanyl OR Actiq OR Duragesic OR Fentora OR Abstral OR Onsolis OR Hydrocodone OR "Hysingla ER" OR "Zohydro ER" OR Lorcet OR Lortab OR Norco OR Vicodin OR Hydromorphone OR Dilaudid OR Exalgo OR Meperidine OR Demerol OR Dolophine OR Morphine OR Kadian OR "MS contin" OR Morphabond OR Oxycodone OR OxyContin OR Oxaydo OR Percocet OR Roxicet OR Tramadol OR Ultram OR Heroin) AND (SU(“substance use disorder”) OR AB(disorder* OR addict* OR dependen* OR misus* OR abus* OR overdos*))))

AND (AB("prevention and control" OR prophyla* OR prevent* OR "drug therapy" OR pharmacotherap* OR screening* OR detect* OR test* OR "Red flags" OR risk OR risks OR "health correlat*" OR attitude* OR opinion* OR stigma* OR belief* OR stereotyp* OR

satisfaction OR preference* OR "Patient-Centered" OR "patient centered" OR "patient-focused" OR "patient focused") OR

SU("drug therapy" OR "drug abuse detection") OR (AB(drug OR drugs OR pharmacolog* OR medication*) AND AB(therap* OR treatment*))))

Cochrane

Note: 3 results: all 3 were reviews of effectiveness of opioid medications

Title, Abstract, Keyword

(pharmacist* OR pharmacy OR pharmacies)

AND ((opioid* OR opiate* OR heroin OR morphine OR opium OR biodone OR Dolophine OR Metadol OR Metasedin OR Symoron OR Methadone OR Hydrochloride OR Methadose OR Methex OR Phenadone OR Physeptone OR Phymet OR Pinadone OR Amidone OR Methaddict OR Codeine OR Fentanyl OR Actiq OR Duragesic OR Fentora OR Abstral OR Onsolis OR Hydrocodone OR "Hysingla ER" OR "Zohydro ER" OR Lorcet OR Lortab OR Norco OR Vicodin OR Hydromorphone OR Dilaudid OR Exalgo OR Meperidine OR Demerol OR Dolophine OR Morphine OR Kadian OR "MS contin" OR Morphabond OR Oxycodone OR OxyContin OR Oxaydo OR Percocet OR Roxicet OR Tramadol OR Ultram OR Heroin) AND (disorder* OR addict* OR dependen* OR misus* OR abus* OR overdos*))

AND (prophyla* OR prevent* OR pharmacotherap* OR ((drug OR drugs OR pharmacolog* OR medication*) AND (therap* OR treatment*)) OR screening* OR detect* OR test* OR "Red flags" OR risk OR risks OR "health correlat*"

OR

attitude* OR opinion* OR stigma* OR belief* OR stereotyp*

OR

satisfaction OR preference*

OR

"Patient-Centered" OR "patient centered" OR "patient-focused" OR "patient focused")

APPENDIX 3

RECRUITMENT ANNOUNCEMENT

Good afternoon PearlRx members,

Please see the message below from Dr. Olayinka Shiyanbola and Ms. Deepika Rao regarding a research opportunity:

We are recruiting community pharmacists practicing in Wisconsin for 60-min interviews exploring pharmacist perceptions and needs regarding an opioid misuse screening and brief intervention. Your views and experiences as a community pharmacist are extremely valuable in designing this pharmacy-based intervention.

You will receive $50 on completion of the in-person or virtual interview. Please see the attached information sheet for more details about study procedures. This study is part of a student dissertation project at the UW-Madison School of Pharmacy and your participation is highly appreciated.

If you are interested in the study, please click on the link below:

Follow this link to the Survey:

Take the Survey

Or copy and paste the URL below into your internet browser:

https://uwmadison.co1.qualtrics.com/jfe/form/SV_2c0J1RG4HIBrep8?Q_DL=Xy4IvhTKDTUcU9c_2c0J1RG4HIBrep8_MLRP_71jNT1jgU5Vjx0G&Q_CHL=email

Follow the link to opt out of future emails about this study:

Click here to unsubscribe

Thank you for your time.

APPENDIX 4

PHARMACIST INFORMATION SHEET

University of Wisconsin-Madison
Research Subject Information Sheet

Research Study Title: Developing a patient-centered opioid misuse screening and brief intervention for community pharmacy

Principal Investigators (the person in charge)**:** Olayinka Shiyanbola, PhD, Deepika Rao BPharm, MS

How to contact the study staff: 608-263-9664 or email at dmrao@wisc.edu

Who to call if you have questions about being a research subject: University of Wisconsin Hospital and Clinics Patient Relations Representative at 608-263-8009

This sheet provides key information you need to know about this research study. Taking part in a research study is voluntary. You don't need to take part in this study. You can stop taking part in this study at any time without any penalty. Feel free to contact the researchers with any questions you have about this study.

What is the purpose of the research study?
We want to explore community pharmacist perceptions about a screening and brief intervention for prescription opioid misuse. We are asking pharmacists practicing in Wisconsin in community/retail settings to provide your perspectives so that intervention development can address your needs and any barriers you may have regarding the intervention.

What will you do if you join this research study?
If you choose to join this study, you will participate in a semi-structured interview where open-ended questions regarding your perspectives about such an intervention and any relevant experiences will be asked.

Audio recordings will be made of the interview. Only the researchers will have access to these recordings. The researchers or someone hired by the researchers will listen to the recording and write down what people said during the interview. The transcription will be saved but the recording will be destroyed. No information that could identify you will be included in the transcription.

Number study visits and how long study visits will be:
You will only have 1 visit to complete the interview. The visit will take up to 60 minutes and be conducted in a location convenient to you such as a nearby public library. This can also be done virtually using Webex or via telephone if you prefer.

Main risks of taking part in this research study:
There are no legal, economic, or physical risks for participating in this study. The main risk of joining this study is that someone who is not supposed to see your information might see it. The study team has done everything it can to protect your information. You can skip any questions that you do not want to answer. Even if you start the interview, you are not required to complete it. You can stop at any time. All your answers will be confidential and will not be shared with anyone outside the research team.

Will I be paid for my participation in the study?
You will receive $50 cash or gift card. If you do not complete the study, you will not receive the incentive.

APPENDIX 5

STUDY FLYER

Are you taking opioid medications?

Please tell us about your experiences!

What is the purpose of this study?

- We are developing a program to improve care for patients who are taking opioids

Why are we asking you to participate?

- Your views are important to help us develop a program that can meet the needs of patients like you

What does this study involve?

- One 30-40min recorded discussion
- Can be a virtual/phone/in-person disccussion (based on your preference)
- You will receive **$30** if you complete the discussion

Interested in participating?

- Call: Deepika at 608-263-9664 and leave a message
- Or Email at: dmrao@wisc.edu

If you have questions about being a research participant: Call University of Wisconsin Hospital and Clinics Patient Relations Representative at 608-263-8009

APPENDIX 6

INTERVIEW GUIDES

Pharmacist Interview

Informed Consent Script

Hello, my name is [NAME], I'm a researcher working at the UW School of Pharmacy on a study with [PearlRx] developing a patient- centered opioid misuse screening and brief intervention for community pharmacy settings.
The information you share with me will be really valuable for our research project to understand what barriers pharmacists face and what your needs are regarding the intervention. Our hope is that this study will help us design an intervention that can be implemented within community pharmacies.

All information collected in this study will be kept confidential. Neither your name nor any other identifiable information will be kept after the end of this study. Our discussion will last for about an hour. You can stop the interview at any time or skip any questions that you do not feel comfortable answering. If you decide not to do the interview, it will not affect your employment through the UW Madison and its affiliates. Please let me know if you need to take a break at any point.

I would like to make a recording of our discussion, so that I can have an accurate record of the information that you provide to me.
(If WebEX and participant has switched on camera: The recording will also capture your video, but only your audio recording will be used for analysis).
It will be transcribed and we'll keep the transcripts confidential and securely in our possession. I will erase the recording after it has been transcribed. Unidentified excerpts from the transcriptions may be published as part of research papers in scientific journals. May I record our discussion?

By completing this interview, you are consenting to participate in the interview.

Introduction:

Do you have any questions before we begin the interview?

Great, thank you, then let's begin.

For the first couple of questions, I'll be focusing on your practice setting and educational background:

- How would you describe your practice setting? (Location/type/size/patient demographic/role)

- What is your educational background? (degrees/ experience/ Continuous Education activities)
- Could you please describe your experiences as a pharmacist in prevention or treatment of OPIOID use disorders?
    - Probe: What is the pharmacist's role in P&T of opioid use disorders?
- Could you describe the exact process that a patient would go through when they want to fill an opioid prescription at your pharmacy?
    - Probe: As part of your regular practice, do you check PDMP, medication review component, do you talk to patients?

Sample Interview questions for pharmacists based on CFIR:

CFIR Domain: Inner Setting

Thank you. For the next couple of questions, I would like to learn more about your organization or practice setting.

Construct: Culture

1. Let's talk about the general culture of your workplace. How would you describe the culture of your pharmacy?

   Probe: To what extent are new ideas embraced and used to make improvements in your organization?

Construct: Network/Communication

2. Can you describe your working relationships with your colleagues?
   Probe: With managers/ leaders?
3. How do you typically find out about new information?
4. When you need to solve a problem, what do you do?
   Probe: Who are your "go-to" people?

CFIR Domain: Individual Characteristics:

Thank you for that information. For the following questions, I am going to discuss a potential screening and brief intervention for opioid misuse. I will refer to them as SBIs.

Construct: Knowledge and Beliefs:

5. What do you know about SBIs? Have you heard about it?
6. SBIs developed for drugs including alcohol and even nicotine. Imagine this SBI model is going to be implemented in your pharmacy, what would screening for opioid misuse look like ideally? Can you describe what the screening/ brief intervention components should be? What does the ideal SBI look like?
7. How do you feel about this SBI for opioid misuse implemented within pharmacies?

8. What challenges do you think will occur when trying to implement this intervention?

Construct: Self-Efficacy & Motivation:

9. How confident are you that you will be able to provide the SBI?
10. What would motivate you to provide the SBI?

CFIR Domain: Outer Settings

Construct: Patient needs and resources

11. How well would this SBI meet the needs of your current patients?

CFIR Domain: Inner Setting

Thank you. Now that we've talked about your own views about the SBI in general, I want to ask you about the SBI implemented in your particular pharmacy.

Constructs: Structural Characteristics & Change Tension:

12. What kinds of infrastructure changes will be needed to accommodate the intervention?
13. Is there a strong need for this intervention?
    Probe: How essential is this intervention to meet the needs of the patients and practicing pharmacists?

Constructs: Goals, Compatibility & Incentives:

14. How does the SBI align with your organization goals?
15. How well does the SBI fit with existing work processes and practices in your setting?
16. What incentives would you need to provide the intervention?

CFIR Domain: Innovation Attributes:

Thank you for the information. Now that we have discussed your views of the SBI and how it could be implemented within your pharmacy, let's talk about areas of improvement in the SBI model that could be helpful.

Constructs: Adaptability, Complexity, Relative Advantage, Cost

17. What kinds of changes do you think you will need to make to the SBI so it will work effectively in your pharmacy?
18. How complicated is it to provide the SBI? (duration, scope, radicalness, disruptiveness, centrality, and intricacy and number of steps required)
    Probe: How can it be made simpler?

19. What other programs for opioid misuse exist in your pharmacy?
    Probe: How does the SBI compare to other similar existing programs in your pharmacy? Is there another intervention that people would rather implement?
20. What costs will be incurred to implement the SBI?
    Probe: How do costs compare to benefits?

Is there anything we haven't discussed related to SBIs that you would like to talk about?

Patient Interview

Informed Consent Script

Hello, my name is [NAME], I'm a researcher working at the UW School of Pharmacy on a study developing a patient- centered opioid safety program for community pharmacy settings.

The information you share with me will be really valuable for our research project to understand what needs patients have about their opioid medications. We are developing a pharmacist led program for opioid medication safety and would like to understand your views as a patient. Our hope is that this study will help us design a program that is acceptable to patients.

All information collected in this study will be kept confidential. Neither your name nor any other identifiable information will be kept after the end of this study. Our discussion will last about 30 minutes. You can stop the interview at any time or skip any questions that you do not feel comfortable answering. If you decide not to do the interview, it will not affect the health care you receive through the UW Madison and its affiliates. Please let me know if you need to take a break at any point.

I would like to make a recording of our discussion, so that I can have an accurate record of the information that you provide to me.

(If WebEX and participant has switched on camera: The recording will also capture your video, but only your audio recording will be used for analysis).

It will be transcribed and we'll keep the transcripts confidential and securely in our possession. I will erase the recording after it has been transcribed. Unidentified parts from the transcriptions may be published as part of research papers in scientific journals anonymously. May I record our discussion?

By completing this interview, you are consenting to participate in the study. Do you have any questions before we begin the interview?

Introduction:

Great, thank you, then let's begin.

For the first couple of questions, I want to learn about your experience with opioid medicines.

1. Approximately how long ago were you first given an opioid medication?
2. How has your experience been in taking the medication?

Probe: What problems/ issues/ side-effects have you experienced? Any problems getting the medications?

Sample Interview questions for patients based on CFIR:

CFIR Domain: Inner Setting

Thank you. For the next couple of questions, I would like to learn more about your relationship with your pharmacist/providers.

Construct: Network/Communication

3. When you have questions about your opioid medicines, what steps do you take to seek out answers?
4. Have you ever talked with your pharmacist about opioid medications?

If yes, what has your experience been in communicating with your pharmacist about opioid medicines?

If not, what inhibits your willingness to talk with your pharmacist?

CFIR Domain: Individual Characteristics:

Thank you for that information. Now, I am going to ask you some general questions about opioid medicines. There are no right or wrong answers. Please feel free to tell me whatever you know or have experienced.

Construct: Knowledge and Beliefs:

5. What do you know about taking opioid medicines safely?
6. How do you feel about your pharmacist talking to you about opioid medicines?

Construct: Self-Efficacy:

7. How confident are you in taking your opioid medicines correctly?

Probe: What makes you feel confident? /

If not confident: How can pharmacists improve your confidence? Why do you feel this way?

For the following questions, I am going to discuss a potential program for helping patients take their opioid medicine safely. The program will involve your pharmacist asking you 3-4 questions about how you use your opioid medications and then give you information to help use it safely.

Construct: Motivation:

8. If such a program is developed, would you be interested in participating? Why?

Probe: What would motivate you to participate in the program?

CFIR Domain: Outer Settings

Construct: Patient needs and resources

9. What do you need to help you take your opioid medicine safely?

Probe: How well would this program meet your needs? Why?

CFIR Domain: Innovation Attributes:

Thank you for the information. Now that we have discussed your views of the program, let's talk about areas of improvement in the program that could be helpful to patients.

Constructs: Relative Advantage, Adaptability, Complexity, Cost

10. What other pharmacy-based programs for opioid medicines do you know about?

Probe: How does this program compare?

11. So, the program has two parts; the first is where patients answer questions about how they take their opioid medicines. How would patients like to answer these questions do you think? (conversation/survey/form on electronic device/phone)

Second part based on the patient's answers, the pharmacist can talk to them, give more information on things like Narcan, call their doctor on your behalf if there are problems with prescriptions. What do you think the pharmacist to do to help patients?

Probe: What kinds of changes would you prefer in the program so it will work effectively for you?

12. What barriers do you think will stop patients from participating in the program? How can we prevent these barriers?

Probe: How complex is the program?

For interviewer: (in terms of duration, scope, radicalness, disruptiveness, centrality, and intricacy and number of steps required)

13. What are some possible ways this program may be beneficial? What disadvantages do you see in participation?

CFIR Domain: Inner Setting

Thank you. Now that we've talked about your own views about the program in general and areas of improvement, I want to ask you about the program being done in your local pharmacy.

Constructs: Structural Characteristics:

14. Imagine that you are picking up your opioid medicine from your local pharmacy. Your pharmacy is offering this program. How should the program be conducted in your pharmacy, for you to comfortably participate in the program?

Constructs: Compatibility:

15. This program is being developed to help patients take their opioid medicines safely. How do you feel about this program being conducted in your local community pharmacy? What makes you feel that way?

Is there anything we haven't discussed related to SBIs that you would like to talk about?

APPENDIX 7

FACE VALIDITY QUESTIONS

1. The purpose of the questionnaire is to act as a pre-implementation measure to evaluate pharmacist perceptions of CFIR constructs specific to the intervention. Did the questionnaire achieve its purpose? If no, please elaborate.
2. Were any of the questions unclear? If yes, please elaborate.
3. Were any of the response options unclear? If yes, please elaborate.
4. Are there any other questions that you think are missing from the questionnaire?
5. Did the response options appear to be complete? Are there any other response options you would like to add in any of the questions?
6. Please add any other comments you would like to make regarding the questionnaire here.

APPENDIX 8

DEVELOPED QUESTIONNAIRE

Please rate the following factors on a scale of Poor- Fair- Adequate- Good- Excellent

1. Your working relationships with your pharmacy colleagues
2. Your communication with your pharmacy supervisors

Please rate your agreement with the following statements regarding the culture of your pharmacy on a scale of Strongly agree – Strongly disagree

3. I can easily learn about new initiatives in my pharmacy.
4. I can provide feedback about new initiatives undertaken at our pharmacy.
5. The culture of our pharmacy is progressive.
6. Our pharmacy organization is close-minded about new initiatives.

SBI Description

Please answer the following questions about your experiences with the SBI

7. How aware are you of screening and brief interventions?
    a. Not aware - Somewhat aware - Moderately aware – Mostly aware- Extremely aware
8. How would you rate your current knowledge regarding SBIs for opioid misuse?
    a. Poor- Fair- Adequate- Good- Excellent
9. How often do you provide the following services for patients when they pick up opioid prescriptions on a scale of Never- Rarely-Sometimes-Often- Always?
    a. Dispense Narcan (naloxone) to patients who may benefit from it
    b. Counsel patients regarding opioid safety issues (such as storage, disposal)
    c. Counsel patients regarding opioid misuse
    d. Contact prescribers for safe opioid prescribing

Please rate the following factors on a scale of Poor- Fair- Adequate- Good- Excellent:

10. The education you have received regarding screening for the following:
    a. substance misuse
    b. opioid misuse
11. The training you have received regarding screening for the following:
    a. substance misuse
    b. opioid misuse

Please rate the helpfulness of the SBI on the following factors on a scale of Not helpful- Somewhat helpful- Moderately helpful- Very helpful- Extremely helpful:

12. Helpfulness of the SBI in improving patient outcomes.
13. Helpfulness of the SBI in improving opioid safety.

Please rate your agreement with the following statements

14. My role as a pharmacist includes watching for opioid-misuse.
15. The SBI gives me an opportunity to use my clinical skills more than usual.
16. Most pharmacists are skeptical of patients misusing opioids when they pick up opioid prescriptions.
17. Most pharmacists are negatively biased against patients picking up opioid prescriptions.

Please answer the following questions about providing the SBI at your pharmacy

18. How motivated are you to provide the SBI in your pharmacy?
    a. Not motivated – Somewhat motivated- Moderately motivated- Very motivated- Extremely motivated
19. Please rate how important each of the following factors are in increasing your motivation to provide the SBI on a scale of Not important- Somewhat important- Moderately important- Very important- Extremely Important.
    a. Improved patient care and outcomes as a result of the SBI
    b. Opportunity to provide more clinical services
    c. Opportunity to connect with patients

d. Reimbursement for providing the SBI

20. How confident are you in providing the SBI at your pharmacy?
21. Please rate the importance of the following factors in making you confident to implement the SBI on a scale of Not important- Somewhat important- Moderately important- Very important- Extremely Important.
    a. Opportunity to address your concerns through practice
    b. Compatibility of SBI with your setting/workflow
    c. Prior experience with similar interventions

Please answer the following questions about implementing the SBI at your pharmacy

22. How important is reimbursement as an incentive for providing the SBI
    a. Not important- Somewhat important- Moderately important- Very important- Extremely Important.
23. <u>If important:</u> How much incentive is adequate to provide the SBI?_$_____
24. How well does the SBI align with your pharmacy organization's goals?
    b. Not at all aligned- Somewhat aligned-Moderately aligned- Very aligned-Extremely aligned
25. How well does the SBI meet the needs of your patients?
    c. Not at all - Somewhat – Moderately well - Very well -Extremely well
26. How would you describe the costs involved in implementing the SBI?
    d. Insignificant-Minor-Moderate-Major-Severe
27. How complicated is providing the SBI at your pharmacy?
    a. Not complicated-Somewhat complicated- Moderately complicated-Very complicated-Extremely complicated

Please rate your agreement with the following statements regarding implementing the SBI at your pharmacy

28. A strong need for the SBI exists at our pharmacy.
29. The SBI is similar to other initiatives implemented at our pharmacy.
30. Incentives beyond increased clinical care time with patients would be necessary to provide the SBI.
31. We can use existing work processes to implement the SBI at our pharmacy.

32. We need physical infrastructure changes to implement the SBI at our pharmacy.
33. The SBI can act as a resource for patients to obtain thorough and consistent pharmacist interaction.
34. Costs to implement the SBI outweigh its benefits.
35. Providing the SBI would be time-consuming.
36. The SBI offers more opportunity for individualized patient care as compared to other opioid safety interventions implemented at our pharmacy.