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Preoperative Deprescribing for Medical Optimization of Older Adults Undergoing Surgery: A Systematic Review

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Abstract

Objective: To summarize the evidence for preoperative deprescribing and its effect on postoperative outcomes in older adults undergoing surgery.

Design: Systematic review

Setting and Participants: All available studies.

Methods: We searched EMBASE, Cumulative Index of Nursing and Allied Health (CINAHL), and PUBMED from inception to January 12, 2021. Settings included outpatient settings during the waiting period for surgery (i.e., preoperative clinic) through to the preoperative period in the hospital. Participants who were older adults 65 and older undergoing planned or emergency surgery with deprescribing or medication-related interventions were included for review.

Results: We identified 3 different methods of deprescribing intervention delivery during the preoperative period: geriatrician-led (n = 2), interdisciplinary team-led (n = 8), and pharmacist-led (n = 6). Outcomes were related to healthcare utilization, patient outcomes, and medication changes; however, results were difficult to compare due to heterogeneous outcomes within the topics. Overall, results were either positive or neutral.

Conclusions and Implications: The evidence for deprescribing during the preoperative period for older adults undergoing surgery is weak due to heterogeneity of intervention delivery and outcomes, inclusion of non-operative cases in some studies, and low power. This review highlights the need for future research, which may consider the following: 1) interdisciplinary approach, 2) coordination of deprescribing efforts with primary care provider from the waiting period for surgery up to after discharge, and 3) validated deprescribing criteria such as STOPP/START that

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is easy to implement. It is important to note that results yielded positive and neutral results, not negative ones, which should reassure clinicians to implement deprescribing for older adults during the surgical period. Additionally, policy initiatives such as integrated electronic medical records (EMR) or increased reimbursement of deprescribing efforts for primary care providers and/or hospitals should be pursued to prevent adverse postoperative events for this population.

Brief summary:

Older adults with multimorbidity undergoing surgery are at a higher risk for adverse drug events. Current limited evidence for deprescribing, medication optimization, during the surgical period warrants high-quality research.

Keywords

preoperative; deprescribing; older adults; polypharmacy; surgery

INTRODUCTION

Increasing number of older adults have multimorbidity[1] and complex medication regimens.[2] Poor coordination of care due to multiple clinicians' involvement and transitions of care (i.e. hospital to home) worsens this problem.[3] Polypharmacy is the presence of five or more medications[4] and is frequently associated with the use of inappropriate and unnecessary medications.[5,6] Its prevalence has doubled in the United States from 1999 to 2012.[2]

Adverse drug reactions complicate approximately 2 million hospitalizations, prolong hospital length of stay,[7] and result in 106,000 deaths.[8] Overall, more than 2000 medications are associated with adverse drug reactions.[9] The mechanism through which polypharmacy is associated with adverse outcomes may be attributed to aging physiology of older adults and varying metabolism and clearance among different drugs and heterogeneity in older adults. Reduced functional reserve in older adults[10–12] may affect drug absorption, metabolism, and clearance.[13,14] The following most commonly used drug classes are associated with adverse drug events: antihypertensives,[9,15–18] anticholinergics,[19] antipsychotics,[17–20] antibiotics,[15,17] oral anticoagulants,[15] analgesics,[15,17] and oral anti-diabetics.[15,16] Potentially inappropriate medications (PIMs) as delineated through the Beer's criteria[21] are associated with adverse drug reactions[22] and mortality, and include some very commonly used drugs involving others that are used less frequently.[23]

Deprescribing is "the process of withdrawal, dose reduction/substitution of an inappropriate medication, supervised by a health care professional to manage polypharmacy and improve outcomes."[24] It is a promising approach to improve health and wellbeing outcomes among older adults. Results of deprescribing studies in community and institutional settings, however, have been mixed with some positive and some neutral results[25–28] with respect to the number of PIMs,[26–28] falls,[25,26] mortality,[25,26] hospitalizations,[25,28] and quality of life.[25,28] Moreover, heterogeneity of outcomes and low quality of evidence limit interpretation of results.

The surgical period may be an optimal time for deprescribing to prevent adverse postoperative outcomes which are burdensome for patients, providers, and affect the healthcare system; however, the evidence is sparse. Older adults with aging physiology,[10–13] comorbidities,[1] and polypharmacy[4] are at an increased risk of postsurgical complications during the surgical period. Specific drug classes have the potential to increase this risk in older adults through drug-drug interactions from pharmacodynamics and/or pharmacokinetics of each drug through cytochrome P450 enzyme activation or inhibition.[29] For instance, opioids and psychoactive medications increase the risk of postoperative delirium[30,31] and selective serotonin reuptake inhibitors are associated with surgical bleeding and transfusion.[32–35] Moreover, studies have demonstrated the association between polypharmacy and surgical complications.[10] Postoperative complications found in the literature include delirium,[12,30,36,37] falls,[18,38,39] postoperative infection,[36] and mortality.[40–43] These are more prevalent in emergency surgeries due to their urgency and unavoidable lack of preoperative optimization.[44]

Recent systematic reviews of surgical interventions for older adults have focused on the effect of multi-faceted (physical, cognitive, and psychosocial) interventions on postoperative outcomes.[45,46] However, to our knowledge, there is currently no systematic review exploring the effect of deprescribing during the preoperative period for older adults undergoing surgery. Thus, this review will appraise the evidence for deprescribing interventions during the preoperative period for this population.

METHODS

A systematic review of the literature was conducted adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[47] (Supplementary Data).

Data Sources and Search Strategy

The first author consulted an experienced medical librarian for search terms and strategy design. The following databases from inception to January 12, 2021 were searched: EMBASE, CINAHL, and PUBMED (Table S1).

Eligibility Criteria

Studies involving patients aged 65 and older undergoing elective or emergency surgery with deprescribing or medication-related interventions were included for review. We included any surgery-related settings such as preoperative clinics, hospital admission pre-surgery, and patient-anesthesiologist interaction prior to surgery. Only studies written in English were included. Reviews, guidelines, abstracts, case studies and studies not in English were excluded.

Data Extraction and Synthesis

The first and second authors conducted screening of titles and abstracts of studies obtained through the databases independently using Covidence software, an online collaborative team-based software for systematic reviews. Full text of select studies were assessed

again by two authors for final inclusion. Discrepancies were discussed and resolved. The following information from the final articles that met the inclusion criteria were extracted: publication year, study design, number of participants, participant mean age, country, surgical procedure, form of intervention delivery (i.e., geriatrician, pharmacist, interdisciplinary team), outcomes, and target medication classes.

To explore the effect of deprescribing interventions, results were grouped based on outcomes. Subgroup analyses could not be performed for outcomes due to variable study designs and heterogenous outcomes.

Quality Assessment

The Johns Hopkins Nursing Evidence-Based Practice Appendix E: Research Evidence Appraisal Tool[48] was used for quality assessment (Table 1). Randomized controlled trials (RCTs) were assessed with the Cochrane risk of bias tool[49] and classified as low, medium, or high risk of bias (Table 3). Quasi-experimental studies were assessed with the Robin-I tool and classified as low, moderate, serious, or critical risk of bias (Table 3).[50] Observational studies were assessed with the Newcastle-Ottawa Scale (Table 4).[51] The first author performed the quality assessments of each study independently.

RESULTS

Study Selection

The search resulted in 1905 studies. After removal of duplicates, 1551 studies remained; of these, 1333 studies were excluded during title and abstract screening. In total, 218 full texts were reviewed for inclusion. Finally, 202 studies were excluded and a total of 16 met the inclusion criteria (PRISMA diagram, Supp.2).

Study characteristics

Included studies used the following study designs: RCTs[52,53] (n=2), quasi-experimental studies[54–59] (n=6), and observational studies[60–67] (n=8). Studies were published from 2011[55] to 2020.[66] Sample sizes ranged from n=44[59] to n=495[58] with mean ages ranging from 54 to 83 years. Studies were conducted in: Canada,[66] Germany,[56,62] Iran,[58] Japan,[63] Norway,[53] Saudi Arabia,[60] the Netherlands,[52] UK,[57,61,67] and U.S.[54,55,59,65] Study settings were either preoperative clinics (n=5)[52,55,59,65] or inpatient hospital settings (n=11).[53,54,67,56–58,60–63,66] Study interventions were led by the following parties: geriatricians (n=2),[52,57] interdisciplinary teams (n=7),[53–55,59,62,65,67] and pharmacists (n=6).[56,58,60,61,63,66] Comprehensive geriatric assessments were used for global assessment of participants in four studies.[53,57,64,67] Decision support tools were used for deprescribing in six studies.[28,34,35,39,40,43] Among those, three studies used the START/STOPP criteria for determining PIMs.[28,39,40] Non-operative cases were included in seven studies.[54,57–59,63,64,66] Outcomes observed in studies were related to healthcare utilization,[54,57,62,66,67] patient outcomes,[52–55,61,64,65,67] and medication changes[52,53,66,67,56–63] (Table 2). Two studies[52,64] mentioned involvement of primary care providers; however, this involvement was limited to providing deprescribing recommendations before/after surgery without follow up.

Quality of Studies

Both RCTs demonstrated high risk of bias.[52,53] Quality assessments for quasi-experimental studies showed moderate[54–56,58,60] and serious[57,59] risk of bias. Quality assessment for case-control and cohort studies showed overall quality assessments of mostly good[61–64,66,67] and fair[65] (Table 3 and 4).

Healthcare Utilization

Outcomes related to healthcare utilization in the form of hospital length of stay (LOS) and readmission was reported in seven studies.[54,57,58,61,62,65,67]

Six studies[54,57,61,62,65,67] reported hospital LOS as an outcome. Reduction in mean LOS was reported in five studies[57,61,65–67] though only two studies demonstrated statistically significant reductions.[61,65] For the studies[61,65] that showed statistically significant difference in LOS, deprescribing occurred through a pharmacy service focusing on medication optimization for chronic illness management and perioperative drug management[61] or through an interdisciplinary team focusing specifically on perioperative drug management.[65] Both studies focused on high-risk medications such as anti-platelets,[61] anticoagulants,[61] angiotensinconverting enzyme,[61] and anticholinergics.[65] Both focused on patients undergoing elective surgeries, but for high-risk patients;[61,65] one study[61] had 50% of patients who were considered high-risk and another study[65] included patients with cognitive disorder, recent weight loss, multimorbidity, polypharmacy, and visual or hearing impairment.

Another outcome related to healthcare utilization was readmissions. Readmissions were reported in three studies.[54,65,67] Two studies did not find any statistically significant differences,[54,67] whereas one study found statistically significantly lower 7-day and 30-day readmission rates in the intervention group.[65]

In short, the two studies[61,65] that demonstrated statistically significant improvement in healthcare utilization for the intervention group focused on: 1) high-risk surgical patients with high illness burden and polypharmacy and 2) high-risk medications. Only one of the studies measured outcomes related to both LOS and readmission,[65] which made direct outcome comparison difficult.

Patient Outcomes

Patient outcomes related to quality of life, function, mortality, and postoperative complications were reported in nine studies.[52–55,61,64–67]

Two studies reported outcomes on quality of life and function.[53,55] One study[53] showed no statistically significant difference between groups regarding quality of life or functional measures. Another study[55] showed statistically significantly different functional scores between the intervention versus control group (0.45 versus 2.28, respectively, $p<0.01$).

For mortality, no statistically significant difference was observed, or results were not compared with a control group in four studies that reported mortality as an outcome.[52,54,64,65]

For postoperative complications, no statistically significant difference was observed between intervention and control group, or the control group was absent in four studies thereby limiting significant results.[54,61,66,67] However, one study[65] showed fewer all-type complication rates in the intervention versus control group (44.8% versus 58.7%, respectively, p<0.001); unfortunately, the same study showed higher rates of delirium in the intervention group (28.4% versus 5.6%, respectively, p<0.001).

In summary, the two studies that showed statistically significant difference in postoperative functional outcomes and complication rates between intervention and control groups,[55,65] had several similarities: 1) focus on vulnerable elderly, 2) led by interdisciplinary teams, 3) early intervention of up to 30 days before surgery, and 4) patients undergoing elective surgeries.

Medication Changes

Medication change as an outcome was reported in twelve studies.[52,53,56–63,66,67] Only three studies showed statistically significant difference in medication changes between the intervention and control group;[52,53,62] the results of the remaining studies were not significant. Several similarities are worth noting: 1) two studies focused on orthogeriatric fractures for emergency surgeries,[53,62] 2) two studies used the comprehensive geriatric assessment to identify areas that might require intervention,[52,53] 3) STOPP/START criteria was used in all three studies to identify PIMs.[52,53,62]

DISCUSSION

This systematic review evaluated deprescribing interventions during the preoperative period and their impact on healthcare utilization, postoperative outcomes, and medication changes among older adults undergoing surgery. The interventions were led by geriatricians, interdisciplinary teams, and pharmacists. Overall, there were inconsistencies in outcomes related to healthcare utilization, patient outcomes (i.e., postoperative complications), and medication changes. However, similarities were noted among studies that showed positive results. In general, the majority of studies had the following characteristics: 1) participants who are vulnerable or at-risk older adults 65 and older with multimorbidity, 2) elective cases,[53,55,61,65] 3) intervention through interdisciplinary teams,[53,55,62,65] and 4) intervention delivery during the inpatient period.[53,55,61,62,65] It is important to note though that two studies that encompassed up to 30-day preoperative to hospitalization[55,65] and two studies with emergency cases involving orthogeriatric trauma[53,62] also showed statistically significant findings. Studies that instituted the STOPP/START criteria demonstrated statistically significant findings in medication changes.[52,53,62] These findings underscore the importance of a multifaceted deprescribing approach by an interdisciplinary team for high risk older adults undergoing surgery during hospitalization with a validated guideline for deprescribing such as the STOPP/START criteria.

Deprescribing in Older Adults

Our findings are consistent with results of studies for non-surgical populations reporting the effect of deprescribing interventions on patient outcomes and healthcare utilization. In a

systematic review of deprescribing interventions for community-dwelling older adults,[25] only interventions involving comprehensive medication review demonstrated reduced mortality in the intervention group compared to the control group. There was otherwise no effect on falls, hospitalization, or quality of life. Similarly in two other systematic reviews[27,28] observing the effect of deprescribing interventions on polypharmacy and patient outcomes in older adults in various settings (hospital, primary care, and nursing homes), patient-specific interventions were able to significantly reduce mortality and the number of PIMs in one systematic review;[27] however, had little or no effect on the number of PIMs, hospital admissions, and quality of life in another systematic review.[28] Lastly, in a systematic review of deprescribing interventions for older adults in nursing homes, deprescribing interventions reduced the number of PIMs, falls, and mortality.[26] The follow up of studies in each of the systematic reviews varied and were up to 12 months,[26] 13 months,[28] 24 months,[25] and 48 months.[27]

In summary, deprescribing evidence in general, outside of the perioperative period have shown either positive or neutral results, which is consistent with our review of deprescribing studies during the preoperative period. Limitations of these studies include heterogeneity of outcomes and moderate to low quality of evidence, which is also consistent with studies in our review.

Interventions for Older Adults Undergoing Surgery

To our knowledge, this is the first systematic review to address the effect of preoperative deprescribing interventions on outcomes for older adults undergoing surgery. Our findings are consistent with findings from previous systematic reviews of multi-faceted interventions. A systematic review of geriatric interventions in non-orthopedic older adults undergoing surgery demonstrated clinically meaningful benefits in reduced complication rates, postoperative delirium rates, and hospital LOS; however, there was no impact on readmissions or mortality.[46] These interventions comprised exercise therapy (including prehab), multi-component geriatrics program, and interventions from comprehensive geriatrics assessments. Another systematic review[45] of interventions from comprehensive geriatric assessments showed reduced mortality and institutionalization; however, heterogenous results for LOS and little or no effect on rates of readmissions, complications, and delirium. Additionally, these two systematic reviews[45,68] attributed conflicting results to limitations of heterogeneous outcomes and low quality of evidence, which was also consistent with our review. Though these reviews[45,68] included medication optimization as a component of the interventions during the perioperative period, they did not isolate the effect of deprescribing. The follow up of the studies varied and were up to 3 months[45] in one study and 1 year in another.[46]

Six studies[52,53,55,61,62,65] with the inclusion of vulnerable elderly with multimorbidity and polypharmacy showed statistically significant difference between intervention and control group in the realms healthcare utilization, patient outcomes, and medication changes. The studies that showed positive findings in our review[52,53,55,61,62,65] partially corroborate findings from deprescribing literature involving frail older adults.[69] In a systematic review of deprescribing for frail older adults in community, hospital, residential care settings,[69]

results demonstrated the following: 1) no significant changes in mortality, adverse events, hospitalizations, and quality of life, 2) positive impact on mental/physical function including frailty, 3) mixed results on falls and cognition, and 4) decrease in the number of PIMs. Though direct outcome comparison is difficult due to heterogenous outcomes, the general trend we found was similar. Similar to the systematic review of deprescribing or frail older adults,[69] there were no significant changes in mortality, quality of life and decrease in the number of PIMs. However, studies from our review found positive or neutral results in healthcare utilization (LOS and readmissions), functional scores, and postoperative complications.

Medication classes that were targeted involved: antihypertensives,[52–54,56,58,60–63] thyroid agents,[60] antiepileptics,[53,60] bronchodilators,[56] proton pump inhibitors,[52,56,66] anti-inflammatory,[62,63] antidepressant,[52,58] analgesics,[52,56,62] anticholinergics,[53,62,63,65] statins,[56,58,60,62] and anticoagulants/antiplatelets.[53,54,56,58,60,61,63] Studies that demonstrated statistically significant findings for healthcare utilization, patient outcomes, and medication changes either did not target specific medications[55,61] or targeted the following medications: anticholinergics,[65] antihypertensives,[65] anticoagulants,[65] or medications in the STOPP/START criteria.[52,53,62] Though there were many medications that were targeted quite broadly, three studies[52,53,62] showed positive outcomes targeting PIMs based on validated criteria such as STOPP/START. In general, deprescribing recommendations were generated if there was no one in the team with prescriptive authority (i.e., attendings) who can deprescribe. Surgery type was not related to deprescribing recommendations.

There may be an association between the nature of surgery (i.e., elective versus emergency) and outcomes. Studies that showed positive results were mostly elective surgeries;[52,55,61,65] two studies were emergency orthogeriatric fracture surgeries.[53,62] Due to heterogeneity in different aspects (i.e., study design, intervention delivery) among studies, it is hard to say that the nature of surgery alone influenced outcomes. Three studies[53,54,62] included emergency orthogeriatric fracture surgeries in the inpatient setting delivered by an interdisciplinary team. Two of these studies[53,62] demonstrated statistically significant results in changes in the number of medication changes[53] and reduction of PIMs[62] between the intervention versus the control group.

Research Implications

The current state of evidence for preoperative deprescribing illuminates several areas of future research focus. Understanding the process of shared decision-making in deprescribing for the providers and the older adults during the surgical period may reveal motivations that can be targeted such as the desire to prevent postoperative complications. Studies exploring patient- and provider-related barriers during the surgical period may also help develop targeted interventions. Additionally, as the surgical period involves medication changes due to withholding certain medications preoperatively (i.e., beta blockers and blood thinners) and prescribing during the postoperative period (i.e., opioids), deprescribing in this population may be more challenging than in more stable circumstances such as in primary care. A few studies in this review that included the perioperative spectrum addressed this by focusing on medication optimization of pre-existing medications preoperatively. Finding the

optimal timing, process, and target medications for deprescribing during the surgical period may be warranted.

Our review highlights the process of caring for older adults during the surgical period, which adds to the literature and may guide future interventions. Some studies instituted continuity of care during the preoperative time period of up to 30 days[55,65] and an effort to coordinate care between either the primary care provider[52,64,66] or the surgical team.[55,58–60,62,63] This underlines the importance of coordinated efforts among providers in a more systematic way, which may enhance care of this population and not only elevate but also sustain the effect of deprescribing. These efforts could be enhanced by several measures not limited to but including: 1) integrated electronic medical system (EMR), 2) expansion of pre-existing clinical information exchange such as CRISP (in Maryland and DC) to include medication updates directly from the EMR, 3) deprescribing based on validated criteria such as START/STOPP, or 4) interdisciplinary approach that follows the patient through the perioperative period and promote communication with primary care provider to allow continuity of care. To reduce fragmentation of care, all key players during the surgical period including the primary care provider, specialists, and the surgical team should be involved. Although current deprescribing efforts are limited due to fragmentation of care, the preoperative period where the patient requires clearance from all providers involved may provide the perfect venue for communication. With these foundations in place, the effect of deprescribing may be more powerful and increase policy-level initiatives. Limitation of these studies is the lack of long-term follow up to gauge the effect of deprescribing on longer term outcomes like physical and cognitive functioning. Most study follow up included in this review was limited to the hospitalization period,[52,54,56–58,60–63,66] though some studies had follow up of 30 days[55,65,67] to 4 months[53] postoperatively. Therefore, it is hard to gauge long-term outcomes of deprescribing, especially after surgery. This prompts a call for more research involving long-term outcomes (i.e., more than 24 months) for older adults undergoing surgery who are deprescribed. o, dramatic improvements in outcomes were hard to detect with longstanding chronic illnesses. Having longer-term follow up may allow detection of deprescribing impact more clearly.

Overall, studies demonstrated positive and neutral results, but not negative ones. This demonstrates the lack of harm of deprescribing. For clinician who are wary of deprescribing because of the potential for harm, these results should allay such concerns.

Strengths and Limitations

This review has several limitations and strengths. Bias may have resulted due to only including published findings and those written in English. This review was limited to studies that delivered deprescribing interventions during the preoperative period; deprescribing during the postoperative period or transitions of care may have yielded different findings. The results are limited by heterogenous intervention delivery methods, surgical procedures, study designs, and outcomes. Additionally, studies were generally of low quality. However, strengths include: 1) using the PRISMA diagram to ensure systematic review of the literature on this topic, and 2) report of evidence quality through quality appraisal.

CONCLUSIONS AND IMPLICATIONS

Current evidence for deprescribing interventions during the preoperative period is inconclusive due to conflicting results from heterogeneity of outcomes, inclusion of non-operative cases, and inadequate power. However, this review highlights some take-away points for clinicians and policymakers from studies with positive outcomes. Deprescribing of commonly used medication classes for chronic illnesses and/or PIMs with a validated criteria such as STOPP/START seemed to be easiest to implement. Deprescribing interventions involved perioperative management for medications as well as optimization of chronic illnesses with the intent of making permanent changes although long-term outcomes were not measured. Future deprescribing efforts for older adults undergoing surgery may benefit from: 1) an interdisciplinary approach, 2) coordinating deprescribing efforts with primary care provider from the waiting period for surgery up to after discharge, and 3) using validated deprescribing criteria such as STOPP/START that is easy to implement. It is important to note that results yielded positive and neutral results, not negative ones, which should reassure clinicians to implement deprescribing for older adults during the surgical period. Additionally, policy initiatives such as integrated electronic medical records (EMR) or increased reimbursement of deprescribing efforts for primary care providers and/or hospitals should be pursued to prevent adverse postoperative events among older adults undergoing surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

of deprescribing studies during the preoperative period (n=16)

	Study Design, Level of Evidence[1]	Age (yrs)	Country	Procedure Type				Intervention Setting		Intervention						Target Medication Classes									
				ER	ELC	OGT	UC	Clinic	Inpatient	IDT	PharmD	GERI	EMR/ Tool	UC	Blood	HTN	AC	PPI	AD	AN	NSAID	BRC	STA	AE	Thy
Randomized controlled trials																									
	RCT N=397 •Level I A•	IG=83.4 CG=83.2	Norway	★		★			★	★					★	★			★				★	★	
	RCT, cluster N=65 •Level I A•	IG=77.8 CG=79	The Netherlands		★			★				★	★		★			★	★	★					
Quasi-experimental studies																									
	Quasi-Exp N=69 •Level II A•	Mean 78.8	US		★			★	★	★						★		★	★	★					
	Quasi-Exp N=105 •Level II A•	>65 (49%)	Germany				★		★		★		★		★	★							★	★	★
	Quasi-Exp study N=184 (adults) N=190 (pediatrics) •Level III A•	Adults Mean 52.8	Saudi Arabia	★	★				★		★				★	★	★				★	★	★	★	
	Quasi-Exp N=177 •Level II A•	Mean 80.1	US	★		★			★	★					★	★									
	Quasi-ExP N=447 •Level II A•	Mean 81	UK	★					★			★		★											
	Quasi-Exp N=495 •Level II A•	Mean 60.4	Iran				★		★		★		★		★			★							

	Study Design, Level of Evidence[1]	Age (yrs)	Country	Procedure Type				Intervention Setting		Intervention						Target Medication Classes									
				ER	ELC	OGT	UC	Clinic	Inpatient	IDT	PharmD	GERI	EMR/ Tool	UC	Blood	HTN	AC	PPI	AD	AN	NSAID	BRC	STA	AE	Thy
	Quasi-Exp N=44 •Level II A•	Mean 71.5	US				★	★		★			★			★		★		★			★		
Observational studies																									
	Cohort study N=300 •Level III A•	Mean 81.5	UK	★	★				★	★				★											
	Cohort study N=48 •Level III A•	Mean 71.9	US		★			★		★				★											
	Case-control N=183 •Level III A•	IG=75.6 CG=71.9	US		★			★	★	★							★								
	Cohort study N=246 •Level III A•	≥60 (83.3 %)	UK		★				★		★				★	★									
	Cohort study N=95 •Level III A•	IG=83.39 CG=81.54	Germany	★		★			★	★						★	★			★	★		★		
	Cohort study N=230 •Level III A•	Mean 75.4	Japan				★		★		★				★	★	★				★				
	Cohort study N=470 •Level III A•	Mean 78.6	Canada				★		★		★		★		★	★	★	★						★	

dence assessed with Johns Hopkins Nursing Evidence Appraisal Tool (Appendix E)

† Procedure Type: **ER**- Emergency, **ELC**- Elective, **OGT**- Orthogeriatric Trauma, **UC**- Unclear

† Intervention: **IDT**- interdisciplinary team, **GERI**- Geriatrician

† Target Medication Classes: **UC**- Unclear, **Blood**- Blood thinners (anticoagulants/antiplatelets), **Htn**- Antihypertensive, **AC**- Anticholinergics, **PPI**- Proton Pump Inhibitors, **AD**- Antidepressants, **AN**- Analgesics, **NSAID**- Anti-inflammatories, **BRC**- Bronchodilators, **STA**- Statins, **AE**- Antiepileptics, **Thy**- Thyroid agents

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Table 2.

Summary of outcomes (n=16)

Author, year	Healthcare Utilization	Patient Outcomes	Medication Changes
Cronin, 2011		Vulnerable Elder Survey score decreased significantly in the postintervention group compared to the preintervention group (0.45 versus 2.28, p<0.01).	
Hohn, 2014			Among pharmacists' recommendations for medication change, 75% were implemented by the physician.
Al-Jazairi, 2017			Pharmacy residents made 260 recommendations and 200 (76.92%) were accepted.
Heltne, 2017		No significant difference between the two groups regarding all other QoL or functional measures.	• Proportion of polypharmacy in the interventiongroup at admission changed from 32.8% to 84.3% at discharge • Proportion of polypharmacy in the control group atadmission changed from 39.7% to 70.6% at discharge • However, 209 withdrawals of pre-existing meds in the intervention group and 82 med withdrawals in control group noted (p<0.0001). • Anticholinergic burden did not show statistically significant difference between the two groups. • Intervention group compared to control group used significantly fewer analgesics (0.0001), anxiolytics (p=0.0001), and hypnotic and sedative drugs (p=0.0015) at discharge.
Vilches-Moraga, 2017	• Mean LOS reduced from 14.6 to 12.5 days for post-intervention group. • No group differences between pre- and post-intervention groups in 30-day readmission rates.	26% developed postoperative delirium, 32.6% acute kidney injury, and 37% constipation.	Significant reduction in meds at discharge (7.6 versus 6.4).
Cortez, 2018	Readmission (1.3% vs 0%) and LOS (6.58±8.0 vs 5.03±3.8) was higher in the pre- versus post-intervention group but not statistically significant.	Higher complication rates (22.5% vs 15.6%), mortality (7.5% vs 6.5%) for postintervention group versus preintervention group, but not statistically significant.	
Lin, 2018		Overall survival rate was 9% for 100 days and 78% at 1-year follow up.	
Mason, 2018	Mean LOS was reduced by 0.55 bed days.		Medication stopped in 40% of cases and started in 28% of cases.
McDonald, 2018	• Shorter median LOS for intervention versus control group (4 days vs 6 days; P < .001). • Lower readmission rates for the intervention group at 7 days (2.8% vs 9.9%; p=0.001) and 30 days (7.8% vs 18.3%; p=0.001).	Fewer all-type complication rates in the intervention group versus control group (44.8% vs 58.7%; p<0.001) and no statistically significant different in mortality rates; however, higher rates of delirium (28.4% vs 5.6%; p<0.001).	
Bansal, 2019	Significant reduction in median LOS in: hepatobiliary (−4.5; IQR: −7,−1; p=0.001), vascular (−2; IQR: −4, 0; p=0.043), and lower GI (−2, IQR: −4, 1.8; p=0.038)	• 48% experienced complications postop (22.2% with postop nausea, 18.2% with infection, 9.1% with cardiac issues,1.5% death, and 6.5% delirium before discharge)	420 interventions by pharmacists and 44.3% related to medication optimization and 55.7% related to perioperative management.

Author, year	Healthcare Utilization	Patient Outcomes	Medication Changes
Boersma, 2019		3-month mortality did not differ significantly between groups.	• More medication changes were implemented in the intervention group versus control group (PIMs 46.2% *vs* 15.3%, *P* < .005). • Most frequently recommended medications for change were: vitamin D, ACE-I, statins, PPIs, benzodiazepines, analgesics, and antiplatelet drugs.
Gleich, 2019	Mean LOS was not statistically significantly different between groups.		• 85.4% with PIMs in the control group and 22.2% with PIMs in the intervention group (p<0.001). • No adjustments in the control group, but 48.1% of medications adjusted in the intervention group by the geriatrician.
Kimura, 2019			• PIMs defined by STOPP-J were 232 and 61 (26%) were recommended for modification by a physician and 82% were accepted, while 50 (22%) were discontinued by the pharmacist. • PIMs defined by STOPP version 2 were 133 and 61(46%) were recommended for modification by a physician and 89% were accepted, while 54 (41%) were changed by the pharmacists.
Shafiekhani, 2019	Mean LOS for patients with drug-drug interactions was 7.00 ± 4.00 days and those without drug-drug interactions was 5.80 ± 2.20 days (p<0.001)		• 62% of the intervention for medication change was accepted by physicians. • 7.5% drug interactions were prevented due to intervention.
Zulig, 2019			Referral generated to pharmacy in 89% of cases, 26% received services.
Mehta, 2020		Non-naïve users: 2.9% developed C difficile infection Naïve users: 1% developed C difficile infection	Non-naïve users: Overall deprescribing rate was 10% (general surgery was 4% and orthopedic surgery was 7%). Naïve users: Overall deprescribing rate was 26% (general surgery was 50% and orthopedic surgery was 0%).

Table 3.

Quality of assessment of RCTs with Cochrane risk of bias tool (n=2) and quasi-experimental studies with Robin-I tool (n=7)

Randomized Controlled Trials (n=2)							
Author, year	**Sequence Generation**	**Allocation Concealment**	**Participant Blinding**	**Assessor blinding**	**Incomplete outcome data**	**Selective reporting**	**Other bias**
Boersma, 2019	L	H	H	L	H	L	L
Heltne, 2017	L	H	H	H	L	L	L

Quasi-experimental Studies (n=7)								
Author, Year	**Confounding**	**Selection**	**Classification**	**Deviation from intervention**	**Missing data**	**Measurement of outcomes**	**Selection of outcomes**	**Overall**
Al-Jazairi, 2017	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Cortez, 2018	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Cronin, 2011	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Hohn, 2014	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Mason, 2018	Serious	Moderate	Moderate	Moderate	Moderate	Serious	Moderate	Serious
Shafiekhani, 2019	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Zullig, 2019	Serious	Moderate	Moderate	Moderate	Moderate	Serious	Serious	Serious

L= low risk of bias, H= high risk of bias, U = unclear risk of bias

Table 4.

Quality assessment of case-control study (n=1) and cohort studies (n=6) with the Newcastle-Ottawa scale

Case-Control (n=1)		**Author, Year**
Criteria		McDonald, 2018
Selection	Is the case definition adequate?	★
	Representativeness of the cases	★
	Selection of controls	NA
	Definition of controls	NA
Comparability	Comparability of cases based on design or analysis	NA
Exposure	Ascertainment of exposure	★
	Same method of ascertainment for cases and controls	★
	Non-response rate	NA
Overall quality	Total number of stars (0–10)	4

Cohort (n=6)		**Author, Year**					
Criteria		Bansal, 2019	Gleich, 2019	Kimura, 2019	Lin, 2018	Mehta, 2020	Vilches-Moraga, 2017
Selection	Representativeness of the exposed cohort	★	★	★	★	★	★
	Selection of the nonexposed cohort	NA	★	★	★	NA	★
	Ascertainment of exposure	★	★	★	★	★	★
	Demonstration that outcome of interest was not present at the start of the study	★	★	★	★	★	★
Comparability	Comparability of cohort based on design or analysis	NA	★	NA	NA	NA	★
Outcome	Assessment of outcome	★	★	★	★	★	★
	Was follow-up long enough for outcomes to occur	★	★	★	★	★	★
	Adequacy of follow-up of cohorts	NA	NA	NA	NA	NA	NA
Overall quality	Total number of stars (0–13)	5	7	6	6	5	7