#### SYSTEMATIC REVIEW



# Prevalence of and Risk Factors for Drug-Related Readmissions in Older Adults: A Systematic Review and Meta-Analysis

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#### Abstract

**Background** Older adults are at an increased risk of drug-related problems, especially following discharge from hospital. Drug-related readmissions place a large burden on the patient and the healthcare system. However, previous studies report inconsistent results on the prevalence and associated risk factors for drug-related hospital readmissions in older adults.

**Objectives** We aimed to assess the prevalence of drug-related readmissions in older adults aged 65 years and older and investigate the drug classes, preventability and risk factors most associated with these readmissions.

**Methods** A systematic review and meta-analysis were undertaken to answer our objectives. A search of four databases (MEDLINE, Embase, CINAHL and Scopus) was conducted. Three authors independently performed title and abstract screening, full-text screening and data extraction of all included studies. A meta-analysis was conducted to calculate the pooled prevalence of drug-related readmissions across all studies, and a subgroup analysis was performed to explore heterogeneity among studies reporting on adverse drug reaction-related readmissions.

**Results** A total of 1978 studies were identified in the initial search, of which four studies were included in the final synthesis. Three studies focused on readmissions due to adverse drug reactions and one study focused on readmissions due to drug-related problems. A pooled prevalence of 9% (95% confidence interval 2–18) was found for drug-related readmissions across all studies, and a pooled prevalence of 6% (95% confidence interval 4–10) was found for adverse drug reaction-related readmissions. Three studies explored the preventability of readmissions and 15.4–22.2% of cases were deemed preventable. The drug classes most associated with adverse drug reaction readmissions included anticoagulants, antibiotics, psychotropics and chemotherapy agents. Polypharmacy (the use of five or more medications) and several comorbidities such as cancer, liver disease, ischaemic heart disease and peptic ulcer disease were identified as risk factors for drug-related readmissions. **Conclusions** Almost one in ten older adults discharged from hospital experienced a drug-related hospital readmission, with one fifth of these deemed preventable. Several comorbidities and the use of polypharmacy and high-risk drugs were identified as prominent risk factors for readmission. Further research is needed to explore possible causes of drug-related readmissions in older adults for a more guided approach to the development of effective medication management interventions.

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# **1** Introduction

Older adults are at an increased risk of experiencing drugrelated problems (DRPs), owing to a high prevalence of multimorbidity and subsequent polypharmacy [1–5]. Up to 45% of community-dwelling older adults live with polypharmacy [6], with several studies highlighting the high prevalence of DRPs in this population [7, 8]. Drug-related problems include adverse drug events (ADEs), adverse drug reactions (ADRs), medication errors (MEs), potentially inappropriate prescribing and drug interactions, which are associated with adverse health outcomes [9, 10].

Drug-related readmissions are a significant adverse outcome for patients discharged from hospital, where newly initiated medications and changes in medication regimes are

#### **Key Points**

This review found 9% of older adults discharged from hospital experience a drug-related readmission with up to 22% of these being preventable.

Polypharmacy and several high-risk drug classes including anticoagulants, antibiotics, psychotropic and chemotherapy agents were associated with an increased risk of readmission.

Further research into targeted interventions to reduce potentially preventable drug-related problems in at-risk older adults is needed.

common. Past reviews suggest that the rate of MEs occurring after discharge is up to 53% and almost 20% of patients are affected by ADEs [11]. Reoccurring admissions due to DRPs can impact patient safety and place a large financial burden on both the patient and healthcare system, highlighting the need to understand the prevalence and nature of drug-related readmissions. Although the prevalence of drug-related admissions has been studied previously [12–14], few studies have focused on drug-related readmissions, with existing studies reporting largely variable results. Past reviews have found that the prevalence of drug-related readmissions in the general adult population has ranged from 0.09 to 64% [15, 16]. Further, the characteristics and risk factors associated with drug-related readmissions are understudied [15, 16]. An understanding of these factors is necessary to inform the implementation of effective policy and clinical interventions to improve patient care, decrease medication-associated harms and reduce healthcare costs [17, 18].

The inconsistency in results from prior research highlights the need for an updated review on the prevalence of drug-related readmissions, with a particular focus on older adults. Thus, this systematic review and meta-analysis primarily aim to assess the prevalence of drug-related readmissions in older adults. Secondary objectives that will be investigated include the preventability, implicated drug classes and potential risk factors associated with drugrelated hospital readmissions in older adults.

# 2 Method

A systematic review was conducted on the prevalence of and risk factors for drug-related readmissions in older adults in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines. "Drugrelated" is a broad term that encompasses ADRs, ADEs and MEs (Table 1). For this review, any study that reported on a drug-related problem that resulted in a hospital readmission was included in the screening process. This systematic review was registered in PROSPERO (CRD42023409005).

# 2.1 Inclusion and Exclusion Criteria

Studies were included in this review if they were published peer-reviewed articles from January 2013 to April 2023 (to ensure recency and relevancy of included studies); that examined drug-related readmissions in participants aged 65 years and over; and contained data that could allow for the calculation of prevalence such as the number of participants, all-cause readmissions and drug-related readmissions. Studies were excluded if they focused on drug-related issues such as drug abuse, intentional overdose or any illicit drug use; were case reports, case series or qualitative studies where calculating prevalence was difficult; or were studies not available in the English language.

#### 2.2 Search Strategy

To identify relevant studies for the review, a search of MED-LINE, Embase, CINAHL, and Scopus was conducted. A search strategy was developed based on three key searchable concepts including 'DRPs', 'readmissions' and 'older adults'

 Table 1 Definitions of key terms associated with drug-related harms

Term	Definition
DRPs	"an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes." [19]
ADEs	"An injury resulting from the use of a drug. Under this definition, the term ADE includes harm caused by the drug (adverse drug reac- tions and overdoses) and harm from the use of the drug (including dose reductions and discontinuations of drug therapy)." [20]
ADRs	"Response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function." [20]
MEs	"Errors in the process of prescribing, dispensing, or administering the medications that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer" [15, 21, 22]

ADEs adverse drug events, ADRs adverse drug reactions, DRPs drug-related problems, MEs medication errors

(see Tables 1–4 of the Electronic Supplementary Material [ESM]). The studies were collated in Endnote (EndNote 20; Clarivate, Philadelphia, PA, USA) and uploaded to Covidence (Veritas Health Innovation, Melbourne, VIC, Australia), where title and abstract screening was conducted by three independent reviewers (NP, EL, IW) as per the inclusion and exclusion criteria. Any conflicts regarding inclusion and exclusion were resolved by discussion among all reviewers. Three independent reviewers (NP, EL, IW) conducted full-text screening of the remaining studies to determine the final eligible studies for the review. Conflict regarding inclusion of studies was resolved by discussion between all authors.

# 2.3 Data Extraction and Quality Assessment

Data extraction was done independently by three reviewers (NP, EL, IW). Extracted data included the author, country, study design, setting, sample size, mean age, definition of DRP, type of DRP that resulted in readmission, number of drug-related readmissions, total number of readmissions, drug classes, clinical presentations, preventability, reported risk factors and method of causality assessment. Risk factors associated with drug-related readmissions were extracted and presented adjusted odds ratios or hazard ratios (HRs) with 95% confidence intervals, as reported by the study. Quality assessment of included studies was conducted independently by two authors (NP, EL) based on the checklist for prevalence studies developed by The Joanna Briggs Institute. Any discrepancies were resolved by discussion with all authors.

#### 2.4 Statistical Analysis

The prevalence of drug-related readmissions was calculated by the number of drug-related readmissions divided by the total number of participants in the study. Only statistically significant findings were included where a 95% confidence interval that did not include the null value of 1 was considered statistically significant. Preventability was calculated as the number of drug-related readmissions deemed preventable divided by the number of drug-related readmissions. A meta-analysis was conducted using Meta-XL 5.3 (http:// www.epigear.com) to calculate the pooled prevalence of drug-related readmissions across all studies, and  $I^2$  statistics were used to assess degree of heterogeneity. Subgroup analyses were performed to examine heterogeneity between studies involving ADR-related readmissions in terms of study design, sample size, study objective, setting, causality assessment, identification method and time to readmission.

#### **3 Results**

#### 3.1 Study Selection

The initial screening process identified 1978 studies that was narrowed down to 1668 studies after de-duplication as shown in Fig. 1. Following title and abstract screening, 58 studies were eligible for full-text review and six studies were selected to be included in the paper. The authors of two papers were contacted for further details to allow for the calculation of drug-related readmissions specifically in the older population; however, they did not respond, leaving four studies that were included in the final review.

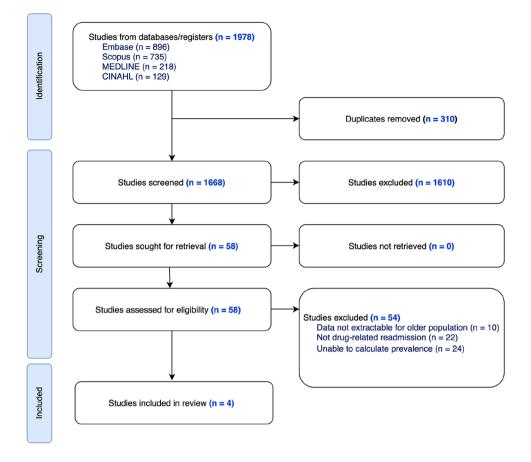
#### 3.2 Characteristics of Studies

A total of four studies [23-26] were included in the review including two prospective cohort studies [25, 26], one retrospective cohort study [23] and one post-hoc analysis of a randomised controlled trial [24]. The studies were conducted across Sweden [24, 25], France [23] and the UK [26], and were based in general (n = 2) or teaching hospitals (n = 2). The cohort sizes ranged from 390 to 2637 participants and the mean age ranged from 77 to 86 years. The time between index admission and readmission varied between 30 days and 1 year. Three studies focused on ADR-related readmissions [23, 25, 26] and one study focused on DRP-related readmissions [24]. No studies were found that focused on MEs or ADEs. Two studies identified drug-related readmissions using clinical judgement including the assessment of individual cases by senior clinicians [25] as well as senior geriatricians, senior pharmacists and senior researchers [26]. Two studies identified drug-related readmissions using International Classification of Disease, Tenth Revision (ICD-10) codes to identify the initial hospital admissions. Hospital readmissions were identified using either ICD-10 codes related to ADRs [23] or a review of all cases by an expert panel [24] (Table 2).

### 3.3 Prevalence

Data extracted from all four studies [23-26] were used to calculate prevalence rates. Three studies [23, 25, 26] focused on ADRs while one study [24] focused on DRPs. The study design also differed in each subgroup where the studies focusing on ADRs were cohort studies and the study focusing on DRPs was a post-hoc analysis of a randomised controlled trial. The total calculated pooled prevalence across the four studies was 9% (95% CI 2–18) with an  $I^2$  value

Fig. 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) diagram outlining the selection of studies for the review



of 99% suggesting considerable heterogeneity (Fig. 2). The calculated pooled prevalence of the ADR subgroup was 6% (95% CI 4–10) with an  $I^2$  value of 87% highlighting considerable heterogeneity between the studies.

## 3.4 Subgroup Analysis

A subgroup analysis was performed on the ADR subgroup [23, 25, 26] to identify possible sources of heterogeneity, as shown in Table 3. Prospective studies presented a lower readmission rate compared with retrospective studies, and non-teaching hospitals had a lower readmission rate compared with teaching hospitals. The use of a published method of assessing causality (Naranjo) and identifying cases (ICD codes) also resulted in a lower readmission rate.

# 3.5 Risk Factors

Two studies [23, 24] explored risk factors associated with DRP-related readmissions using multivariate logistic regression as shown in Table 4. Neoplasm (odds ratio 7.69, 95% CI 4.59–12.88) was identified as the only statistically

significant risk factor for ADR-related readmissions [23]. One study [24] found several comorbidities that increased the risk of DRP-related readmissions. Liver disease (HR 2.46, 95% CI 1.15–5.24), peptic ulcer disease (HR 1.86, 95% CI 1.10-3.14) and ischaemic heart disease (HR 2.06, 95% CI 1.32–3.21) were the conditions with the highest risk of DRP-related readmissions. Patients taking five or more medications were also found to be more likely to be readmitted than those taking fewer than five medications (HR 1.45, 95% CI 1.06-1.98), and the risk increased for patients taking ten or more medications (HR 1.69, 95% CI 1.22–2.32). Dementia (HR 0.55, 95% CI 0.39–0.78), urinary tract infections (HR 0.60, 95% CI 0.39-0.92) and injuries, intoxications and certain other complications or external factors (HR 0.50, 95% CI 0.31-0.83) were identified as protective factors for DRP-related readmissions.

## 3.6 Drug Classes

Two studies [23, 25] identified drug classes and specific medications that were associated with drug-related readmissions as shown in Table 5. The most implicated

		<b>Iddie z</b> Characteristics of included studies $(n = 4)$	(n = 4)									
Author, year	Country	Country Study design	Setting (num- ber of beds)	Sex (%)	Sex (%) Mean age (years)	Time to readmis- sion	Definition of "drug- related"	No. of partici- pants	Total no. of all-cause read- missions	No. of drug-related readmissions	Causality	Identification method
Ekerstad et al., Sweden Prospective 2017 cohort	Sweden	Prospective cohort	2 Tertiary hos- F ( pitals (610 beds)	F (57)	85.7 (SD: 5.1) 30 days	30 days	ADR	390	96	13 (3.3)	Naranjo	Clinical judge- ment
Hauviller et al., 2016	France	France Retrospective cohort	1 Teaching hospital (6880 beds)	F (51.5)	(51.5) 77.6 (SD: 7.4) 1 year	1 year	ADR	1000	553	87 (8.7)	Not assessed	ICD-10
Kempen et al., Sweden Post-hoc 2022 analysis an RCT	Sweden	Post-hoc analysis of an RCT	4 Tertiary hospitals	F (51)	81 (IQR: 74–87)	1 year	DRP	2637	Not reported	582 (22.1)	AT-HARM10 ICD-10	ICD-10
Parekh et al., 2018	UK	Prospective cohort	5 Teaching hospitals	F (58)	82 (IQR: 75.5-86.9)	8 weeks	ADR	1116	Not reported	87 (7.8)	Naranjo	Clinical judge- ment
<i>ADR</i> adverse dı Disease, <i>IQR</i> in	rug reactio terquartile	n, <i>AT-HARM10</i> , strande, <i>RCT</i> rand	ADR adverse drug reaction, AT-HARM10 Assessment tool for hospital admissions related to medications, 10 questions, DRP drug-related problem, F female, ICD International Classification of Disease, IQR interquartile range, RCT randomised controlled trial, SD standard deviation	or hospital 1 trial, <i>SD</i>	l admissions relations standard deviation	ted to medic	cations, 10 que	stions, DRP	drug-related prob	lem, F female, I	CD Internationa	l Classification of

drug classes identified include anticoagulants (13.8% and 15.6%), psychotropics (6.9% and 23.1%) and antibiotics (4.6% and 7.7%). One study [23] noted a large representation of chemotherapy agents that caused drug-related readmissions. Specific agents were not mentioned; however, common clinical presentations included aplasia, agranulocytosis, polyneuropathy and osteoporosis. Both studies identified anticoagulants, antibiotics and antipsychotics as prominent causes of drug-related readmissions. Anticoagulants were associated with clinical presentations such as gastrointestinal bleeding, abdominal pain, haematoma, anaemia and epistaxis. Implicated drugs included warfarin, fluindione, standard heparin and enoxaparin. The presentations associated with antibiotics were predominantly fever, diarrhoea and dyspnoea and the implicated medications varied including clindamycin, cotrimoxazole, norfloxacin, ceftazidime and linezolid. The implicated psychotropics were antidepressants, antiepileptic agents and antiparkinson medications. Some clinical presentations identified were constipation and falls, and the implicated medications varied across all classes.

# 3.7 Preventability

The preventability of drug-related readmissions was explored by three studies [23-25] and ranged from 15.4 to 22.2%. Two studies [24, 25] used the Hallas criteria [27] to determine the preventability of readmissions where cases classified as 'definitely avoidable' by the scale were considered preventable. Along with the Hallas criteria, one study [24] used the Helper criteria proposed by Howard et al. [28] to determine preventability. One study [23] used Olivier's scale [29] as the method of determining preventability. Further analysis by the definition of readmission shows that 22.2% and 15.4% of cases were considered preventable for ADR-related readmission, respectively [23, 25], and 21.3% of DRP-related readmissions were considered preventable. One study [24] identified the cause of potentially preventable readmissions in the study as inadequate treatment (undertreatment, low dose or lack of treatment, wrong or inappropriate treatment), lack of monitoring or follow-up, and lack of investigations or diagnostics.

#### 3.8 Quality Assessment

The quality assessment conducted using the Joanna Briggs Institute checklist for prevalence studies presented a mean score of 8.75/9. All studies scored full marks, except one study where a low response rate was not explained by the authors [25]. See Table 5 of the ESM for more detail.

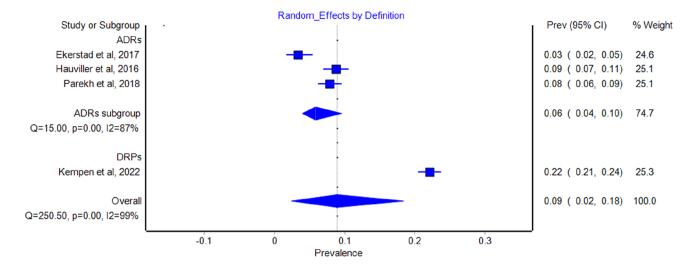


Fig. 2 Forest plot showing the prevalence of drug-related readmissions in older adults across all studies and based on the definition of drug-related readmissions including adverse drug reactions (ADRs) and drug-related problems (DRPs). CI confidence interval

 Table 3
 Prevalence of adverse drug reaction-related readmission by subgroups

Subgroup	Studies (n)	% Readmission (95% CI)	$I^2$
Study design			
Retrospective	1	9 (7.0–10.5)	_
Prospective	2	5.4 (1.6–10.3)	91
Sample size			
< 1000	1	3.3 (1.8–5.4)	_
$\geq 1000$	2	8.1 (7.1–9.4)	0
Setting			
Non-teaching hospital	1	3.3 (1.8–5.4)	_
Teaching hospital	2	8.1 (7.1–9.4)	0
Causality assessment			
Naranjo	2	5.4 (1.6–10.3)	91
Nil (reviewed ICD)	1	8.6 (7.0–10.5)	_
Identification method			
ICD coding	1	8.6 (7.0–10.5)	_
Independent assessment	2	5.4 (1.6–10.3)	91
Days to readmission			
$\leq 2$ months	2	5.4 (1.6–10.3)	91
> 2 months	1	8.6 (7.0–10.5)	_

CI confidence interval, ICD International Classification of Diseases

# 4 Discussion

This systematic review and meta-analysis found the pooled prevalence of drug-related readmissions in older people was 9%, with a range from 3.3 to 22.2%, while the prevalence of ADR-related readmissions in older people was 6%, with a range from 3.3 to 8.7%. Overall, 15–22% of drug-related

readmissions were deemed to be preventable. Several risk factors associated with an increased risk of readmission were identified including comorbidities such as cancer, liver disease, peptic ulcer disease and ischaemic heart disease, polypharmacy and specific drug classes including antibiotics, anticoagulants, psychotropics and chemotherapy agents.

A total pooled prevalence of almost one in ten was found for drug-related readmissions, and importantly, a significant proportion of cases were deemed preventable. Importantly, 15–22% of cases were deemed preventable. Past reviews focusing on the entire adult population reveal a large variation in the prevalence of drug-related readmissions, with ranges from 3 to 64% and from 0.09 to 64%, respectively [15, 16]. One systematic review found a median prevalence of 21% (interquartile range 14-23) for drug-related readmissions, which is higher that the prevalence determined by this study. Although the preventability of drug-related readmissions has not been extensively studied, a systematic review [15] found a preventability rate of 69% in DRP-related readmissions, which is higher than the prevalence rate found in this study. Because of significant heterogeneity between studies including variations in target populations and methods of calculating prevalence, it is difficult to compare the prevalence found in this review to past studies. However, it must be noted that a large variation in study designs does not allow for an accurate prevalence rate to be calculated. Despite these differences, it is evident that a significant proportion of older adults experience preventable drug-related hospital readmissions. Exploring risk factors associated with drug-related readmissions can provide insight into

Table 4	Risk factors	associated	with	drug-related	readmissions	(n = 2)	2)
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Study	Risk factor	OR/HR (95% CI)
Hauviller et al., 2016 <sup>a</sup>	Neoplasm	OR 7.69 (4.59–12.88)
Kempen et al., 2022 <sup>b</sup>	Diabetes mellitus	HR 1.25 (1.03-1.52)
	Atrial fibrillation	HR 1.42 (1.18–1.71)
	Heart failure	HR 1.48 (1.21-1.81
	COPD	HR 1.27 (1.01-1.60)
	Peptic ulcer disease	HR 1.86 (1.10-3.14)
	Liver disease	HR 2.46 (1.15-5.24)
	Charlson Comorbidity Index score	HR 2.46 (1.15-5.24)
	Medications 5–9	HR 1.45 (1.06–1.98)
	Medications $\geq 10$	HR 1.69 (1.22-2.32)
	Previous hospital admissions $(\geq 1)$	HR 1.45 (1.21-1.73)
	Previous ED visits (≥1)	HR 1.22 (1.03-1.45)
	Ischaemic heart disease	HR 2.06 (1.32-3.21)
	Dementia	HR 0.55 (0.39-0.78)
	Urinary tract infections	HR 0.60 (0.39-0.92)
	Injuries, intoxications and certain other complications or external factors	HR 0.50 (0.31–0.83)

CI confidence interval, COPD chronic obstructive pulmonary disorder, ED emergency department, HR hazard ratio, OR odds ratio

<sup>a</sup>Adjusted for age, sex, delay of first hospitalisation, Charlson Comorbidity Index, diabetes, mild liver disease, peripheral vascular disease, congestive heart failure, kidney disease, metastatic cancer, lung disease, stroke, dementia, paraplegia, connective tissue damage, diabetes with end organ damage, acute myocardial infarction, peptic ulcer disease, moderate or severe liver disease and AIDS

<sup>b</sup>Adjusted for all other variables listed in the table

Drug class	Study	No. of cases (% of total drug-related readmis- sions)	ADR-related readmission cause/ clinical presentation (number of cases)	Implicated medications (number of cases)
Anticoagulants	Ekerstad et al., 2017	2 (15.4)	GI bleeding (1), abdominal pain (1)	Warfarin (2)
	Hauviller et al., 2016	12 (13.8)	GI bleeding (10), hematoma (3), anaemia (2), epistaxis (1)	Fluindione (4), heparin (4), enoxa- parin (3), warfarin (1)
Antibiotics	Ekerstad et al., 2017	1 (7.7)	Fever and diarrhoea (1), diar- rhoea (1), dyspnoea (2)	Clindamycin (1)
	Hauviller et al., 2016	4 (4.6)	-	Cotrimoxazole (1), norfloxacin (1), ceftazidime (1), linezolid (1)
Psychotropics	Ekerstad et al., 2017	3 (23.1)	Constipation (1), fall (2)	Citalopram (1), carbamazepine (1), duloxetine (1)
	Hauviller et al., 2016	6 (6.9)	-	Valproate sodium (1), bromazepam (1), tramadol (1), loxapine (1), benserazide (1), levodopa (1)
Chemotherapy agents	Hauviller et al., 2016	69 (79.3)	Aplasia, agranulocytosis, poly- neuropathy, osteoporosis	-

<b>Iddle 5</b> Most implicated drug classes associated with ADR-related readmissions ( $n =$	Table 5	rug classes associated with ADR-related readmissions $(n = 2)$
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ADR adverse drug reaction, GI gastrointestinal

certain populations groups at a greater risk of readmissions than others to allow for targeted interventions to be implemented.

Several comorbidities were found to be associated with an increased risk of drug-related readmissions. Cancer

was found to increase the risk of readmission for ADRrelated cases [23]. Chemotherapy agents are known to be associated with a high level of toxicity and ADRs. Agerelated physiological changes, multiple comorbidities and drug-drug interactions may further increase the risk of experiencing an ADR, thus the increased risk of readmission is not an unexpected finding [30]. However, multiple comorbidities were linked to DRP-related readmissions with liver disease presenting the highest risk [24, 31]. Older adults suffer from a poorer prognosis of liver conditions because of age-related changes in liver cells [32]. An increased risk of hepatotoxicity from the use of drugs predominantly metabolised by the liver can explain the increased risk of DRPs. Furthermore, changes in pharmacotherapy to account for decreased metabolic ability of the liver can increase the risk of ADEs. Interestingly dementia, urinary tract infections and injuries, intoxications and certain other complications or external factors were identified as protective factors. However, this may be because of dementia being classified as "caused by the progression of the disease" rather than as a DRP. Other protective factors identified are relatively unrelated to pharmacotherapy compared with other identified comorbidities [24]. These protective factors may act as a confounder or possibly compete with the risk of readmissions where patients readmitted for these causes are less likely to have the opportunity for a drug-related readmission. A systematic review has identified the Charlson Comorbidity Index score as a prominent risk factor of drug-related readmissions, although specific conditions were not explored further. Conflicting results have been found in past papers regarding age and sex; however, this review found no association between these factors and readmissions [15].

Use of high-risk medications, often to treat comorbidities such as those identified in this review, has also been associated with an increased risk of readmission. Anticoagulants, antibiotics, psychotropics and chemotherapy agents were the most common drug classes identified by this review [23, 25]. Past reviews identified these drug classes as risk factors in past reviews along with other drug classes such as opioids, antihypertensives, diuretics and corticosteroids. In particular, anticoagulants were found to be most associated with preventable drug-related readmissions [15, 16]. These drug classes align with the APINCHS [33] (Antimicrobials, Potassium, Insulin, Narcotics and other sedatives, Chemotherapeutic agents, Heparin and other anticoagulants and Systems) acronym classifying high-risk medications [34]. In particular, anticoagulant and psychotropic use is often seen in longer term care of older patients, increasing the likelihood of ADEs [34–36]. Gastrointestinal bleeds and falls were the most common clinical presentations identified in this review, which are potentially preventable ADRs of anticoagulants and psychotropics.

Along with specific medication classes, taking an increasing number of medications was linked to an increased risk of readmission. Polypharmacy is a well-established issue, particularly in the older population, which is associated with an increased risk of medication regimen complexity, ADEs, MEs and drug–drug interactions, which can lead to an increased burden on individual health and the healthcare system [37]. Importantly, DRPs that can occur from polypharmacy can be prevented through rational prescribing and deprescribing initiatives [38–40].

Risk factors including the use of high-risk medications and polypharmacy can be managed through the implementation of targeted interventions addressing these issues. One study [24] suggests the causes of potentially preventable readmissions were inadequate treatment (undertreatment, low dose or a lack of treatment, wrong or inappropriate treatment), a lack of monitoring or follow-up and a lack of investigations or diagnostics. Past studies suggest that communication issues and a lack of medication management are barriers to effective transitions in care that can possibly increase the risk of hospitalisation [41–43]. Pharmacist-led interventions during hospital stay, discharge and post-discharge may reduce potentially inappropriate medication use and ADEs. Interventions that have been studied in the past include improved discharge planning, medication reconciliation and patient education, a medication care plan on discharge and follow-up monitoring by a pharmacist [44–47].

#### 4.1 Strengths and Limitations

This review had several strengths, particularly the extensive search strategy and extraction of data. The extensive search strategy included multiple databases that minimised the chances of relevant studies being missed by the search. The screening and extraction process involved three independent reviewers that minimised the risk of bias. However, there were some limitations in this review. The heterogeneity between the studies included in the review and the number of studies included suggests the calculated prevalence should be interpreted with caution. The search was limited to the English language and excluded unpublished articles, which increased the likelihood of excluding relevant studies. Some studies did not report on the risk factors and/or drug classes associated with drug-related readmissions, which may have led to underestimation or underreporting of information. The studies included in the review present data from European countries and therefore the results from this study may not be generalisable to healthcare systems in other countries. Furthermore, ICD-10 codes were used by a few studies to identify cases of drug-related readmissions; however, this method of identification has limited sensitivity and specificity, which may have missed eligible cases in the identification process [48].

# 4.2 Implications for Practice, Policy and Future Research

Despite its high impact on health burden and healthcare costs, there is currently a lack of studies exploring drugrelated readmissions in older adults and current studies are difficult to compare. A recent systematic review suggests further investigations using a more standardised approach to define drug-related readmissions and preventability to help gain a deeper understanding of possible causes and risk factors associated with readmissions [15]. This review has also emphasised the role of comorbidities and polypharmacy in contributing to drug-related readmissions; however, further investigations are required to identify other possible risk factors, including sociodemographic and environmental factors, which can contribute to readmissions. Further research is also required to investigate other common DRPs including ADEs and MEs. An increased understanding of risk factors and causes of preventable readmissions will help inform the development of targeted interventions in healthcare settings to optimise the quality use of medicines in older adults.

# 5 Conclusions

This systematic review and meta-analysis found that almost one in ten older adults discharged from hospital experienced a drug-related hospital readmission, with one fifth of these being preventable. Several comorbidities and the use of polypharmacy were identified as prominent risk factors for readmission, with the most common drug classes involved including anticoagulants, antibiotics, chemotherapy agents and psychotropics. Further research is needed to explore possible causes of drug-related readmissions in older adults for a more guided approach to the development of effective medication management interventions.

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#### Declarations

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