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Pharmacist Interventions to Deprescribe Opioids and Benzodiazepines in Older Adults: a Rapid Review

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Abstract

Background: Many older adults are prescribed opioids and benzodiazepines (BZDs), despite increased susceptibility to adverse events. Challenges of deprescribing include fragmented care and lack of knowledge or time. Pharmacists are well-positioned to overcome these challenges and facilitate deprescribing of these medications.

Objectives: We sought to evaluate interventions utilizing pharmacists to deprescribe opioids and BZDs in older adults.

Methods: We conducted a rapid review following a comprehensive literature search to identify interventions with pharmacist involvement for deprescribing opioids and BZDs in older adults. Studies were included based on: (1) inclusion of patients ≥ 65 years old receiving BZDs and/or opioids, (2) evaluation of feasibility or outcomes following deprescribing (3) pharmacists as part of the intervention. We included randomized, observational, cohort, and pilot studies. Studies that did not report specific results for BZD or opioids were excluded.

Results: We screened 687 abstracts and included 17 studies. Most (n=13) focused on BZD deprescribing. Few studies focused on opioids (n=2) or co-prescribing of opioids and BZDs (n=2). The most common intervention was educational brochures (n=8), majority being the EMPOWER brochure for deprescribing BZDs. Other interventions included chart review with electronic notes (n=4), pharmacist-led programs/services (n=2), and multifactorial interventions (n=3). Many studies were underpowered or lacked suitable control groups. Generally speaking, interventions utilizing educational materials and those in which pharmacists engaged with patients and providers

were more effective. Interventions relying on electronic communication by pharmacists were less successful, due to low acceptance or acknowledgement.

Conclusions: We identified a number of feasible interventions to reduce BZD use, but fewer interventions to reduce opioid use in older adults. An optimal approach for deprescribing likely requires pharmacists to engage directly with patients and providers. Larger well-designed studies are needed to evaluate the effectiveness of deprescribing interventions beyond feasibility.

INTRODUCTION

Opioid use is a serious public health problem in the United States and has contributed to many deaths over the past two decades.^{1,2} Benzodiazepines (BZDs) are frequently co-prescribed with opioids and contribute to increased risk of adverse events.³⁻⁶ Older adults, specifically, are being prescribed both opioids and BZDs at an increasing rate.^{7,8} From 2006 to 2015, the rate of opioid prescribing during office visits for older adults increased from 5.9% to 10.0% while BZD prescriptions increased from 4.8% to 6.2%. Rates of co-prescription of opioids and BZDs in older adults increased from 11.7% to 19.9%.⁸

Older adults are poor candidates for opioids and BZDs as long-term solutions to manage chronic pain, anxiety, or insomnia due to their greater susceptibility to central nervous system (CNS) adverse effects, and the resulting impact on falls.⁹⁻¹¹ Use of CNS-active drugs increases the risk of falls in older adults and co-prescribing of opioids and BZDs exponentiates this risk.¹²⁻¹⁴ Older adults are also at an increased risk of opioid misuse due to increased healthcare utilization and are more likely to be treated for pain than younger patients.¹⁴⁻¹⁶ A substantial number of older adults are prescribed both opioids and BZDs, despite the known risk for severe adverse effects that can lead to death.^{5,8,14,17-19}

The importance of deprescribing medications for older adults is increasingly emphasized in clinical care. Deprescribing is defined as a supervised process of dose reduction or cessation of medication that may cause harm or may no longer be beneficial.²⁰ Limited evidence is available, but several studies have shown deprescribing to be feasible and safe.^{21,22} Several barriers to deprescribing from the perspectives of prescribers have been identified, including devolved responsibility, fragmented care, fear of harming the provider-patient relationship or causing patient harm, and lack of knowledge and time.²³⁻²⁷ Considering these barriers, it is reasonable to assume that successful interventions for deprescribing require a multifaceted approach. In fact, prior studies have found that single interventions for deprescribing benzodiazepines that relied on or targeted physicians alone were less likely to be successful than multifaceted interventions drawing on interdisciplinary expertise.²⁸ Tools and resources exist to facilitate deprescribing by engaging with patients and other healthcare providers, specifically pharmacists.²¹⁻²³ An approach to deprescribing that utilizes pharmacists has the potential to overcome many of the aforementioned barriers.²⁹ Pharmacists are well-positioned to determine whether opioids or BZDs are indicated and develop individualized tapering schedules to facilitate deprescribing.²⁹⁻³¹

There are still numerous gaps in the literature, including best practices for tapering opioids and BZDs in older adults and the efficacy of targeted pharmacist interventions for deprescribing.³² Non-targeted interventions aimed at addressing polypharmacy or

medications from the Beers Criteria may only produce modest improvements in clinical outcomes,³³ particularly for high-risk medications that may be more difficult to deprescribe, due to the potential for dependency. Additionally, some prescribers may feel overwhelmed with non-targeted, non-prioritized deprescribing recommendations from pharmacists or feel that such recommendations come with inherent uncertainties,³⁴ thereby limiting their responsiveness to the recommendations. Given the focus of various outcome metrics on opioid and BZD prescribing and the documented harms of long-term overuse,³⁵⁻³⁷ targeting opioid and BZDs for deprescribing with pharmacist support is a logical step towards achieving improved outcomes.³⁸ To date, there are no reviews that summarize the evidence related to deprescribing opioids and BZDs, specific to older adults. The goal of this review is to evaluate and synthesize current literature on targeted pharmacist interventions that facilitate opioid and BZD deprescribing in older adults.

METHODS

We developed our research question using the population, intervention, comparison, and outcome (PICO) format, which was used to guide a literature search and develop a screening process for relevant articles. The research question was: “What is the feasibility and success of targeted interventions involving pharmacists to deprescribe opioids or benzodiazepines in older adults?”.

We conducted a rapid review,³⁸⁻⁴⁰ after a comprehensive literature search that used a combination of subject headings and keywords for opioids, BZDs, deprescribing, pharmacy, and geriatrics. Our research question, literature search, and eligibility criteria were developed with input from our study team, comprised of physicians, pharmacists, and researchers. A health sciences librarian (RC) consulted with the study team to develop the comprehensive search strategy, which was employed in PubMed via National Libraries of Medicine (NLM), Embase via Elsevier, and Cumulated Index to Nursing and Allied Health Literature (CINAHL) Plus via EBSCO from date of database inception to February 18, 2020. No filters or limits were applied to the PubMed and CINAHL searches while conference abstracts were excluded from the Embase search. See the Supplementary Materials for the details of each search.

A two-stage screening was completed independently by two authors (BC and JDN). Search results were loaded into Covidence, a web-based software platform designed to facilitate the systematic review process for screening. Reasons for exclusion were incorporated into Covidence screening forms and noted for each study. Titles and abstracts were screened and after initial screening, full texts were reviewed by both reviewers. Bibliographies of review articles were manually inspected to identify additional studies. Discrepancies were discussed by both parties to reach a decision.

Inclusion/Exclusion Criteria.

Inclusion criteria were: (1) inclusion of patients ≥ 65 years old receiving BZDs and/or opioids, (2) evaluation of deprescribing feasibility or outcomes following deprescribing (3) mention of pharmacists as part of a targeted intervention for opioids and/or BZDs. We included randomized trials, observational studies, cohort studies, and pilot studies.

Qualitative studies, case studies, or papers without full text available in English were excluded. Studies that did not report specific results to BZD or opioid deprescribing were excluded.

The complete screening strategy is outlined in Figure 1. Among abstracts initially identified, (n=687), 70 studies were included for full text screening. At this stage, studies that did not address opioids or BZDs nor include older adults were eliminated. This resulted in 15 studies to be included. Finally, we identified two additional references meeting criteria from two systematic reviews^{41,42} (n=17).

Data Extraction.

Key information was extracted from each study by one member of the study team (BC) and subsequently verified for accuracy by another (JDN). Information extracted from each study included: (1) title, author, and publication year, (2) sample and care setting, (3) study design and intervention, and (4) results. Most studies were designed to evaluate implementation or feasibility and reported an array of outcomes that could not be pooled across studies. For this reason, we provide a narrative summary with no formal statistical analysis. A simplified risk of bias assessment based on study design, sample, and analyses was conducted and is presented in supplementary materials (Table S2).

RESULTS/SUMMARY

Overview of Included Studies.

Tables 1 and 2 provide a summary of data extracted from included studies. The majority of studies examined BZD deprescribing (n=13), while two studied opioids, and two studied BZD and opioid co-prescribing. Uncontrolled before and after designs were the most common (n=9), followed by randomized trials (n=5), and non-randomized trials (n=3). Most studies were conducted in the outpatient (n=9) or acute care setting (n=6). Three studies were conducted in long-term care settings. Sample sizes varied between studies. Most studies had sample sizes between 100-500 individuals. The smallest and largest were 12 and 12,157 individuals, respectively. Most studies focused on the feasibility of reducing BZD/opioid use. However, several (n=5) focused on outcomes other than medication use, including health status, patient symptoms, communication acceptance, and cost.

The most common type of intervention was patient educational brochures (n=8), with five studies specifically using the EMPOWER (Eliminating Medications Through Patient Ownership of End Results) brochure. This was followed by pharmacist chart review and electronic notes (n=4), pharmacist-led programs/services (n=2), and multifactorial interventions (n=3). Key findings from each study are summarized below based on the type of intervention.

Summary of Studies.

Educational Brochures or Other Materials.—In total, eight studies utilized educational brochures to facilitate deprescribing of BZDs across community, inpatient,

and long-term care settings. All except one were conducted specifically in older adult populations.

Five studies used the EMPOWER brochure,⁴³⁻⁴⁷ an educational resource encouraging patients to discuss discontinuing their BZDs with their physician or pharmacist. The team involved in creating the brochure was an interdisciplinary collaboration that included pharmacists. The first two papers analyzed data from the original EMPOWER study,^{43,44} a cluster randomized study which evaluated the effect of direct consumer education on BZD discontinuation in community-dwelling older adults in Canada. The study included older adults taking five or more medications and at least one chronic BZD prescription.⁴³ A total of 303 patients were randomized in a 1:1 ratio to receive the EMPOWER brochure or usual care. The primary outcome was complete cessation of BZDs as measured by pharmacy refill records. In the first study, those receiving the EMPOWER brochure had a higher rate of discontinuation compared to controls (27% vs. 4.5%, risk difference = 23% [CI 14%-32%]). The second paper⁴⁴ was a post-hoc analysis of the aforementioned trial⁴³ that assessed whether cognitive status may affect the success of the EMPOWER brochure. The study included individuals from the intervention arm and controls who received the EMPOWER brochure following a 6-month waiting list period. Cessation of BZDs was compared across individuals with (n=122) and without (n=139) mild cognitive impairment. The rate of total cessation of BZDs at six months was lower for the individuals with MCI compared to those without MCI (32% vs. 38.1%), but this was not statistically significant (adjusted OR 0.79, 95% CI [0.45–1.38]). No safety outcomes were reported in either study.

Three additional studies used the EMPOWER brochure to target hospitalized older adults.⁴⁵⁻⁴⁷ The first study was a non-randomized trial in which investigators examined the effectiveness of the EMPOWER brochure in reducing sedative use (BZD and non-BZD sedatives) among hospitalized older adults who regularly used sedative medications.⁴⁷ The intervention group was compared to a cohort of historical controls who received usual care. The primary outcome was discontinuation of BZDs during hospitalization. Sleep quality was measured as a safety outcome. Among the 50 patients who received the brochure, 72% (n = 36) successfully stopped sedatives within 30 days after discharge versus 20.8% (n = 42) controls (p < 0.01). No significant worsening in sleep quality was reported. The second study⁴⁵ conducted among hospitalized older adults was an uncontrolled before and after comparing cessation of BZDs before and after receiving the EMPOWER brochure and an individualized discussion with the pharmacist. The pharmacist also led weekly medication reviews that were presented to the team and was responsible – solely or with the healthcare team - for creating individual tapering schedules for patients. The primary outcome was cessation of BZDs. Six of twelve total individuals achieved total cessation and seven received alternate medications. No safety outcomes were studied. The third study⁴⁶ was a randomized trial in which 42 hospitalized older adults were randomized in a 1:1 ratio to receive the EMPOWER brochure. The primary outcome was BZD use at 1-month post-discharge. There was no difference in reduction of BZDs between groups at one month (p > 0.05) although high rates of cessation were observed (46.2% intervention, 53.8% control). No safety outcomes were studied.

The remaining studies used other educational brochures or materials. D-PRESCRIBE⁴⁸ (Developing Pharmacist led Research to Educate and Sensitize Community Residents to the Inappropriate Prescriptions Burden in the Elderly) was a randomized trial of community dwelling older adults receiving one or more high-risk medications (sedative-hypnotics, first-generation antihistamines, glyburide, or nonsteroidal anti-inflammatory drugs). This study used patient educational brochures with pharmacists providing their ‘pharmaceutical opinion’ directly to physicians. A pharmaceutical opinion is a legal and reimbursable activity by a pharmacist that is intended to facilitate pharmacist-physician communication. The primary outcome was complete cessation of prescriptions in the 6 months after intervention and adverse withdrawal events were measured as safety outcomes. Among the 301 individuals taking a BZD, zopiclone, or zolpidem, higher rates of cessation were observed in the intervention group compared to controls at 6 months (43.2% vs. 9%, risk difference 34% (95% CI [25% to 43%]). However, 38% of those who attempted to taper sedative-hypnotics reported withdrawal symptoms.

Another study⁴⁹ assessed the impact of printed educational materials and pharmacist-led educational sessions for providers, staff, and family members on BZD and psychotropic medication use among older adults in long-term care facilities in Canada. In this non-randomized trial, a psychotropic deprescribing algorithm and education about nonpharmacologic interventions for mood and behavioral management were provided to providers, nursing staff, and caregivers. Facilities were selectively allocated to receive the intervention based on geographic location. The primary outcome was the proportion of residents receiving BZDs and the dosage prescribed six months post-intervention. No safety outcomes were measured. The intervention did not reduce the percentage of residents receiving BZDs nor the dosages administered in the six months after the intervention ($p > 0.05$).

The final study to use educational brochures⁵⁰ was an uncontrolled before and after pharmaco-economic evaluation of a deprescribing intervention. This study included a broader population of adults, not just older adults, in the United Kingdom. Letters were mailed to all patients with long-term BZD use from two practices and included education on complications associated with long-term BZD use with encouragement to reduce intake. BZD usage and costs were compared in the years before and after the 12-month intervention period using defined daily dosages (DDD) prescribed. Of the 242 individuals included, 31% discussed BZD use with their general practitioner and 9.9% had dose or drug changes made. Following the intervention, there was a 17% reduction in BZD use, with 5% completely discontinuing. The authors reported modest cost savings due to reduced prescribing of medications but argued that the intervention is justified given the avoidance of potential negative outcomes of long-term BZD prescribing.

Pharmacist Chart Reviews—In four studies,⁵¹⁻⁵⁴ pharmacists conducted chart reviews or used automatically generated reports to identify candidates for deprescribing and make recommendations. Although the studies using this type of intervention included older adults, none were specific to this population.

The first study⁵¹ was a randomized trial evaluating the impact of a deprescribing intervention for anticholinergics and BZDs on reducing delirium in adult ICU patients. Two interventions were used: 1) computerized decision support alerts on order entry and 2) pharmacist review of medication orders and communication with providers. Specifically, pharmacists conducted medication reviews twice a day and communicated alternatives directly with the medical or surgical team. Primary outcomes were delirium duration and severity, while secondary outcomes were mortality and length of stay. However, the study team also measured the proportion of patients receiving BZDs as well as the median dose prescribed. Ultimately, this study found no significant difference in the number of patients receiving BZDs or the median dose of lorazepam equivalents prescribed. No significant differences were observed for other safety outcomes. However, the lack of difference may be due to the fact that clinical pharmacists were already staffed on teams involved in the intervention.

The only two studies to target concurrent use of opioids and BZDs also relied on chart reviews. The first study⁵² was an uncontrolled before and after study that evaluated community pharmacist messages to prescribers via fax or electronic health record (EHR) messaging, including alerts about prescription dispensing history and evidence-based recommendations to reduce opioid and BZD prescribing. The primary outcome was any change to prescription dispensing in the 3 months following the intervention. No safety outcomes were evaluated. A total of 137 prescribers of 121 patients were contacted via fax or electronic health record (EHR). After four weeks, 34 pharmacist recommendations were sent and 32 responses were received. Most recommendations were rejected (59%) with few BZD and opioid tapers accepted (15% and 6%, respectively). After 3 months, 35 prescriptions were changed, most being opioid or BZD tapers or discontinuation (63%).

The second study to target co-prescribing of opioids and BZDs⁵³ was also an uncontrolled before and after study evaluating the success of pharmacist-initiated tapers in a Veteran population. Pharmacists reviewed charts of eligible patients and submitted notes on tapering recommendations or alternative therapies via the EHR. Primary outcomes included acknowledgement of recommendations and initiation of tapering schedules. No other outcomes were evaluated. More than 75% of individuals were over the age of 55. Less than half (48%) of recommendations were acknowledged and just 11% either initiated or indicated commitment to tapering. Authors concluded that despite electronic notes being a common communication method, recommendations were frequently disregarded and thus insufficient as a primary intervention for reducing long-term combination BZD and opioid use.

Harden and colleagues⁵⁴ conducted an uncontrolled before and after study to evaluate the clinical implications of tapering chronic opioids in a Veteran population with a primary outcome of reduction in morphine milligram equivalents (MMEs) and a secondary endpoint of pain perception. This chart review included 50 patients with tapering plans. Tapers were implemented by PCPs, an outpatient pain service, or pharmacists, but the study did not specifically differentiate which was most successful. Over a 12-month period, opioids were reduced by 46%. Thirty-nine percent of patients (n=19) increased the number of adjuvant medications they were taking (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs

(NSAIDs), topical analgesics, antidepressants, tramadol, and muscle relaxants). Conversely, 39% (n=19) reported no change in the number of adjuvant medications and 22% (n=11) actually reduced their number of adjuvant medications. Change in dosing of adjuvant medications was not reported. Most patients noted no increases in pain, with 70% reporting less or no pain at 12 months. Overall, 47 of 50 patients were successfully tapered with 13% completely discontinued at 12 months.

Pharmacist-Led Teams.—In two studies, deprescribing was facilitated by pharmacist-led teams. Neither were exclusive to older adults. The first study⁵⁵ was an uncontrolled before and after study that examined whether pharmacist-led multidisciplinary team meetings were effective in reducing the dosages of BZDs on two inpatient psychiatric units. Clinical pharmacists conducted comprehensive medication reviews and then led weekly multidisciplinary conferences with the medical team to direct proper usage of BZDs. Primary outcomes included changes in the number of BZD doses, dosages prescribed, and discontinuation. No safety outcomes were measured. A total of 273 patients were evaluated. Recommendations from this pharmacist-led service resulted in a statistically significant decrease in the number of BZD doses administered as well as the average equivalent diazepam doses prescribed in post-intervention periods compared to pre-intervention periods. The rate of discontinuation ranged from 27% to 47% across units.

Furbish and colleagues⁵⁶ conducted an uncontrolled before and after study to describe a pharmacist-led service to improve safe use of BZDs. Individuals with a prescription for BZD therapy for >3 months were identified using the electronic health record. PCPs had the option to refer to the pharmacy service to manage BZDs and other medications for anxiety under a collaborative drug therapy management protocol. In addition to prescribing power the pharmacy service ordered lab work and administered screening tools to track patients' progression. Primary outcomes included rates of BZD discontinuation or change. Severity of anxiety symptoms was measured as a safety outcome. Among referred patients (n=235), only 29 were seen by the pharmacy service. More than half of individuals seen by the pharmacy service (n=15) had their BZD prescription changed, reduced, or discontinued. Patients reported improved anxiety symptoms; however the study was underpowered to detect significant differences in clinical outcomes due to the small proportion of patients enrolled.

Multi-factorial Interventions.—Finally, three studies used multi-factorial interventions that included the use of pharmacists to reduce BZD and opioid use. All three studies focused specifically on older adults.

The first two studies took place in the long-term care setting as part of the RedUSE (Reducing Use of Sedatives) trial – an interdisciplinary program in Australia to reduce BZD and antipsychotic prescribing rates in residential aged care facilities. The RedUSE project included two medication audit and feedback cycles by pharmacists for nursing home residents. Pharmacists led group educational sessions for nursing staff or individual educational sessions for physicians. The RedUSE educational intervention also used pamphlets developed for patients or their family members. Lastly sedative reviews were

conducted and allowed for notes by pharmacists, nurses, and physicians to encourage interdisciplinary communication.

The first study⁵⁷ was a non-randomized study of 25 nursing homes in Tasmania. Primary outcomes included prescribing rates of BZDs with dosage reductions and discontinuations as secondary outcomes. No data on safety outcomes was collected. Over the six-month study period, there was a significant reduction in the percentage of residents in the intervention group regularly taking BZDs (31.8% to 26.9%, $p < 0.005$). Dose reductions or cessations of BZDs were greater in the intervention group versus controls (39.6% vs 17.6%, $p < 0.0001$). The second study⁵⁸ was an expansion of the RedUSE program in 150 Australian residential aged care facilities using a before and after study design. The same outcomes were measured as in the prior study. The program included an enhanced staff training by pharmacists with the addition of a “champion nurse” role. At six months, the prevalence of BZD use significantly declined from 22.2% to 17.6% ($p < 0.001$) and the mean equivalent diazepam dose declined from 1.4 to 1.1 mg/resident/day ($p < 0.001$).

The final study⁵⁹ evaluated an interdisciplinary pain rehabilitation program (IPRP) that included pharmacists focused on opioid deprescribing. Using an uncontrolled before and after design, individuals were followed for up to 6 months and were divided into three age groups, with 78 patients making up the older adult group (age 60+). Pharmacists completed medication reconciliation upon admission and calculated daily dosage of opioids in MMEs. Primary outcomes included assessments of pain and depression as well as the types and dosages of opioid and non-opioid medications prescribed. Over half (57.7%) of all older adults in the program were taking opioids on admission. At discharge, only 6.8% of older adults remained on opioids. Among those who continued opioids at discharge, the average daily doses were substantially reduced compared to admission (157.1 vs 219.6 MMEs). Six months after discharge, use of NSAIDs, muscle relaxants, anticonvulsants, and tricyclic antidepressants (TCAs) had decreased, while use of SSRIs and other non-TCA antidepressants had increased among older adults in the program. No differences were shown across age groups. Participants in the older adult group reported significant improvements in depressive symptoms, pain catastrophizing, pain interference, perceived health, and physical, emotional, and social functioning at discharge and six months post-treatment.

Risk of Bias Assessment.

Risk of bias in each study was assessed in consideration of the study design and analyses. The majority of studies relied on self-controlled study designs or failed to identify a control group altogether. Only 5 of 17 studies identified used a randomized design with a suitable control group. A number of studies also lacked sufficient long-term follow-up to evaluate deprescribing, which likely required a tapering period of several months. We also noted that the majority of studies did not evaluate safety outcomes of deprescribing, which greatly limits the ability to determine the feasibility of targeted deprescribing interventions. Finally, generalizability was a concern across studies, given that all interventions were only evaluated within a single facility or healthcare system.

DISCUSSION

In a rapid evidence synthesis, we identified a number of studies evaluating targeted pharmacist interventions for deprescribing BZDs in older adults, but few studies of deprescribing opioids in this population. The most common targeted intervention was the EMPOWER brochure, targeted to patients.⁴⁴ Other targeted interventions included electronic pharmacist communications to providers, pharmacist-led deprescribing services, and multimodal behavioral and pharmaceutical interventions. Although all of the interventions demonstrated feasibility, direct comparison of the successes across intervention type was difficult due to heterogeneity in study designs, populations, and measures of deprescribing. Pharmacists are well-positioned to bridge the gap between prescribers and patients to achieve successful deprescribing. In fact, a number qualitative studies have emphasized the importance of pharmacists to help facilitate deprescribing in older adults.²⁵⁻²⁷ Pharmacists are arguably the most accessible health professionals⁶⁰ and highly trusted by both prescribers and patients to manage medications. The optimal role for pharmacists in deprescribing opioids and BZDs is uncertain. However, our review provides some important food for thought.

We observed that targeted interventions relying on pharmacist chart reviews with electronic communication to providers were generally less successful in reducing opioid or BZD use, primarily due to a low acceptance/implementation or acknowledgement of the communication. Targeted interventions utilizing educational brochures to engage patients, pharmacist-led teams, and multimodal interventions were more effective in reducing opioid and BZD use. This suggest that an optimal approach likely requires pharmacists to engage directly with patients and providers in order to successfully deprescribe opioids and BZDs, as suggested by qualitative studies which emphasize trust as a key factor in successful deprescribing.²⁷ However, we only observed one study in which it was clear that pharmacists had prescriptive authority that allowed them to modify orders under a collaborative practice agreement.⁵¹ Otherwise, the level of responsibility delegated to pharmacists was unclear across most studies. This expanded role of pharmacists may be worth exploring in future studies.²⁷

The lack of studies utilizing pharmacists to deprescribe opioids in older adults was surprising, given that the dangers of opioid misuse are highlighted the media⁶¹ and that pharmacists are highly trained and accessible medication specialists.⁶² Guidelines caution against the use opioids and BZDs individually and in combination in older adults at risk for falls⁹, yet there is a paucity of guidance or best practices to reduce use, particularly opioids. While most overdose deaths involve opioids, the risk of drug mixing is often underemphasized and few studies actually addressed co-prescribing of opioids and BZDs.

We hypothesize that disparities in resources for deprescribing opioids versus BZDs contributes to the imbalance of studies included in our review. The National Academy of Medicine states “tapering long-term opioid analgesics is a practice area in which clear evidence and authoritative guidance remains limited”.⁶³ Guidelines from the Centers for Disease Control and Prevention (CDC),⁶⁴ the US Department of Veterans Affairs (VA),⁶⁵ and the American Academy of Family Physicians (AAFP)⁶⁶ offer little guidance on opioid

tapering except to reduce dosages by 10%–50% per week/month. Reducing opioids in older adults is further complicated by the adverse effects of alternative medications such as NSAIDs, antidepressants, and anticonvulsants which are less optimal in older adults with significant comorbidities.⁶⁴ Few studies included in our review actually reported on the change in number of non-opioid analgesics used after an opioid taper.^{54,59} Further research examining the overall change in dosage of these medications, not just the number of medications used, is warranted to evaluate the overall improvement in safety with opioid tapers.

While opioids can be used appropriately for chronic pain, use of BZDs for long-term treatment is usually inappropriate. The Beer's Criteria recommends to avoid BZDs due to increased risk of cognitive impairment, delirium, and falls.⁹ BZDs are only considered appropriate for severe anxiety when other drugs or therapies have failed.^{9,67} In contrast to opioids, there are several well-designed BZD deprescribing tools available, with specific tapering schedules. Examples include the EMPOWER trial brochure⁴³ and a BZD and Z-Drug Deprescribing Algorithm from the Bruyère Deprescribing Guidelines Research Team⁶⁸.

The majority of studies in this review occurred in the outpatient setting (n = 9), followed by the acute care (n = 6) and long-term care settings (n = 3). No studies investigating opioid use were conducted in the long-term care setting. This may be due to increased focus on appropriate use of BZDs and antipsychotics in this setting, with requirements for documenting gradual dose reductions and limits on duration of use. The inpatient setting allows for close oversight of deprescribing and direct communication between patients, team members and prescribers. However, targeted interventions in the outpatient or long-term care setting may be more impactful in reducing opioid and BZD use over time due to longitudinal continuity of care.

We acknowledge several limitations. We conducted a rapid review with streamlined elements of a systematic review. Given the variable study designs and outcomes measured, we did not evaluate the bias in individual studies and did not conduct a meta-analysis. Many studies had small sample sizes and thus were underpowered to evaluate the impact of interventions. Additionally, few studies measured clinical outcomes following BZD and/or opioid deprescribing. Larger randomized studies are needed to evaluate the impact of targeted pharmacist deprescribing interventions for opioids and BZDs on patient-focused outcomes such as falls, pain, and sleep quality. We also acknowledge that our review is narrow in scope. Our focus on interventions targeting opioids and BZDs specifically, may have omitted other studies with relevance to our research question, despite having a broader focus. Additionally, we acknowledge that non-pharmacist interventions may also be effective for deprescribing opioids and BZDs in older adults. Thus, the studies presented in this paper may not be representative of the feasibility or success of all deprescribing interventions. Finally, several studies in our review evaluated deprescribing of opioids and BZDs in younger adults and thus may be less generalizable to the older adult population. Future studies should also seek to evaluate which subpopulations beyond age strata are most suitable for deprescribing and the efficacy and tolerability of alternative agents.⁶³

CONCLUSIONS

We identified feasible targeted interventions to reduce BZD use, but fewer interventions to reduce opioid use in older adults. The most common targeted interventions were educational brochures and materials targeted towards patients and prescribers. Interventions were more effective when pharmacists engaged with patients and providers to facilitate deprescribing. Larger well-designed studies are needed to evaluate the effectiveness of targeted deprescribing interventions for opioids and BZDs beyond feasibility outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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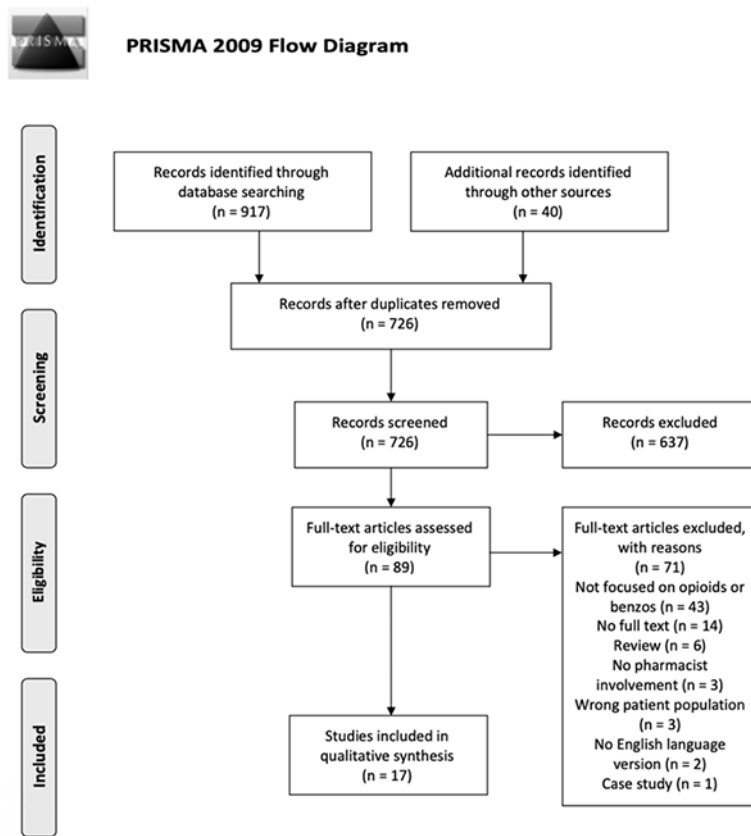


Figure 1. Screening Strategy

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097
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Table 1
Studies Utilizing Educational Materials for Deprescribing of Benzodiazepines or Opioids

Study	Target	Intervention	Pharmacist Role	Sample	Main Results
<i>Educational Brochures or Other Materials</i>					
Tannenbaum, 2014	BZDs	EMPOWER brochure. Deprescribing tool sent via mail, encouraging patients to discuss deprescribing with physician or pharmacist.	Created educational materials. Patients encouraged to speak with pharmacists about deprescribing.	Older adults with 5 prescriptions and benzodiazepine use for 3 months. (n=148 intervention; n=155 control)	In intervention group, 27% achieved discontinuation versus 5% in control group (CI 14%-32%). Higher likelihood of cessation in intervention group (8-fold).
Martin, 2017	BZDs	EMPOWER brochure.	Created educational materials. Patients encouraged to speak with pharmacists about deprescribing.	Sub-group of individuals with mild cognitive impairment from EMPOWER trial (Tannenbaum). (n=122 intervention; n= 139 control)	Comparable rates of total cessation or dose reduction in patients with mild cognitive impairment (46.8%) and without (45.1%). No significant differences among individuals with mild cognitive impairment between control and intervention groups (CI 0.62-1.83).
Wilson, 2018	BZDs	EMPOWER brochure.	Medication histories. Created educational materials. Patients encouraged to speak with pharmacists about deprescribing.	Inpatients 65 years old with sedative prescription. (n=50 intervention; n=202 control)	72% of patients stopped sedatives for 30 days following discharge in intervention group compared to 20.8% in control group (p<0.01).
Carr, 2019	BZDs	Four components: (1) structured medication review by hospital pharmacist, (2) EMPOWER brochure, (3) consult with physician and then pharmacist/healthcare team, (4) information sent to PCP.	Medication histories and tapering schedules presented weekly to team. Patient counseling.	Newly hospitalized older adults with benzodiazepine prescription who consented to deprescribing (n=12).	Half (6/12) of patients completely discontinued, and 5/12 had partial depression. More than half of patients who initiated deprescribing were switched to other medications; statistical tests not performed.
Gnjidic, 2019	BZDs	EMPOWER brochure.	Created educational materials. Patients encouraged to speak with pharmacists about deprescribing.	Older adult inpatients who had 1 or more benzodiazepine prescription (n=42).	No significant difference seen (p>0.05) in benzodiazepine withdrawal between control and intervention group at 1-month follow-up.
Martin, 2018	BZDs	Educational brochures created by pharmacists that targeted patients and physicians.	Sent brochures to patients. Sent PCPs pharmaceutical recommendations.	Patients 65 years old with a prescription for 1 or more sedative hypnotic medication for 3 months (n=465 intervention; n=155 control).	Among sedative hypnotic users, 43.2% in the intervention group completely discontinued vs. 9.0% in control (CI 25%-43%).
Hagen, 2005	BZDs	Educational brochures and in-person, pharmacist-led education to facility staff and family members.	Delivered education to staff or patients' family members.	Long-term care facilities in Southern Alberta (n=1,124 intervention; n=1,190 control).	Intervention did not result in a statistically significant reduction in the proportion of residents receiving benzodiazepines nor the total doses received compared to control facilities (p>0.05)
Morgan, 2002	BZDs	letter mailed to patients detailing complications associated with long-term benzodiazepine use and encouraging discontinuation.	Developed educational materials. Available for counseling.	Patients receiving benzodiazepines for > 1 year (n=242).	Benzodiazepine use was discussed with PCPs for 31% of patients. Dosages were changed for 9.9% and 5.0% had no prescriptions following intervention. Total benzodiazepine use decreased by 17%. Cost savings was £1.20 per patient; number needed to treat was 20.

Table 2
Studies Utilizing Other Interventions for Deprescribing of Benzodiazepines or Opioids

Study	Target	Intervention	Pharmacist Role	Sample	Main Results
Pharmacist Chart Review					
Campbell, 2019	BZDs	Computerized prescribing alerts and pharmacist decision support.	Reviewed medication orders. Recommended alternatives directly with medical/surgical team.	ICU patients with dementia (n=200).	No difference in median total benzodiazepine dose, delirium rates, or severity between intervention and control groups.
Luchen, 2019	Opioids & BZDs	Pharmacist-driven communications, including patient dispensing history and standardized recommendations.	Recommendations sent to providers via fax or EHR.	Patients with benzodiazepine and opioid co-prescribing for 30 cumulative days (n=122).	In total, 11 benzodiazepine discontinuation/tapers and 11 opioid discontinuation/tapers were implemented for 19 unique patients; 32 prescribers responded to fax while none responded to EHR communication. Statistical tests not performed.
Shayegani, 2018	Opioids & BZDs	Pharmacist chart review and recommendations made via EHR.	Chart review with tapering/alternative therapy recommendations via EHR.	Veterans receiving combination opioid and benzodiazepine therapy for over 90 days (n=61).	Fewer than half of recommendations were acknowledged (48%) and 11% of prescriptions were tapered. Mental health providers were less likely to acknowledge notes or initiate tapering; statistical analysis not performed.
Harden, 2015	Opioids	Pharmacist charts review and taper recommendations.	Pharmacist-run pain management clinic.	Patients on an opioid for at least 90 consecutive days with plan to taper (n=50).	Opioid doses were reduced by 46% over 12 months; 70% of patients reported less pain or no change in pain symptoms; 78% of patients had no change or increase in number of adjunctive medications; statistical tests not performed.
Pharmacist-led Teams					
Geka, 2019	BZDs	Pharmacist-run multidisciplinary team meetings.	Comprehensive medication assessments. Pharmacist-led meetings with medical team on proper benzodiazepine usage.	Patients admitted to psychiatric ward with benzodiazepine prescription (n=273).	Across two inpatient units, number benzodiazepine of doses decreased from 1.6 to 0.85 (p<0.05) and from 1.6 to 1.2 (p<0.05) during intervention. Discontinuation rates were 48% and 27% on each unit.
Furbish, 2017	BZDs	Pharmacist-led benzodiazepine management clinic.	Chart review and referral to outpatient clinic. Pharmacy team manages medications, orders labs, and administers patient screening tools under collaborative practice agreement.	Patients receiving benzodiazepines for 3 months (n=44).	Changes were made to 16 benzodiazepine prescriptions, including 7 complete discontinuations. Statistically significant decreases in generalized anxiety disorder scores for 9 patients (p<0.05).
Multi-factorial Interventions					
Westbury, 2010	BZDs	Multiple pharmacist-led strategies, including staff education, drug use evaluation cycles, targeted sedative reviews, and academic detailing.	Drug use evaluation and feedback cycles. Pharmacist-led education sessions for healthcare staff on sedative use with interdisciplinary review.	Patients across 25 nursing homes (n=898 intervention; n=693 control)	Significant decrease in number of patients with benzodiazepine prescription seen in intervention group (31.8% to 26.9%, p < 0.05) versus an increase in the control group (30.4% to 33%, p = 0.2).
Westbury, 2018	BZDs	RedUse program: interactive staff training, defining provider roles for reviewing medications, creation of "champion nurse" role, and educational outreach.	Drug use evaluation and feedback cycles. Pharmacist-led education sessions for healthcare staff on sedative use with interdisciplinary review.	150 nursing facilities (n=12,157)	Mean rates of benzodiazepine use declined 22.2% to 17.6% in 6 months (p<0.001); mean equivalent diazepam dose declined from 1.4 mg/resident/ day to 1.1 mg/resident/day (p < 0.01).

Study	Target	Intervention	Pharmacist Role	Sample	Main Results
Darchuk, 2010	Opioids	Outpatient interdisciplinary pain rehabilitation program, based on cognitive-behavioral model.	Comprehensive medication reviews with multidisciplinary collaboration.	Patients with chronic, non-cancer pain (n=449 total). Age groups: 60+(n=78), 40-59 (n=230), 18-39(n=141).	At discharge, only 3.4% of patients who completed program continued using opioids. At 6 months post-discharge 15.1% reported using opioids. No significant differences observed between groups in terms of opioid use at 6 months post-discharge.