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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***

- PROPSERO 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.

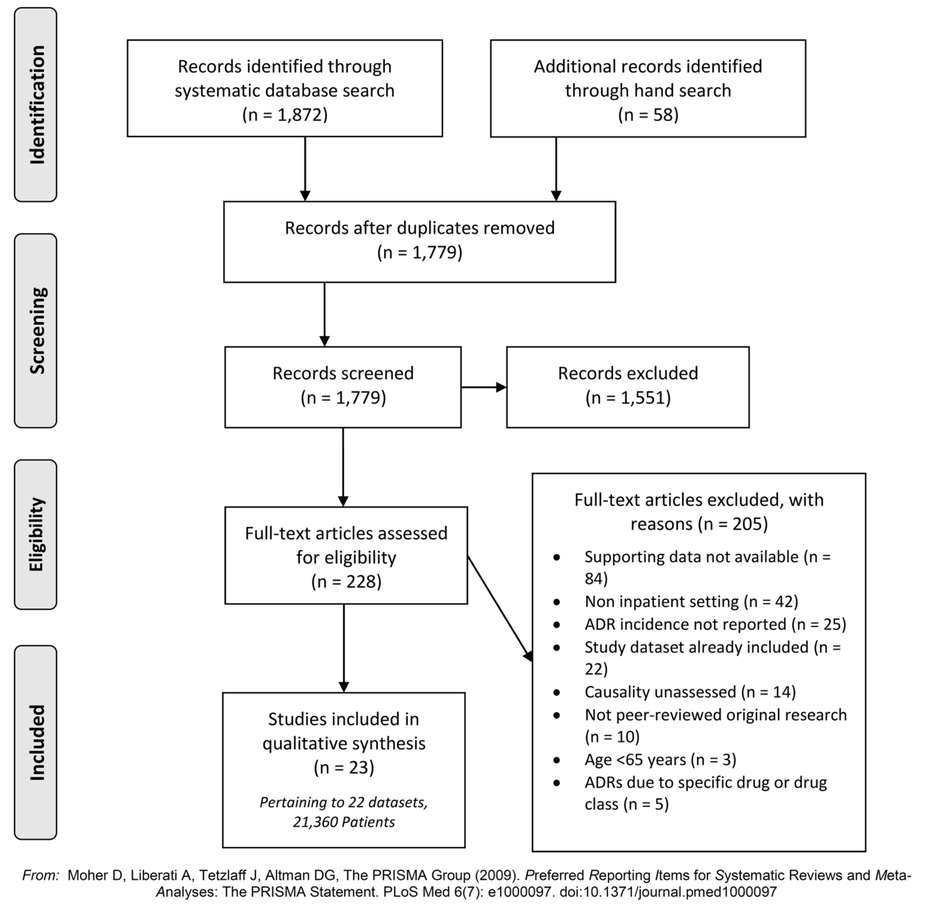
***Study Quality / Risk of Bias Assessment***

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). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: 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) gastro-intestinal 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***.

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