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# In-Hospital Adverse Drug Reactions in Hospitalised Older Adults: A Systematic Review

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## Introduction

- Almost ten percent of older-adults experience an adverse drug reaction [ADR] associated with acute hospitalisation
- Individual studies suggest that up to 1 in 4 experience an ADR in hospital.

This systematic review [SR] aims to evaluate in-hospital ADRs in hospitalised older-adults; frequency, culprit drug classes, severity, and clinical consequence.

## Methods

This SR was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009). Two researchers (EJ, KM) screened all papers for inclusion, risk of bias and data extraction independently.

### Registration

- PROSPERO registration CRD42018079095

### Search Strategy

- Databases – electronic databases [PubMed, Embase and EBSCO-CINAHL, Cochrane Library] and library-hosted academic sources, google scholar, and grey literature.
- Search term stems – aged, ADRs, hospitalized, multi-morbid, polypharmacy and hospital-acquired [search strategy available on request from author]
- Bibliographic hand searches of relevant editorials and systematic reviews.

### Paper Inclusion/Exclusion

- All languages.
- All dates up to and including the date of the final search [15/01/2018] were eligible.
- Any study that reported on ADRs either as a primary or secondary outcome in those aged 65 years or older that were hospitalised at time of ADR occurrence.
  - Review articles, systematic reviews, case reports and letters to the editor were subsequently excluded – their bibliography was hand searched for suitable studies.
- When data reported was for all ages, but there was evidence of ≥65 cohort the author was contacted requesting data for those aged 65 and over.
  - A template document for completion was provided.
  - Two attempts were made to the listed author, followed by an attempt to contact a co-author.

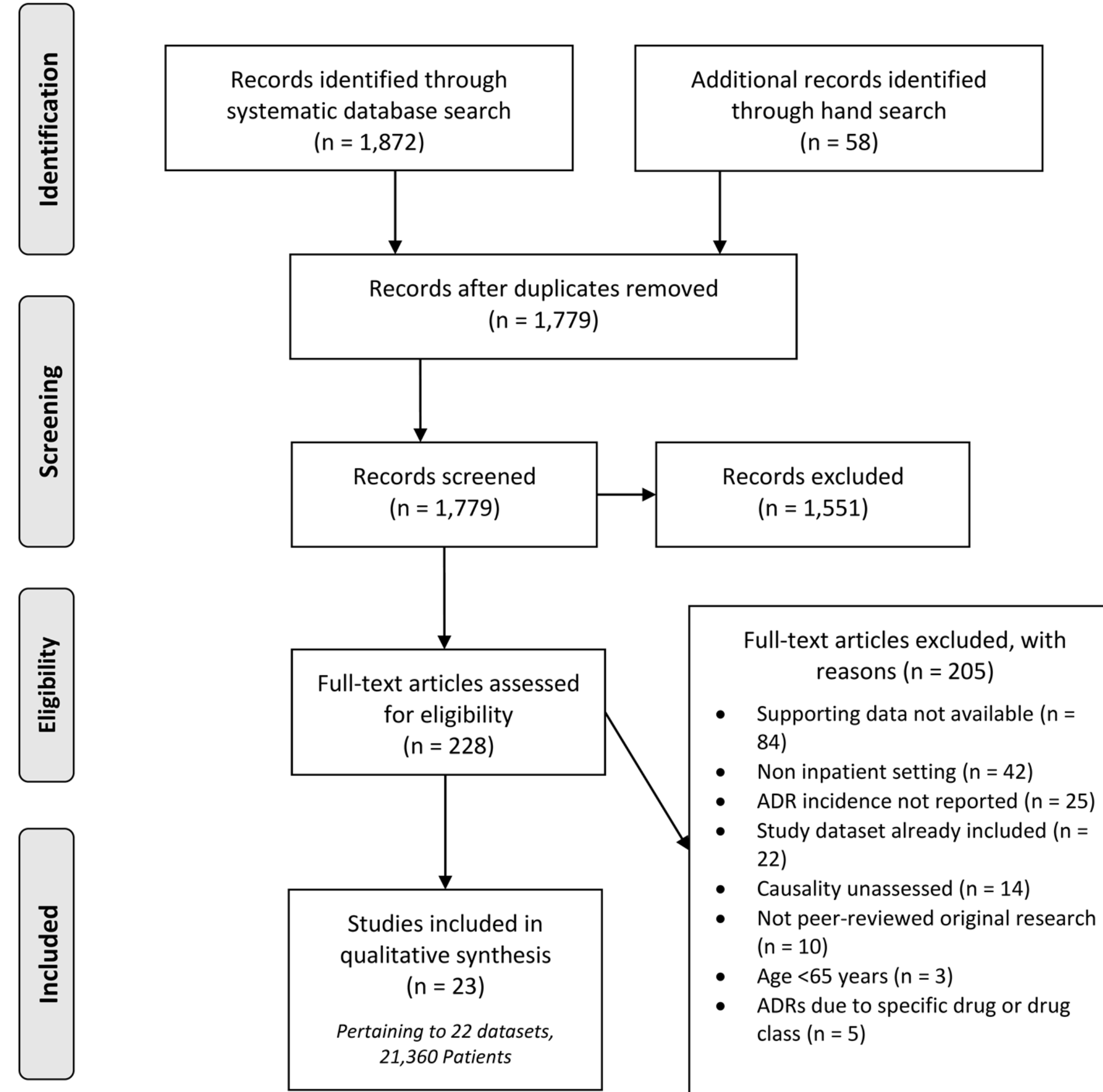
### Study Quality / Risk of Bias Assessment

Included studies were assessed for risk of bias and study quality.

- Cochrane for randomised controlled trials
- STROBE checklist for case cohort studies
- Newcastle-Ottawa Scale for non-randomised studies

### Data Extraction

We extracted data to assess percentage of study cohort ≥ 65 that experienced an ADR, reported presentation of ADRs, Drugs deemed accountable, ADR severity, ADR preventability, any measured outcomes.



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(7): e1000097. doi:10.1371/journal.pmed1000097

**Figure 1.** PRISMA Flowchart outlining study selection

## Results

### Study selection – see PRISMA Diagram [Figure 1.]

1930 abstracts were identified, 1,779 were screened, 228 underwent full-text screening. 23 papers reporting 22 studies were included [1-23] 11 ADRs in participants ≥ 65 years, 11 ADRs all age adults (extractable data for ≥65 available in 5 studies, supplemental data provided by authors in 6 studies)

### Characteristics of Included Studies

21,306 patients were included in the 22 studies; 15,769 (74%) were aged ≥65 years. 50% male, 50% female (reported in 18 studies). Polypharmacy (reported as a mean/median ≥5 medications at baseline) was reported and present in 12 studies. Multi-morbidity (reported as a mean/median number of diagnoses ≥3 at baseline) was reported in 9 and present in 8 studies.

### ADR Rates

22 Studies reported ADR incidence – 2186 patients ≥ 65 years experienced ADRs in-hospital. Median 19.77% [IQR 10.44 – 25.35] Min 4.95% Max 42.19%.

### Reported ADR Presentation

16 studies reported on ADR presentation (n = 13,217, 1,403 ADR presentations). 20% (283) metabolism and nutritional disorders; 17% (246) nervous system disorders; 15% (210) cardiac disorders; 13% (185) gastrointestinal disorders; 10% (148) renal and urinary disorders; 6% (80) blood and lymphatic system disorders.

### ADR Drugs

ADR associated drugs were extractable in 15 papers (1528 reported drugs in 1253 ADR patients). 85% of ADRs were associated with 11 commonly prescribed medications.

### ADR Severity

14 studies reported severity (n = 13,171; reported ADRs = 1,947). 72% of reported ADRs were at least of moderate severity. 29% (560 ADRs) were severe.

### ADR Preventability

5 studies assessed preventability (n = 3602, reporting 672 ADRs), 69% of reported ADRs were preventable.

### Outcomes

5 papers reported on post ADR outcomes [3 length of stay [LOS], 1 LOS-death, 1 functional decline].

**1 in 5 patients ≥ 65 years experiences a clinically significant ADR in-hospital**



**11 commonly prescribed drug classes account for 85% of ADRs**

Diuretics	22%
Anti-thrombotics	14%
Vitamin-K antagonists 10%, Heparin 2%, Platelet aggregation inhibitors 2%	
Antimicrobials	12%
Opioids	11%
Psycholeptics	6%
Drugs used in diabetes	4%
Insulin 3%, oral hypoglycaemic agents 1%	
ACE-I, ARBs	4%
Systemic corticosteroids	3%
Drugs for obstructive airway disease	3%
Cardiac glycosides	3%
Anti-hypertensives	3%

**1 in 4 in-hospital ADRs is severe**

**At least 2 of 3 in-hospital ADRs are preventable**

## Conclusion:

- There is a **lack of consistency** in methodologies used for **ADR** identification, assessment and **reporting in the literature**.
- Incident **ADRs** occurring **in-hospital** in older adults (≥ 65 years) are **common**, occurring in **1 in 5 hospitalised** older adults.
- **11** commonly prescribed **drug classes** account for **85%** of **all ADRs**.

- **1 in 4** of ADRs are **severe**.
- **2 of 3** ADRs could be **preventable**.
- Despite this, there is **under-reporting** of measurable clinical **outcomes** associated with ADRs.
- Development of **drug based ADR prediction** tools may lead to better **ADR prevention**.