RESEARCH BRIEF

DRUG-DRUG INTERACTIONS IN OLDER COMMUNITY-DWELLING ADULTS: A PREVENTABLE SOURCE OF MEDICATION-RELATED HARM?

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EXECUTIVE SUMMARY

This systematic review indicates that drug-drug interactions are highly prevalent in the older community-dwelling population, and provides an insight into some of the clinically important drug-drug interactions commonly reported for this population. Our findings clearly highlight the need for a standardised method to measure drug-drug interaction prevalence, for meaningful comparison across studies. In clinical practice, routine surveillance of prescriptions for the older population should be used to identify and reduce clinically important drug-drug interactions. Further research is warranted to determine the effect of drug-drug interaction exposure on health outcomes in this older population.

SUMMARY OF THE PROBLEM

A drug-drug interaction occurs when the effect of one drug is changed by the use of another drug. Some drug-drug interactions can result in adverse health effects, which may require hospital admission. Such drug-drug interactions are considered to be a predictable, and therefore avoidable, cause of medication-related harm.

The ageing process means that we are likely to develop chronic disease(s) which may require medication(s) to maintain our health. Ageing also results in a decline in some body functions, such our kidneys. The use of multiple medications and reduced body function means that older individuals (aged $\geqslant$ 65 years) are at greatest risk of drug-drug interactions and avoidable medication-related harm.

To date, the overall number (prevalence) of older people living in the community with a potential drug-drug interaction is unknown. Understanding and estimating the prevalence of drug-drug interactions in this population would be helpful to policy and decision makers when planning, developing, and allocating healthcare resources based on population needs.

The aim of this review was to summarise the prevalence of drug-drug interactions in older community-dwelling adults, and to identify common drug-drug interactions in this population.

WHAT DID WE DO?

We conducted a systematic review of the literature to identify published observational studies reporting drug-drug interaction prevalence in older adults aged $\geqslant$65 years in the community setting.

WHAT DID WE FIND?

We found 31 studies reporting drug-drug interaction prevalence in community-dwellers aged $\geqslant$ 65 years across 17

countries. Prevalence estimates varied widely, ranging from 0.8% to 90.6%. Across studies, there was also variation in the method used to identify drug-drug interactions, which meant it was not possible to report a meaningful overall drug-drug interaction prevalence estimate.

Table 1. Commonly Reported Clinically Important Drug-Drug Interactions

Drug-Drug Interaction	**Established Medication-Related Harm Reported in the Literature**
ACE inhibitor-potassium-sparing diuretic	Life-threatening hyperkalaemia, requiring hospitalisation[1]; Renal failure[2]
Amiodarone-digoxin	Digoxin toxicity, arrhythmias[3]
Amiodarone-warfarin	Haemorrhage requiring hospitalisation[4]
Beta-blocker-verapamil	Additive cardiac depressant effects, which can be fatal in some patients[5]
Warfarin-NSAID	Upper gastrointestinal haemorrhage, requiring hospitalisation[6]
ACE inhibitor-allopurinol	Toxic epidermal necrolysis (lyell syndrome)[3]

Almost all of the included studies measured clinically important drug-drug interactions, and drugs routinely used in this older population were commonly implicated (Table 1). These specific DDIs may confer severe and potentially life-threatening harm to the older patient, including hospitalisation for haemorrhage, as has been highlighted by previous studies.[1-6]

WHAT CONCLUSIONS DID WE REACH?

Drug–drug interactions are prevalent among older community-dwelling individuals, and most are classified as clinically important; however, the methodology used to estimate these events varies considerably. Further research, which is uniform in both methodology and reporting, is needed to monitor trends in drug–drug interaction prevalence and related health outcomes in this older population.

RECOMMENDATIONS

1. A standardised methodology is urgently needed to allow meaningful measurement and comparison of drug–drug interaction prevalence in the older population. The use of a common drug–drug interaction identification methodology instead of a static list, which is vulnerable to becoming outdated, may facilitate a more meaningful comparison of drug–drug interaction prevalence across different studies and settings.

2. Healthcare professionals caring for these individuals should be aware of the medications commonly implicated in clinically important drug–drug interactions when prescribing, dispensing, and during medication review.

3. In clinical practice, routine surveillance of prescriptions for the older population represents one measure which can be used to monitor and reduce drug–drug interactions, and avoidable medication-related harm in our ageing population.

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FURTHER INFORMATION

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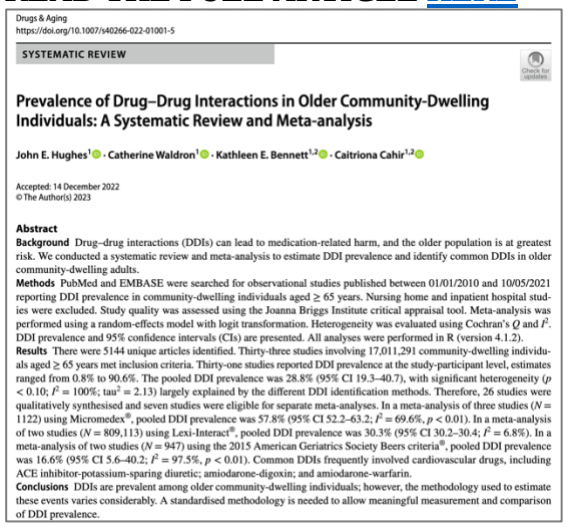

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SYSTEMATIC REVIEW

Prevalence of Drug–Drug Interactions in Older Community-Dwelling Individuals: A Systematic Review and Meta-analysis

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Abstract

Background Drug–drug interactions (DDIs) can lead to medication-related harm, and the older population is at greatest risk. We conducted a systematic review and meta-analysis to estimate DDI prevalence and identify common DDIs in older community-dwelling adults.

Methods PubMed and EMBASE were searched for observational studies published between 01/01/2010 and 10/05/2021 reporting DDI prevalence in community-dwelling individuals aged ≥ 65 years. Nursing home and inpatient hospital studies were excluded. Study quality was assessed using the Joanna Briggs Institute critical appraisal tool. Meta-analysis was performed using a random-effects model with logit transformation. Heterogeneity was evaluated using Cochran's Q and I^2. DDI prevalence and 95% confidence intervals (CIs) are presented. All analyses were performed in R (version 4.1.2).

Results There were 5144 unique articles identified. Thirty-three studies involving 17,011,291 community-dwelling individuals aged ≥ 65 years met inclusion criteria. Thirty-one studies reported DDI prevalence at the study-participant level, estimates ranged from 0.8% to 90.6%. The pooled DDI prevalence was 28.8% (95% CI 19.3–40.7), with significant heterogeneity ($p < 0.10$; $I^2 = 100\%$; $\text{tau}^2 = 2.13$) largely explained by the different DDI identification methods. Therefore, 26 studies were qualitatively synthesised and seven studies were eligible for separate meta-analyses. In a meta-analysis of three studies ($N = 1122$) using Micromedex®, pooled DDI prevalence was 57.8% (95% CI 52.2–63.2; $I^2 = 69.6\%$, $p < 0.01$). In a meta-analysis of two studies ($N = 809{,}113$) using Lexi-Interact®, pooled DDI prevalence was 30.3% (95% CI 30.2–30.4; $I^2 = 6.8\%$). In a meta-analysis of two studies ($N = 947$) using the 2015 American Geriatrics Society Beers criteria®, pooled DDI prevalence was 16.6% (95% CI 5.6–40.2; $I^2 = 97.5\%$, $p < 0.01$). Common DDIs frequently involved cardiovascular drugs, including ACE inhibitor-potassium-sparing diuretic; amiodarone-digoxin; and amiodarone-warfarin.

Conclusions DDIs are prevalent among older community-dwelling individuals; however, the methodology used to estimate these events varies considerably. A standardised methodology is needed to allow meaningful measurement and comparison of DDI prevalence.

Hughes JE, Waldron C, Bennett KE, Cahir C. Prevalence of Drug–Drug Interactions in Older Community-Dwelling Individuals: A Systematic Review and Meta-analysis. Drugs & Aging. 2023 Jan 24:1-8.

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