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Drug-drug interaction among elderly patients in Africa: a systematic review and meta-analysis

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Abstract

Background Elderly patients are at a heightened risk of drug-drug interactions due to their high prevalence of comorbidities, polypharmacy, and age-related physiological changes that alter drug metabolism and excretion. In Africa, these risks are compounded by unique healthcare challenges, including limited access to diagnostic tools, and high burdens of communicable diseases. The aim of this study is to estimate the prevalence of drug-drug interactions and its associated factors among elderly patients in Africa.

Methods Relevant research articles were identified from databases such as HINARI, Science Direct, Embase, PubMed/MEDLINE, Google Scholar, and Research Gate. Data were extracted via a Microsoft Excel spreadsheet and analyzed via STATA version 11.0. Egger regression tests and funnel plot analysis were used to check for publication bias, and the I^2 statistic was used to evaluate statistical heterogeneity. Sensitivity and subgroup analyses were also conducted to identify potential causes of heterogeneity.

Results Fifteen articles were analyzed, and a total of 5651 potential drug-drug interactions (pDDIs) were identified in 1952 patients, resulting in an average of 2.89 pDDIs per patient. The overall prevalence of pDDIs among elderly patients was 52.53% (95% confidence interval (CI): 35.40, 69.66). However, the prevalence of pDDIs ranged widely from 2.8 to 90.1%. When the severity of the interactions was considered, the prevalence of pDDIs was 20.59%, 69.4%, 34.32% and 1.59% for major, moderate, minor, and contraindicated DDIs, respectively. Polypharmacy, long hospital stays, hypertension and diabetes mellitus were identified as factors associated with pDDIs among elderly patients in Africa.

Conclusion DDIs are prevalent among elderly patients in Africa and are often associated with polypharmacy, prolonged hospitalizations, and the presence of chronic comorbidities, particularly hypertension and diabetes mellitus. Moderate-severity interactions were the most prevalent DDIs. The study suggests addressing this issue requires targeted interventions, including improved pharmacovigilance, enhanced prescribing practices, and integration of DDI risk assessment into routine clinical care. The study also suggests that the database itself could have

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modified the DDI prevalence rate. As a result, a single DDI identification database needs to be authorized; otherwise, clinical knowledge should be taken in to account when interpreting the information obtained.

Keywords Drug-drug interaction, Elderly, Africa, Systematic review, Meta-analysis

Background

Drug–drug interactions are the most common types of interactions. It is described as "a pharmacological or clinical response that differs from the anticipated known effects of the two agents when administered separately upon the administration of a drug combination." On the other hand, it is a quantitative alteration that results from the simultaneous administration of two medications and influences the toxicity or effectiveness of one medication [1]. It can be classified as actual DDIs or potential drug–drug interactions (pDDIs). Actual DDIs are identified from patient adverse outcomes; however, pDDIs are those identified through analysis of the pharmacologic profiles of each drug used by patients and identification of possible adverse events due to the association [2]. Not all pDDIs result in an adverse outcome; therefore, the occurrence of actual DDIs is lower than that of pDDIs [3]. DDIs can also be classified on the basis of their severity and the mechanism by which they interact. They can range from mild to severe and can be categorized as pharmacokinetic (PK), pharmacodynamics (PD) or mixed interaction [4, 5].

The occurrence of DDIs is a serious global issue for patient safety, affecting individuals of all age groups. However, older adults aged 60 years and above are particularly vulnerable [6]. Despite this vulnerability, clinical trials are often conducted on younger adults, which can make it challenging to provide appropriate care for the elderly population [7]. Older patients generally take more medications than younger patients do because of the various physiological changes associated with aging and the ensuing health problems [8], which makes aging an independent risk factor for DDIs [9]. This is because physiological changes associated with aging can affect the PKs and PDs of drugs, potentially increasing the risk of drug toxicity and adverse drug reactions [10]. DDIs are therefore often unavoidable in this population. As a result, DDIs are frequently unavoidable in this population, and elderly individuals are particularly vulnerable to the adverse outcomes of these interactions [11].

According to a systematic analysis of the literature, the pooled prevalence of pDDI globally was 28.8% [12]. The number of DDIs per 100 patients varies from 120 to 3060, and the global pooled prevalence of pDDI among older patients ranges from 8.34 to 100% [13]. Similarly, the occurrence of pDDIs among elderly patients is also common in different African countries, however, the prevalence of pDDIs ranged widely [14–16]. A systematic review and meta-analysis conducted in Ethiopia found that the national prevalence of pDDIs among elderly patients was 50.69% [17].

The high prevalence of drug-drug interactions in older patients is influenced by several factors, including patient-specific characteristics such as age, the presence of multiple comorbidities, and polypharmacy. Additionally, the pharmacokinetic and pharmacodynamic properties of medications, along with the impact of illness on drug metabolism, play a crucial role [8, 11, 18]. Prescriber-related factors also contribute significantly to the occurrence of potential DDIs (pDDIs). These include multiple prescriptions from different healthcare providers, limited awareness or inadequate knowledge of DDIs among prescribers, and a failure to recognize their clinical significance [19]. Furthermore, certain drug classes, particularly cardiovascular medications, are frequently implicated in DDIs, further increasing the risk of pDDIs in this population [8, 13, 17, 20].

Globally, DDIs have been identified as a significant contributor to adverse clinical outcomes, including increased hospitalizations, healthcare costs, and mortality [4]. In fact, the incidence of DDI-related ADRs in older adults has been estimated to range from 4.5 to 6.5% [21, 22]. In elderly patients, clinically significant DDIs can also lead to deterioration of overall health, decreased quality of life, longer hospital stays, increased need for ambulatory services, and higher healthcare costs [23–25]. Furthermore, DDIs are responsible for 4.8% of hospital admissions in elderly patients, compared with only 0.57% in the general population [26], and account for 20.79% of deaths in hospitalized elderly patients [27]. Conversely, some DDIs may not immediately cause noticeable changes in patients but can still result in treatment failure [28]. However, in Africa, where healthcare systems often face resource constraints and gaps in pharmacovigilance, the impact of DDIs on elderly patients may be even more pronounced. Limited awareness among healthcare providers, the scarcity of clinical guidelines tailored to polypharmacy in elderly patients, and the widespread use of herbal remedies may also contribute to underreported and poorly managed DDIs.

Despite the implementation of automated DDI alert systems, such as DDI screening software, as an approach to reinforce DDI alert quality, which has helped to decrease the occurrence of DDIs [29], DDI remains an evolving public health problem [30, 31]. However, the numerous alerts produced by these systems can lead to alert fatigue among physicians and pharmacists, resulting in a significant number of overrides of DDI alerts [32]. As

a result, DDIs continue to pose a serious risk to public health.

Given the growing elderly population and the potential impact of DDIs, to date, as per the investigators knowledge no systematic review has explicitly addressed the prevalence of DDIs and its associated factors among elderly patients in Africa. This study provides a comprehensive understanding of the nature and extent of DDI prevalence and associated factors in this growing and vulnerable population in Africa. Therefore, the aim of this study was to estimate the pooled prevalence of DDIs and their associated factors among elderly patients in Africa.

Method

Study protocol

The protocol for this systematic review and meta-analysis has been registered with the international prospective registration of systemic reviews (PROSPERO) with the ID CRD42024563052. The current review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [33].

Search strategy

A systematic review and meta-analysis were conducted to determine the prevalence of potential drug–drug interactions (pDDIs) and their associated factors among elderly patients in Africa. The search for relevant research articles was conducted via databases such as HINARI, Science Direct, Embase, Thesis Bank, PubMed/MEDLINE, Google Scholar, and Research Gate for English-language publications (Table 1). The reference lists of the identified studies were also reviewed for additional relevant research. The study search was done for the published studies from inceptions to June 30, 2024 and the search process was conducted over a six-week period, from May 19, 2024, to June 30, 2024. A search methodology for this systematic review and meta-analysis was crafted by combining free texts with MeSH terms and keywords. A predetermined combination of search terms was used, including "prevalence", "occurrence", "pharmacoepidemiology", "potential drug–drug interactions", "inappropriate medication use", "associated factors", "predictors", "elderly", "elder", "older adults", "aged", and "Africa". After data were retrieved from the articles, we attempted to contact the primary or corresponding authors via email to obtain any missing information.

Table 1 Study search results across various databases

Database	Records identified (*N* = 412)	Duplicates removed (*N* = 216)	Records screened (*N* = 196)	Full-text articles assessed (*N* = 53)	Studies included (*N* = 15)
PubMed	102	52	48	18	8
Scopus	9	7	2	0	0
Embase	92	47	45	13	1
Google Scholar	1,27	76	51	14	4
Thesis Bank	21	12	9	4	1
Research Gate	14	9	5	1	0
HINARI	47	13	34	3	1

Study selection

After TTA, AAT, GWG, and YAW identified the relevant articles through the database searches, citations for the articles were exported into the Endnote program X9 version. Duplicate publications were then removed independently. Next, the three investigators screened the titles and abstracts to determine the eligibility of the articles. Finally, the authors (TTA, AAT, GWG, and YAW) independently assessed the full-text articles using the inclusion and exclusion criteria. Any disagreements were resolved through discussion before the analysis began.

Eligibility criteria

Inclusion criteria

Observational studies (cohort, cross-sectional, and case–control studies) conducted in Africa, which were reported as original articles, theses, and abstracts from scientific events and meetings were included. The articles must be published in English in a peer-reviewed journal with a recognized impact factor or indexed in reputable databases such as PubMed, Scopus, or Web of Science. They should specifically assess the prevalence of potential drug-drug interactions (pDDIs) and its associated factors among elderly patients (aged 60 years and above) admitted to hospital wards or visiting outpatient settings, regardless of their underlying disease.

Exclusion criteria

On the basis of the consensus of the authors, we decide to exclude (a) articles that did not report the prevalence of DDI and/or associated factors but only characterized DDIs in the population of interest. (b) Articles reporting interventions for DDIs but not their prevalence before intervention. (c) Articles analyzed the prevalence of DDIs in adults, including elderly individuals, but did not provide enough data to calculate the prevalence of DDIs in the elderly population of the study, in the original document or after the information was requested. Additionally, pilots, validations, and studies with incomplete data, even after the authors were contacted, were also excluded. If there were doubts about the eligibility of a study, a decision was made by consulting and discussing with second groups of authors (DG, HAS and TM).

Data extraction

Data were extracted and managed in a predesigned form in Microsoft Excel. Following the selection of the articles and the final decisions, TTA, AAT, GWG, and YAW were separately extracted from all relevant data from the articles. The authors entered the following data in a standard data extraction form: the first author's name, publication year, countries in which the study was conducted, study design, pathology (diagnosed disease condition or identified health condition), target population, study setting, interaction database, number of patients, number of patients with DDIs, and lists of medication classes that caused the interactions. Additionally, the outcome of interest (prevalence of pDDIs - major, moderate and minor) and associated factors of pDDIs, as well as measures of effect (odds ratios (ORs)), lower confidence intervals, and upper confidence intervals, were also extracted. In cases where the authors had differing opinions during the data extraction process, a decision to extract was made by consulting and discussing with second groups of authors (ASY, GT, SF, and TBA). The second group of authors independently extracted all relevant data again to ensure that no relevant data were missed. To compare the observed and expected agreements between authors, we used kappa statistics to assess any differences. The calculated kappa value of ≥ 0.6, indicating substantial agreement, was considered acceptable. To determine the reliability of the meta-analytic results, a sensitivity analysis was also performed.

Outcome measurements

The primary aim of the current systematic review and meta-analysis was to assess the pooled prevalence of pDDIs, which can be calculated as the percentage of patients who presented at least one DDI among the total number of patients studied, as well as factors associated with pDDIs. This study also has three secondary outcomes: (i) to characterize pDDIs on the basis of their severity (major, moderate, minor and contraindicated (CI)) and mechanism of action (PK, PD and mixed interactions). (ii) Determine the number of DDIs per patient, defined as the number of DDIs divided by the number of patients with at least one pDDI. (iii) To identify the most common drug class involved in pDDIs.

Quality assessment

Owing to the cross-sectional nature of the studies included, study quality was assessed via the Agency for Healthcare Research and Quality (AHRQ) methodological checklist for cross-sectional and prevalence studies [34]. This assessment tool is an 11-item questionnaire that explores the quality of data collection, inclusion criteria, outcome measurement, and other measurements. The items were answered as yes (+), no (-), or unclear (U) for the study. TTA, ASY, SF, TBA, GT, DG and HSA conducted the quality assessment. Any disagreements between reviewers were resolved through consensus, and the opinion of another reviewer (YAW, AAT, GWG, and TM) was sought if necessary. Study quality was not an exclusion criterion. The quality assessment process was completed on July 05, 2024.

Statistical procedure

After the data were extracted and opened in Microsoft Excel, STATA 11.0 was used for analysis. The outcomes of the primary articles were presented via text, tables, and forest plots. For each original article, we looked at the standard error of prevalence via the binomial distribution. Furthermore, to determine whether there was publication bias in the included articles, two methods were employed. A funnel plot was used to demonstrate the symmetric distribution and lack of publication bias in the included articles. Egger's correlation and Begg's regression intercept tests were employed at the 5% significance level. In the event that our analysis revealed publication bias, we formalized the use of funnel plots, estimated the number and outcome of missing articles, and accounted for hypothetically absent articles via the nonparametric "trim and fill" approach developed by Duval and Tweedie.

Heterogeneity assessment

Der Simonian and Laird's pooled effects of pDDIs were estimated via a random effects meta-analysis approach. Heterogeneity between articles was assessed by considering the I^2 inconsistency statistic. Significant levels of heterogeneity were considered present when the I^2 estimate was greater than or equal to 70%. Additionally, if we found evidence of heterogeneity during analysis, we used a sensitivity analysis, and subgroup analysis to pinpoint its potential cause. We applied a leave-one-out sensitivity analysis to determine the potential cause of heterogeneity in the pooled prevalence of pDDIs.

Subgroup analyses

Subgroup analyses are useful for examining between-group differences or determining how a given group's characteristics affect the prediction of the pooled prevalence and the cause of heterogeneity across studies. In this study, the prevalence of DDIs among elderly patients was examined by subgrouping the country where the study was conducted, the interaction database, the study design, the pathology, and the study setting. The prevalence of DDIs is reported as percentages with 95% confidence intervals (CIs).

Results

Article search results

A total of 412 articles were identified from the database. After removing duplicates, 196 articles remained for screening. Among these, 143 articles were excluded on the basis of their titles and abstracts. The remaining 53 articles were then assessed according to predetermined inclusion and exclusion criteria. After this assessment, 38 articles were excluded. Ultimately, 15 full-text articles that met the eligibility criteria and passed the quality assessment were included in the final systematic review and meta-analysis (Fig. 1).

General characteristics of the included studies

Fifteen primary articles, comprising 4202 individuals, were included in the final systematic review and meta-analysis on the prevalence of DDIs and their associated factors among elderly patients. All the articles included in the current review focused only on the prevalence of pDDIs and did not assess the prevalence of actual DDIs. Among the 15 articles, five focused solely on the prevalence of pDDIs. All of the articles utilized cross-sectional study designs, with eight being retrospective and two being prospective. The designs of the remaining five articles were not specified. The included articles were

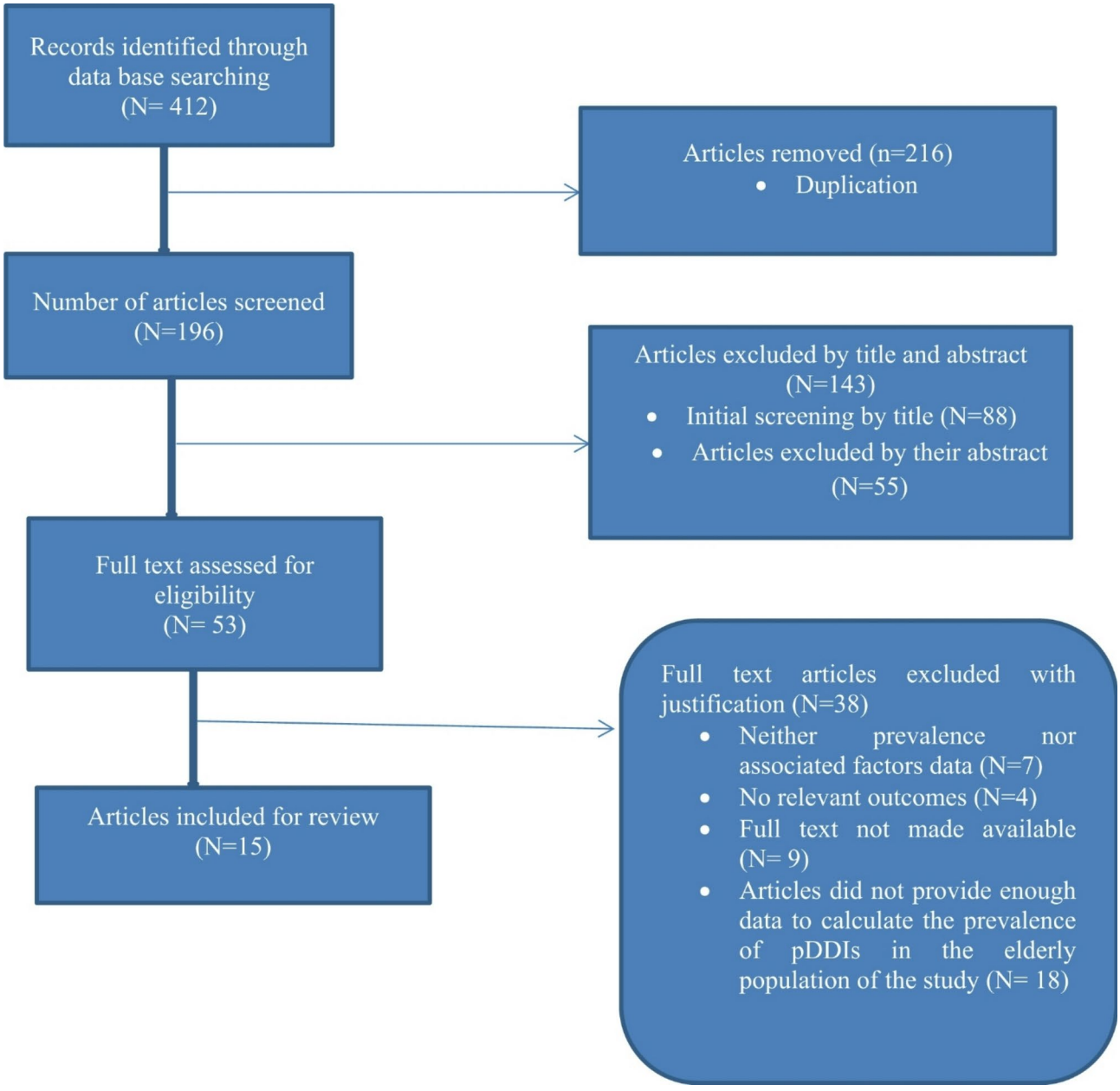

Fig. 1 PRISMA flowchart diagram

published between 2014 and 2023. Geographically, the articles were obtained from five African countries. The included articles examined patients with various diseases receiving treatment in both medical wards and outpatient settings. Eleven articles analyzed patients with all types of pathologies, whereas three articles focused specifically on patients with cardiovascular disorders, and the remaining article focused on patients with benign prostatic hyperplasia. More than half of the articles (nine) studied pDDIs in outpatient settings, four in inpatient settings, and two each in both settings. Nine different databases were used to detect pDDIs, with only six articles utilizing a combination of two databases. The Medscape online database was used in six articles, Micromedex® was used in two articles, the Beers criteria were used in three articles, and the remaining four databases utilized were the EM guidance interaction checker, Hepler and Strand, US-FDA, WebMD, and BNF & Stockley's drug interactions (Table 2).

Quality of the included studies

The quality of the included studies ranged from moderate to high (Additional file 2).

Study outcome measures

Pooled prevalence of pDDI among elderly patients in Africa

To determine the pooled prevalence of pDDIs among elderly patients in Africa, a systematic review and meta-analysis were conducted using 15 published articles [14–16, 30, 35–44]. The results revealed that the pooled prevalence of pDDIs among elderly patients in Africa was 52.53% (95% CI: 35.40, 69.66) (Fig. 2). The included articles reported a wide range of pDDIs, from 2.8% [39] to 90.1% [35]. When the severity of the interactions was considered, the pooled prevalence of pDDIs was 20.59% (95% CI: 6.42, 34.76) for major DDIs, 69.4% (95% CI: 56.15, 82.65) for moderate DDIs, 34.32% (95% CI: 8.44, 60.19) for mild DDIs, and 1.59% (95% CI: -1.56, 4.75) for contraindicated DDIs. Only two articles classified the prevalence of pDDIs on the basis of the mechanism of the interactions, reporting 22.57% (95% CI: 18.57, 26.58) 23) for PK, 73.14% (95% CI: 68.89, 77.39) for PD, and 4.07% (95% CI: 1.91, 6.00) for mixed DDIs [36]. (Table 3 presents the pooled prevalence of different types of pDDIs among elderly patients in Africa). A total of 5651 pDDIs were identified in 1952 patients, resulting in an average of 2.89 pDDIs per patient (calculated by dividing the total number of DDIs by the number of patients with at least one DDI). The number of pDDIs per patient ranged from 0.15 to 12.1.

Factors associated with the prevalence of pDDIs among elderly patients in Africa

Polypharmacy (effect size (ES) = 4.26, 95% CI: 3.46, 5.26), long hospital stays (ES = 3.36, 95% CI: 1.36, 8.27 hypertension (ES = 3.27, 95% CI: 2.07, 5.15), and diabetes mellitus (ES = 4.14, 95% CI: 2.17, 7.90) were identified as significant factors associated with DDIs among elderly patients in Africa. Figure 3 presents a forest plot illustrating the pooled factors associated with pDDIs among elderly patients in Africa.

Table 2 Characteristics of the studies included in this systematic review and meta-analysis on pDDIs among elderly patients in Africa

Authors	Publication year	Study design	Region	Database	Sample size	Pathology	Prevalence of DDI(%)
Adem et al. [35]	2022	RCS	Ethiopia	AGS & MAI	384	CVD	90.1
Assefa et al. [36]	2020	RCS	Ethiopia	Medscape online	168	CVD	86.31
Dagnew et al. [37]	2022	prospective observational	Ethiopia	Medscape online	389	All	58.1
Teka et al. [45]	2016	CS	Ethiopia	Micromedex	140	All	62.2
Teni et al. [38]	2014	RCS	Ethiopia	Micromedex	392	All	24.9
Bhagavathula et al. [39]	2021	CS	Ethiopia	Beers criteria	320	All	2.8
Dagnew et al. [40]	2022	prospective observational	Ethiopia	Medscape online	389	All	30.62
Fadare JO et al. [41]	2016	RCS	Nigeria	Medscape online & Epocrates	350	CVDs	47.6
Yusuff KB et al. [16]	2015	CS	Nigeria	BNF & Stockley's	229	All	65
Abdu N et al. [42]	2019	CS	Eritrea	US-FDA & WebMD	285	All	71.9
Saka SA et al. [43]	2021	RCS	Nigeria	Medscape online	201	BPH	55.8
Alssageer MA et al. [14]	2023	RCS	Libya	Hepler and Strand	195	All	23
Bojuwoye AO et al. [15]	2022	RCS	South Africa	Medscape online & Epocrates	250	All	84.8
Dube SO [44]	2022	CS	South Africa	EMGuidance interaction checker	89	All	80.4
Saka SA et al.	2018	RCS	Nigeria	Beers criteria	352	All	5.7

RCS: retrospective cross-sectional; CS: cross-sectional

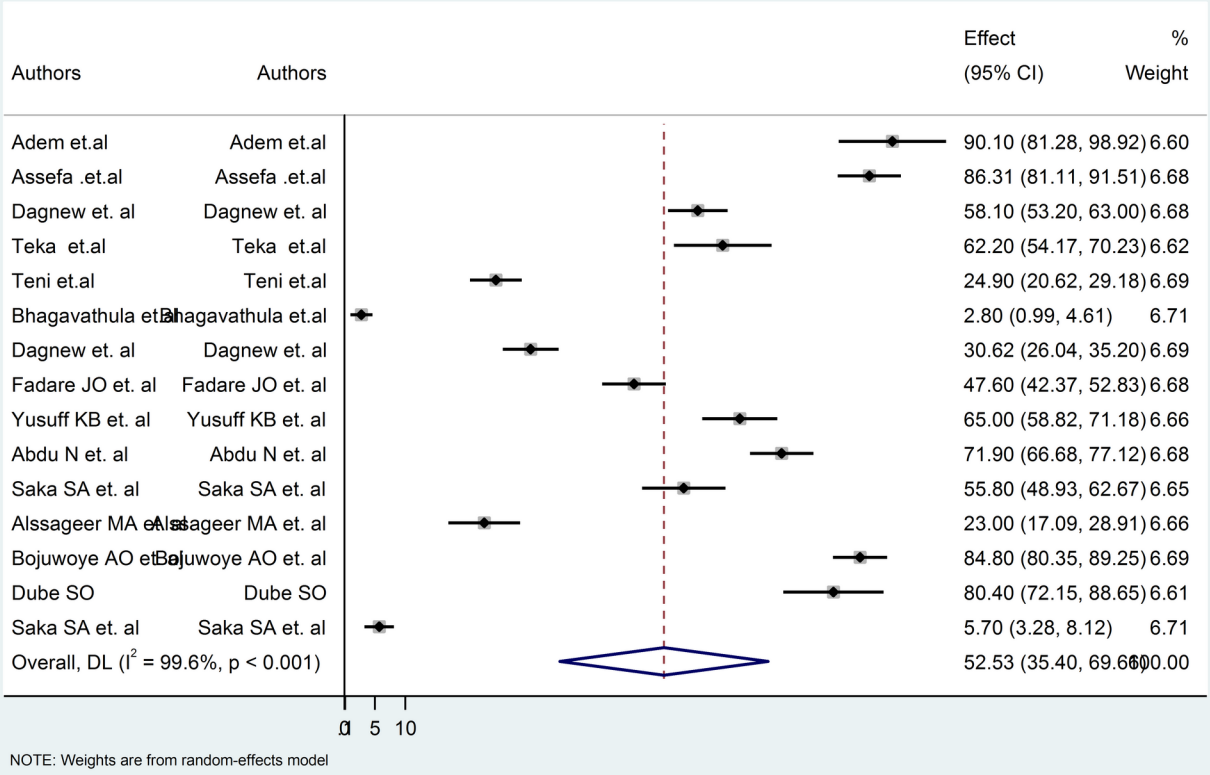

Fig. 2 The pooled prevalence of pDDIs among elderly patients in Africa

Table 3 The pooled prevalence of different types of potential drug–drug interactions (pDDIs) among elderly patients in Africa

Types of DDIs	Number of study	Prevalence (95% CI)	Heterogeneity	
			I2 (%)	*p*-value
Major DDIs	7	20.59 (6.42, 34.79)	99.1	0.000
Moderate DDIs	8	69.40 (56.15, 82.65)	98.8	0.000
Minor DDIs	7	34.32% (8.44, 60.19)	99.6	0.000
Contra indicated DDIs	2	1.59 (-1.56, 4.75)	76.1	0.041
PK DDIs	2	22.57 (18.57, 26.58)	0.0	0.594
PD DDIs	2	73.14 (68.89, 77.39)	0.0	0.975
Mixed (PK& PD) DDIs	2	4.07 (1.91, 6.23)	19.4	0.265

Common interacting drug classes

The study found that the most frequently interacting drug classes include cardiovascular drugs [14–16, 35–37, 39–42, 45, 46], gastrointestinal drugs [14, 35–37, 39, 40, 45], anti-infective drugs [15, 36, 37, 39, 40, 45], endocrine drugs [15, 16, 36, 37, 39, 40, 45], and nonsteroidal anti-inflammatory drugs [15, 16, 42, 44–46]. Additionally, interactions were observed with central nervous system drugs [45, 46] and medications used for benign prostatic hyperplasia (BPH) [43].

Test of heterogeneity and publication bias, subgroups and sensitivity analysis

Heterogeneity and publication bias

The heterogeneity of the fifteen articles included in the current systematic review and meta-analysis was high, as shown by the test statistics (I^2 = 99.7%, p value = 0.000). To determine whether there was publication bias in the included papers, two methods were employed. First, a funnel plot was used to demonstrate the symmetrical distribution and lack of publication bias in the included papers (Fig. 4). Additionally, p = 0.24 indicates that Egger's test was used to verify that there was no publication bias. (Table 4 presents the results of Egger's test for pDDIs among elderly patients in Africa.). To differentiate the causes of heterogeneity, sensitivity analysis and subgroup analysis were employed.

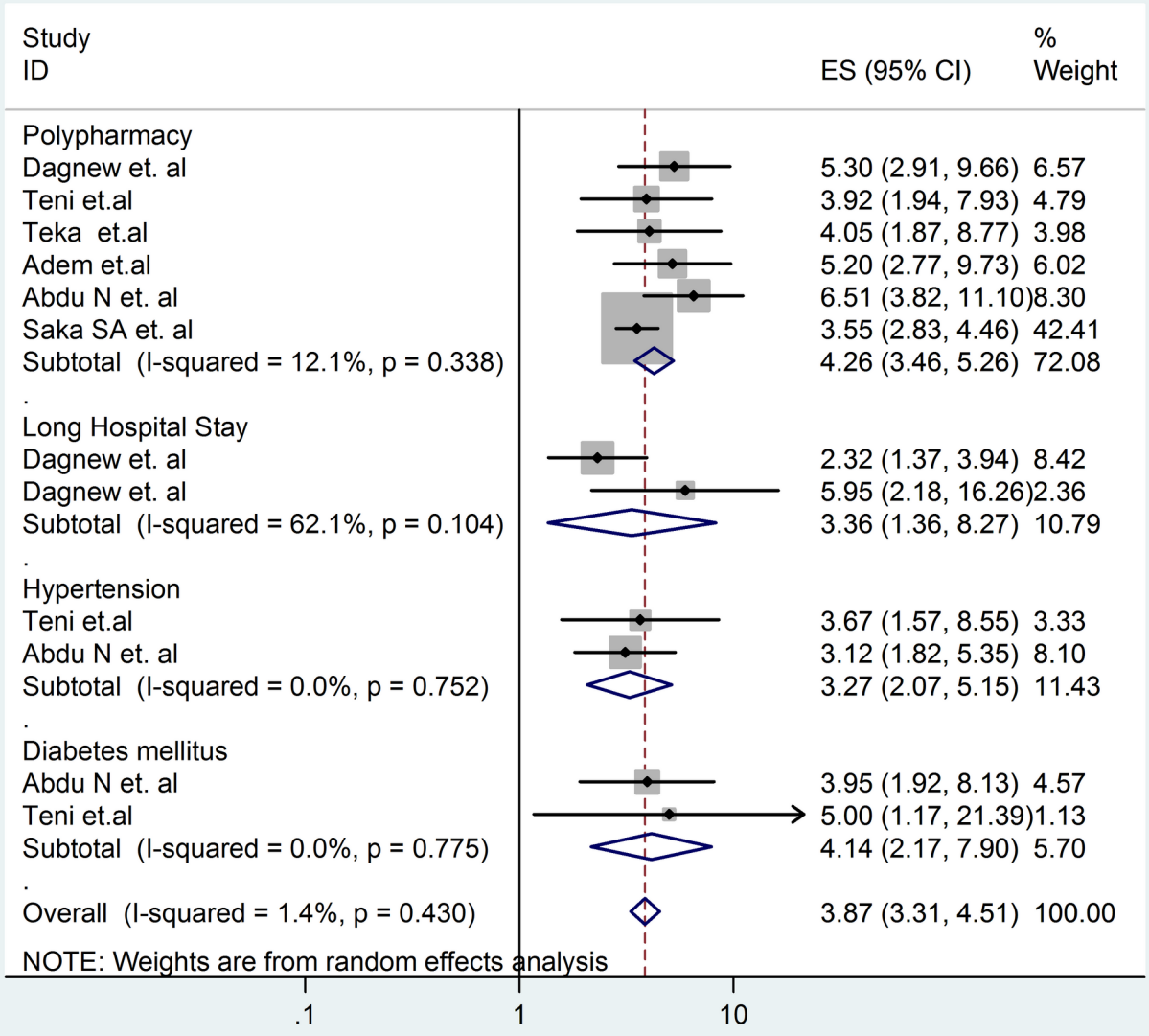

Fig. 3 Pooled factors associated with pDDIs among elderly patients in Africa

Subgroup analysis

To identify the possible sources of heterogeneity, subgroup analysis was conducted on the basis of country, DDI database, study design, pathology, and study setting. The current review revealed that there were differences in the prevalence of pDDIs depending on the DDI database, country where the articles were conducted, study design, pathology, and study setting. Subgroup analysis by country revealed that the highest prevalence of pDDI was found in South Africa, at 83.81% (95% CI: 79.89, 87.72), followed by Ethiopia, with a prevalence of 50.61% (95% CI: 23.94, 77.27). Furthermore, subgroup analysis on the basis of the drug information database revealed that the highest prevalence of pDDI, 66.23% (95% CI: 29.77, 102.68), was detected via the Medscape online database, 57.69% (95% CI: 33.66, 81.72), 43.39% (95% CI: 6.84, 79.94), and 31.97% (95% CI: 9.34, 54.60), was detected via the Micromedex combined database. Additionally, there was a difference in the prevalence of pDDIs based on the number of databases used at a time: more than 63.67% (44.30, 83.04) of the studies utilized a single database (45.06%, 95% CI: 25.57, 64.56). With respect to the study design employed, the highest prevalence of pDDI was observed in studies that utilized a cross-sectional study design (56.39%, 95% CI: 16.78, 96.01), followed by retrospective cross-sectional studies (52.21%, 26.62, 77.81%). Moreover, subgroup analysis was also performed on the basis of the clinical diagnosis of the patients, and the highest prevalence of pDDIs was found in articles that assessed DDI among CVD patients, at 74.56% (95% CI:

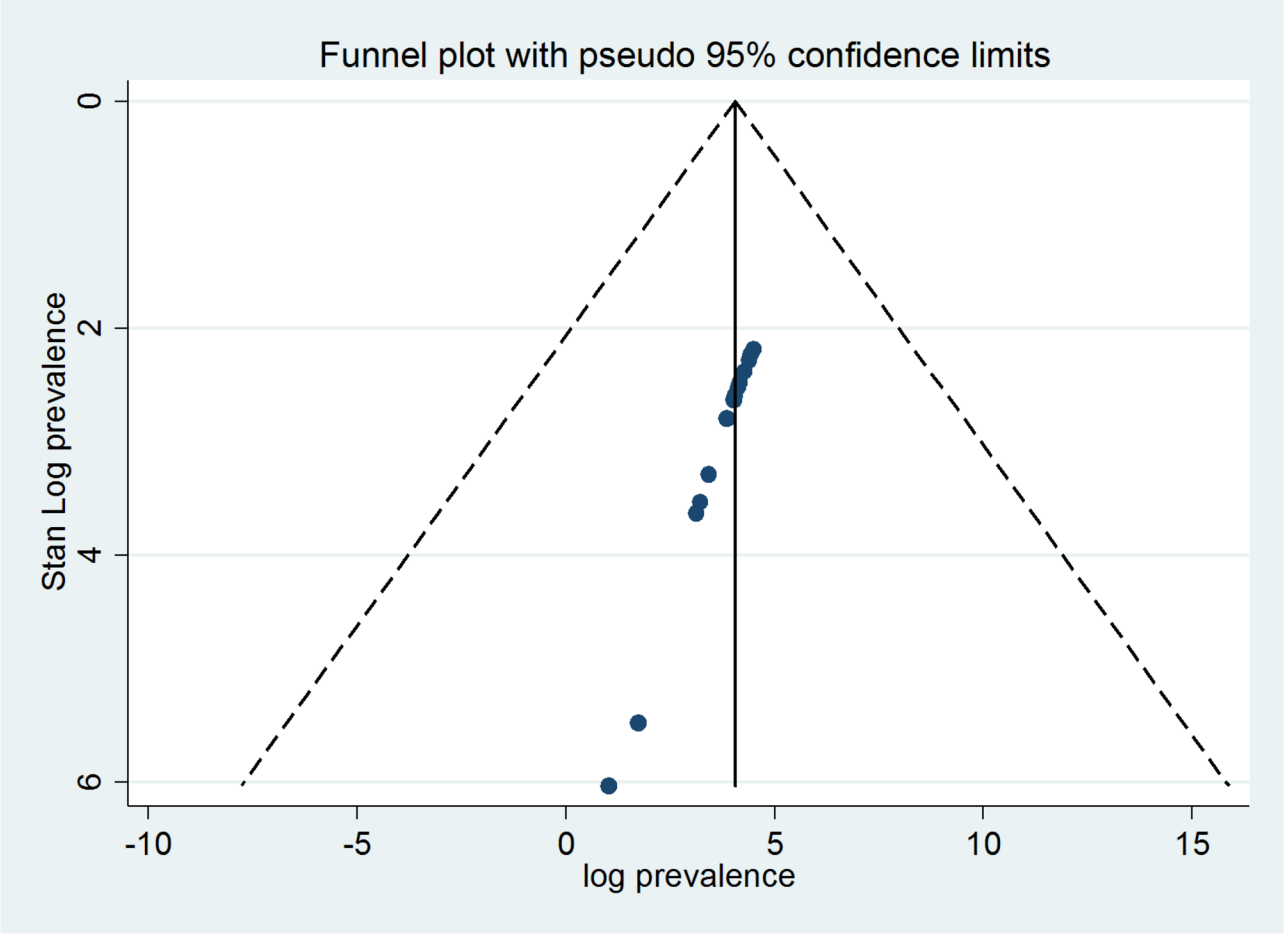

Fig. 4 Random effects funnel plot of logit event rate of pDDIs effect sizes by standard error

Table 4 Egger's test of the PDDI among elderly patients in Africa

Std_Eff	Coef.	Std. Err.	t	*P*>|t|	[95% Conf. Interval]
Slope	-16.95233	11.59376	-1.46	0.169	-42.21296 8.3083
Bias	25.60731	5.188107	4.94	0.24	14.3034 36.91123

46.19, 102.94), compared with 46.22% (27.39, 65.05) in studies that assessed DDI among all clinical conditions. Finally, in the study setting, the prevalence of pDDIs was greater in outpatient settings, at 58.07% (95% CI: 32.23, 83.91), than in inpatient settings, at 43.38% (95% CI: 24.98, 61.78) (Table 5).

Sensitivity analysis

Sensitivity analysis was performed in the current systematic review and meta-analysis to investigate the impact of each study on the pooled prevalence of DDIs among elderly patients. This was accomplished by systematically eliminating one author or one article. The fact that all of the numbers fall within the anticipated 95% CI suggests that the omission of one study did not significantly change the prevalence of this review (Table 6).

Discussion

The objective of the current study was to estimate and offer a quantitative summary of the prevalence of drug–drug interactions, as well as their associated factors, among elderly patients in Africa. The analysis included 15 articles with a total of 4202 individuals. The overall pooled prevalence of DDIs among elderly patients in Africa was 52.53% (95% CI: 35.40, 69.66). This finding is consistent with previous systematic reviews and meta-analyses conducted on adults and the general population in intensive care units (58% and 67% [24, 47], respectively). This may be due to similar healthcare practices, prescribing patterns, and the common use of certain medications across different populations. Furthermore, standard treatment guidelines for various diseases often recommend similar classes of medications, resulting in similar risks of DDIs for patients with the same diseases. The elevated prevalence of pDDIs raises significant concerns in clinical practice, particularly the increased likelihood of adverse drug reactions (ADRs), which can lead to complications such as treatment failure, exacerbation of underlying conditions, or life-threatening events. The

Table 5 Subgroup analysis of the pDDI among elderly patients in Africa

Variable	Subgroup	Number of studies	Prevalence (95% CI)	Heterogeneity	
				I^2%	*p* value
Country	Ethiopia	7	50.61 (23.94, 77.27)	99.6	0.000
	Nigeria	4	43.45 (11.10, 75.79)	99.4	0.000
	South Africa	2	83.81 (79.89, 87.72)	0.0	0.357
	Other	2	47.47 (-0.45, 95.39)	99.3	0.000
Study design	Retrospective cross- sectional	8	52.21 (26.62, 77.81)	99.6	0.000
	Prospective observational	2	44.35 (17.42, 71.28)	98.4	0.000
	Cross-sectional	5	56.39 (16.78, 96.01)	99.7	0.000
Database	Medscape online	4	57.69 (33.66, 81.72)	98.8	0.000
	Beers criteria	3	31.97 (9.34, 54.60)	99.4	0.000
	Micromedex	2	43.39 (6.84, 79.94)	98.5	0.000
	Medscape online & Epocrates	2	66.23 (29.77, 102.68)	99.1	0.000
	Other*	4	52.53 (35.40, 85.16)	98.5	0.000
Number of database used	Single	9	45.06 (25.57, 64.56)	99.6	0.000
	Two	6	63.67 (44.30, 83.04)	98.6	0.000
Pathology	CVDs	3	74.56 (46.19, 102.94)	98.4	0.000
	All conditions	11	46.22 (27.39, 65.05)	99.6	0.000
	BPH	1	55.80 (48.93, 62.67)	-	-
Setting	Outpatients	9	58.07 (32.23, 83.91)	99.6	0.000
	Inpatients	4	43.38 (24.98, 61.78)	97.7	0.000
	Both settings	2	45.97 (-33.03, 124.97)	99.9	0.000

Other = Eritrea and Libya, Other*= EMGuidance interaction checker, Hepler and Strand, US-FDA & WebMD and BNF & Stockley's drug interactions

Table 6 Sensitivity analysis of the pDDI among elderly patients in Africa

Authors	Estimate prevalence (95% CI)	Heterogeneity	
		I2 (%)	*p* value
Adem et al.	49.87 (32.49, 67.25)	99.6	0.000
Assefa et.al	50.10 (33.28, 66.93)	99.5	0.000
Dagnew et al.	52.16 (34.22, 70.04)	99.6	0.000
Teka et al.	51.84 (34.09, 69.60)	99.6	0.000
Teni et al.	52.53 (35.40, 69.66)	99.6	0.000
Bhagavathula et al.	56.10 (39.13, 73.08)	99.4	0.000
Dagnew et al.	54.11 (35.70, 72.51)	99.6	0.000
Fadare JO et al.	52.89 (34.79, 70.99)	99.6	0.000
Yusuff KB et al.	51.64 (33.92, 69.36)	99.6	0.000
Abdu N et al.	51.14 (33.67, 68.61)	99.6	0.000
Saka SA et al.	52.30 (34.44, 70.16)	99.6	0.000
Alssageer MA et al.	54.64 (36.52, 72.77)	99.6	0.000
Bojuwoye AO et al.	50.20 (33.68, 66.73)	99.5	0.000
Dube SO	50.55 (33.05, 68.06)	99.6	0.000
Saka SA et al.	55.90 (37.14, 74.67)	99.5	0.000

management of ADRs resulting from pDDIs can lead to longer hospital stays, increased hospital readmissions, and higher healthcare costs. In resource-constrained African healthcare systems, these additional burdens can exacerbate existing challenges, such as limited healthcare infrastructure, medication shortages, and understaffed facilities.

However, the prevalence of pDDIs in the current study was higher than the pooled prevalence of pDDIs among elderly patients across the globe (28.8%) [12]. Additionally, the prevalence was also higher than that reported in cross-sectional studies conducted in Albania (0.8%) [48], Australia (15%) [49], and the USA (7.7%, 10.4%) [50, 51]. This may be due to socioeconomic factors, such as education levels, healthcare infrastructure, and public health initiatives, which can influence how medications are prescribed and managed. These factors may lead to differences in how drug interactions are handled in different countries. Additionally, differences in clinical conditions, study settings, and criteria used to identify and classify DDIs may also contribute to these discrepancies.

In contrast, the findings of the current study were lower than the pooled prevalence of pDDIs in the general population in Ethiopia (72.2%) [52]. This may be due to differences in the study populations, healthcare practices, and prescribing patterns. Moreover, the prevalence was lower than that reported in a study conducted in Croatia (90.6%) [53]. This may be attributed to the presence and effectiveness of pharmacovigilance systems, which monitor and address adverse drug reactions and interactions. These systems may be more robust in Ethiopia, leading to a lower prevalence of pDDIs. Access to healthcare and medication can also differ, with Ethiopia potentially having limited access to certain drugs, making it easier to recognize and avoid pDDIs. In contrast, Croatia, with potentially better access to a wider range of medications, may have a greater risk of pDDIs. In addition to these factors, differences in healthcare systems and practices, such as prescription practices and the monitoring and

management of drug interactions, can also influence the occurrence of pDDIs. Compared with Croatia, Ethiopia may have stricter guidelines or better monitoring systems, leading to fewer interactions.

In terms of the severity of DDIs, the prevalence rates of major and moderate DDIs were 20.59% and 69.4%, respectively. This finding is in line with other studies that reported similar outcomes. A systematic review across the globe reported pooled prevalence of major and moderate DDIs of 28.9% and 54.4%, respectively [54]. This consistency may be due to similarities in patient demographics, methodologies, and criteria used to identify and classify DDIs. The observed discrepancies in the classification of pDDIs with the expected total prevalence, particularly the prevalence of contraindicated (1.59%) and moderate (34.32%) interactions, may be attributed to several factors, including variations in classification systems, differences in clinical settings, and the choice of drug interaction identification databases used to identify drug-drug interaction. Discrepancies may arise due to different DDI classification systems use varying criteria to categorize interactions based on severity. Some databases may prioritize pharmacokinetic interactions, while others emphasize clinical outcomes. For example, one classification system might label an interaction as "moderate" due to a known pharmacokinetic alteration, whereas another might classify it as "major" if clinical consequences are more frequently reported. Additionally, Drug interaction databases differ in terms of their scope, frequency of updates, and underlying evidence sources. Some databases incorporate extensive clinical data, while others primarily rely on theoretical pharmacological interactions. Consequently, the same drug pair might be categorized differently depending on the database used. If a study utilized a database with more conservative classification criteria, this could explain the lower prevalence of contraindicated DDIs [55, 56]. The study population and clinical setting can also influence the prevalence and classification of pDDIs. Hospitalized patients, for instance, may receive more complex medication regimens compared to outpatients, increasing the likelihood of detecting contraindicated or major DDIs. In contrast, outpatient-based studies might report fewer contraindicated DDIs due to differences in prescribing patterns and medication monitoring [17].

The prevalence estimates for potential drug–drug interactions (pDDIs) in Africa among elderly patients identified in this systematic review and meta-analysis show the wide variation, ranging from 2.8 to 90.1%. The wide variation in prevalence estimates for pDDIs identified by this systematic review is similar to that reported in recent reviews. For example, one review reported that prevalence estimates for pDDIs among elderly patients ranged from 0.8 to 90.6% [12], whereas another reported a range of 8.34–100% [13]. The wide variation in the prevalence of pDDIs in the current systematic review and meta-analysis may be due to differences in clinical conditions, the number of comorbidities and medications, and the sources used to identify pDDIs. Previous research also supports this explanation [57]. The high prevalence of pDDIs reported by some studies may be attributed to prescriber issues such as multiple drug prescriptions by multiple prescribers, inadequate knowledge of prescribers on pDDIs, or poor recognition of the relevance of pDDIs [19]. Additionally, certain types of drugs, such as cardiovascular medications, which are commonly involved in pDDIs [8, 13, 20], may contribute to the wide variation in prevalence estimates of this systematic review, as most articles included in this study measure the prevalence of pDDIs for cardiovascular medications. Therefore, studies reporting a high prevalence of pDDIs should be acknowledged. The significant variation in pDDI prevalence suggests that the potential consequences DDIs such as the elevated risk of ADRs in elderly patients may vary greatly depending on factors such as geographic region, local healthcare practices, and patient demographics. The elevated risk of ADRs could lead to treatment failure, worsening comorbidities, and longer hospital stays, placing additional strain on already limited healthcare resources.

However, when the prevalence estimates were pooled in a meta-analysis, there was significant heterogeneity (I^2 statistic of 99.7%) between studies, meaning the variability in effect sizes is almost entirely due to differences between studies rather than random chance, which could be explained by differences in the databases used to identify pDDIs, countries, study settings, and study designs. Subgroup analyses based on the database used showed wide variation in pooled prevalence estimates, ranging from 31.97 to 56.39%. This finding is consistent with a recent review that also reported differences in prevalence estimates on the basis of the database used [12]. The variation could be linked to differences in the DDI database properties. While several DDI screening software programs are available, one limitation is their lack of clinical relevance, which can result in the over reporting of pDDIs [58]. Additionally, the information obtained from one database may differ from that of another. This means that the software itself may have influenced the prevalence estimates. Ideally, multiple sources should be used, and the information should be interpreted carefully. Micromedex® is considered the gold standard and a generic measurement [59]. However, in this review, only two studies assessed pDDIs with Micromedex®, and six studies evaluated pDDIs via more than one database.

Furthermore, the subgroup analysis revealed that the prevalence of pDDIs differed on the basis of the study setting, which revealed that the occurrence of pDDIs was high in outpatient settings (58.07%, 95% CI: 32.23, 83.91)

versus 43.38%, 95% CI: 24.98, 61.78) in the inpatient setting and in the inpatient and outpatient setting (45.97%, 95% CI: -33.03, 124.97). This finding is supported by a previous systematic review and meta-analysis of the general population in Ethiopia [52]. The occurrence of pDDIs in the outpatient setting is greater than that in the inpatient setting, possibly, because outpatients often manage chronic conditions with long-term medication regimens, which can lead to drug prescriptions from different providers without full knowledge of other medications the patient is taking. Over time, the risk of drug interactions can increase as patients accumulate multiple prescriptions [60]. There may also be self-medications and less rigorous or less frequent medication reviews than in inpatient settings, increasing the risk of unintended drug interactions.

This study was also designed to identify factors associated with pDDIs among elderly patients in Africa. Polypharmacy and long hospital stays were significantly associated with pDDIs. Polypharmacy is a major risk factor for pDDIs. Polypharmacy is more common among elderly patients in African this may be due to healthcare is in some African countries often fragmented, with patients visiting multiple healthcare providers, including private clinics, traditional healers, or hospitals. This can lead to overlapping prescriptions for similar conditions, resulting in polypharmacy. The lack of a comprehensive medication review system further complicates the situation. Furthermore, self-medication practices, and healthcare providers' prescribing habits also play a role [61]. This finding is in line with a systematic review in Ethiopia, which revealed that taking five or more medications is an independent factor that leads to pDDIs [52]. The current findings are also in line with those of cross-sectional studies conducted in Iran, Brazil and India, which indicated that taking six or more medications is an important factor for the occurrence of pDDIs [62–64]. This may be attributed to each additional drug increasing the likelihood of interactions. This is supported by a study from Brazil, which revealed that as the number of medications taken by a patient increased, so did the probability of pDDIs [65]. Elderly patients may also require polypharmacy because of their comorbidities. Managing multiple medications can be challenging and increase the risk of medication errors. Long hospital stays, particularly more than seven days, were also associated with the occurrence of pDDIs, which is consistent with previous research [52, 66]. Hospitalized patients are more likely to have multiple illnesses, comorbid conditions, and chronic therapeutic regimens, as well as frequent changes in their medication regimens, which can increase the risk of pDDIs [67].

Being hypertensive and having DM were also associated with the occurrence of pDDIs. This finding is supported by a cross-sectional study in Brazil and Turkey [68, 69]. This could be attributed to the fact that patients with hypertension and diabetes frequently have other comorbid conditions, such as cardiovascular disease, kidney disease, or dyslipidemia, which further necessitate additional medications [70, 71], and hypertension and diabetes often require multiple medications to manage these conditions effectively [70]. This increased number of medications increases the risk of pDDIs. This is supported by a study from Brazil, which revealed that as the number of medications taken by a patient increased, the probability of pDDIs also increased [65]. Furthermore, hypertensive and diabetic patients may also have lifestyle factors that impact drug metabolism or efficacy and frequent changes in treatment regimens to better control these conditions, which can involve changing doses or adding new medications, thereby increasing the likelihood of drug interactions [72].

The current systematic review and meta-analysis highlights the need to adapt standardized methods to identify DDIs really to narrow the wide range of prevalence across studies. The drug–drug interaction database itself could have modified the prevalence of pDDI. Hence, the use of databases with different sensitivities can overestimate and underestimate the prevalence rate of pDDIs. Therefore, a single DDI identification database needs to be authorized; otherwise, a list of DDIs, which is regularly updated to reflect both current clinical practice and emerging evidence of clinically important DDIs, needs to be developed and maintained. This encourages consistency in reporting the prevalence of DDI and reduces the amount of alerts fatigue among health professionals. Furthermore, the pooled prevalence of pDDIs was high. These findings suggest that elderly patients are a natural high-risk population for pDDIs. DDIs are also frequently unavoidable and often predictable medical issues. As a result, each patient should be evaluated individually, pDDIs should be characterized, the risk–benefit ratio should be weighed, and prompt interventions such as medication reviews, improved healthcare provider education, and regional pharmacovigilance systems are needed to enhance patient safety and optimize care in these settings should be implemented to improve the quality of care for the elderly population. Finally, drugs used to treat cardiovascular disorders are frequently prescribed to elderly individuals to treat conditions associated with aging and are involved in the majority of drug–drug interactions. Therefore, healthcare providers in geriatric cardiovascular treatment facilities should prioritize screening, monitoring, and providing special attention to elderly patients. To mitigate these risks, targeted interventions such as medication reviews, improved healthcare provider education, and regional

pharmacovigilance systems are needed to enhance patient safety and optimize care in these settings.

Suggestion for future researchers

Many individuals in Africa use herbal and traditional remedies alongside prescribed medications, which may increase the risk of DDIs. However, there is a lack of sufficient data on the potential interactions between these substances and modern pharmaceuticals. Therefore, further research is needed to explore the role of herbal and traditional medicines in contributing to DDIs, particularly among elderly patients in Africa. Additionally, future studies should focus on conducting longitudinal cohort studies to assess the long-term health outcomes associated with DDIs in elderly populations, including their impact on mortality, morbidity, and quality of life. Research should also prioritize the development and implementation of artificial intelligence [1]-based technologies and robust pharmacovigilance systems to detect, report, and analyze DDIs in real-time. Furthermore, evaluating the potential of mobile health (mHealth) technologies, electronic prescribing systems, and clinical decision support tools in monitoring and preventing DDIs among elderly patients in Africa will be crucial for enhancing patient safety and healthcare outcomes.

Limitations of the study

However, this study offers important clinical and research advantages. The pooled effect of potential drug–drug interactions (pDDIs) among elderly patients in Africa has several limitations. First, the articles included in this review focused primarily on potential drug-drug interactions and did not examine actual drug-drug interactions, primarily due to the lack of studies that directly assessed real-world interactions. This distinction is crucial, as not every pDDI necessarily leads to an actual adverse interaction. Consequently, the evaluation of pDDIs may overestimate the true incidence of clinically significant DDIs, and the findings should be interpreted with caution, as the real-world impact may be lower than what is reported here. Second, significant heterogeneity was observed across the included studies, which may have influenced the pooled estimates of pDDIs. This variability could stem from differences in study settings, methodologies, and the databases used to identify pDDIs. For example, prevalence rates varied by country, with South Africa showing the highest prevalence, followed by Ethiopia. However, due to the limited number of studies from other African countries, the study did not account for potential regional differences across the continent. This lack of geographical diversity in the included studies means that the findings may not fully represent the situation in all African countries. Further research, incorporating more countries and diverse populations, is needed to provide a clearer, more generalized picture. Third, the severity of pDDIs was categorized differently across the included studies. Different methodologies and criteria were used to classify the severity of interactions, which may have led to inconsistencies in how the interactions were reported. These variations in classification could impact the accuracy of the conclusions regarding the severity of pDDIs among elderly patients. A more standardized approach to categorizing the severity of pDDIs is needed to provide more reliable and comparable data across studies.

Conclusion

The current systematic review and meta-analysis identified a notable prevalence of potential drug–drug interactions among elderly patients in Africa, with moderate severity being the most common category. However, significant heterogeneity between studies was observed, which may be attributed to variations in the databases used to identify pDDIs, as well as differences in countries, clinical conditions, study settings, and designs. Factors such as polypharmacy, prolonged hospital stays, hypertension, and diabetes mellitus (DM) were found to be associated with an increased likelihood of pDDIs in this population. The relatively high prevalence of pDDIs among older patients in Africa suggests potential challenges in clinical practice, including the increased risk of adverse drug reactions (ADRs), longer hospitalizations, medication non-adherence, and higher healthcare costs. To address these issues, healthcare systems may benefit from enhanced drug interaction monitoring, improved pharmacovigilance, routine medication reviews, and refined prescribing practices. Additionally, the choice of DDI database used to identify DDIs interactions could have influenced the reported prevalence rates, emphasizing the need for a standardized DDI identification database, or the integration of clinical expertise in interpreting such data.

Appendix: Search terms used

A predetermined combination of search terms was used, including.

- "Prevalence", "occurrence", "pharmacoepidemiology",
- "Potential drug–drug interactions", "inappropriate medication use",
- "Associated factors", "predictors",
- "Elderly", "elder", "older adults", "aged", and "Africa".

Search strategy and results

The search for relevant research articles was conducted via databases such as HINARI, Science Direct, Embase, Thesis Bank, PubMed/MEDLINE, Google Scholar, and Research Gate for English-language publications.

Abbreviations

ADR	Adverse drug reactions
AGS	American Geriatrics Scale
CI	Confidence interval
CVDs	Cardiovascular diseases
DDIs	Drug–drug interactions
MAI	Medication appropriate index
pDDIs	Potential drug–drug interactions
PKs	Pharmacokinetic
PDs	Pharmacodynamics

Supplementary Information

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Supplementary Additional file 2: Quality scores

Supplementary Additional file 3: Sample data extraction format

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Author contributions
TTA conceptualized the study; conceived the idea and design for the work; and was involved in the interpretation, reporting, and manuscript writing. GWG, AAT, YAW, DG, HAS and TM were involved in the search, data extraction, analysis, and review of the article. GT, ASY, SF and TBA made substantial contributions to the quality assessment of the included studies and the drafting of the manuscript. All the authors contributed to the article and approved the submitted version.

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References

1. Hadjibabaie M, Badri S, Ataei S, Moslehi AH, Karimzadeh I, Ghavamzadeh A. Potential drug–drug interactions at a referral hematology–oncology ward in Iran: a cross-sectional study. Cancer Chemother Pharmacol. 2013;71:1619–27.
2. Marusic S, Bacic-Vrca V, Obreli Neto PR, Franic M, Erdeljic V, Gojo-Tomic N. Actual drug–drug interactions in elderly patients discharged from internal medicine clinic: a prospective observational study. Eur J Clin Pharmacol. 2013;69:1717–24.
3. Magro L, Moretti U, Leone R. Epidemiology and characteristics of adverse drug reactions caused by drug–drug interactions. Exp Opin Drug Saf. 2012;11(1):83–94.
4. Varma MV, Pang KS, Isoherranen N, Zhao P. Dealing with the complex drug–drug interactions: towards mechanistic models. Biopharm Drug Dispos. 2015;36(2):71–92.
5. Bjornsson T, Pharmaceutical Research, Manufacturers of America (PhRMA) Drug Metabolism/Clinical Pharmacology Technical Working Group; FDA Center for Drug Evaluation and Research (CDER). The conduct of in vitro and in vivo drug-drug interaction studies: a pharmaceutical research and manufacturers of America (PhRMA) perspective. Drug Metab Dispos. 2003;31(7):815–32.
6. Marengoni A, Pasina L, Concoreggi C, Martini G, Brognoli F, Nobili A, et al. Understanding adverse drug reactions in older adults through drug–drug interactions. Eur J Intern Med. 2014;25(9):843–6.
7. Davies E, O'mahony M. Adverse drug reactions in special populations–the elderly. Br J Clin Pharmacol. 2015;80(4):796–807.
8. Bastida C, Grau A, Márquez M, Tuset M, De Lazzari E, Martínez E, et al. Polypharmacy and potential drug-drug interactions in an HIV-infected elderly population. Farm Hosp. 2017;41(5):618–24.
9. Routledge PA, O'mahony M, Woodhouse K. Adverse drug reactions in elderly patients. Br J Clin Pharmacol. 2004;57(2):121–6.
10. Chen Y, Zhu L-L, Zhou Q. Effects of drug pharmacokinetic/pharmacodynamic properties, characteristics of medication use, and relevant pharmacological interventions on fall risk in elderly patients. Therapeut Clinic Risk Manag. 2014:43–48.
11. Shetty V, Chowta MN, Chowta KN, Shenoy A, Kamath A, Kamath P. Evaluation of potential drug-drug interactions with medications prescribed to geriatric patients in a tertiary care hospital. J Aging Res. 2018;2018(1):5728957.
12. 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;40(2):117–34.
13. de Oliveira LM, Diel JAC, Nunes A, Dal Pizzol TS. Prevalence of drug interactions in hospitalised elderly patients: a systematic review. Eur J Hosp Pharm. 2021;28(1):4–9.
14. Alssageer MA, Sherif FM, Mohammed ES, Abd Alsalm SA. Pattern of drug prescribed and drug related problems among hospitalized elderly patients. Mediterranean J Pharm Pharm Sci. 2023;2(2):66–78.
15. Bojuwoye AO, Suleman F, Perumal-Pillay VA. Polypharmacy and the occurrence of potential drug–drug interactions among geriatric patients at the outpatient pharmacy department of a regional hospital in Durban, South Africa. J Pharm Policy Pract. 2022;15:1–12.
16. Yusuff KB, Okoh CN. Frequency, types and factors associated with potentially harmful drug interactions in ambulatory elderly patients in Nigeria. Int J Pharm Pract. 2015;23(5):353–6.
17. Alemayehu TT, Wassie YA, Bekalu AF, Tegegne AA, Ayenew W, Tadesse G, et al. Prevalence of potential drug–drug interactions and associated factors among elderly patients in Ethiopia: a systematic review and meta-analysis. Global Health Res Policy. 2024;9(1):46.
18. Schneider KL, Kastenmüller K, Weckbecker K, Bleckwenn M, Böhme M, Stingl JC. Potential drug-drug interactions in a cohort of elderly, polymedicated primary care patients on antithrombotic treatment. Drugs Aging. 2018;35:559–68.

19. Aljadani R, Aseeri M. Prevalence of drug–drug interactions in geriatric patients at an ambulatory care pharmacy in a tertiary care teaching hospital. BMC Res Notes. 2018;11:1–7.
20. Holm J, Eiermann B, Eliasson E, Mannheimer B. A limited number of prescribed drugs account for the great majority of drug-drug interactions. Eur J Clin Pharmacol. 2014;70:1375–83.
21. Obreli-Neto PR, Nobili A, de Oliveira Baldoni A, Guidoni CM, de Lyra Júnior DP, Pilger D, et al. Adverse drug reactions caused by drug–drug interactions in elderly outpatients: a prospective cohort study. Eur J Clin Pharmacol. 2012;68:1667–76.
22. Bucşa C, Farcaş A, Cazacu I, Leucuta D, Achimas-Cadariu A, Mogosan C, et al. How many potential drug–drug interactions cause adverse drug reactions in hospitalized patients? Eur J Intern Med. 2013;24(1):27–33.
23. Qorraj-Bytyqi H, Hoxha R, Krasniqi S, Bahtiri E, Kransiqi V. The incidence and clinical relevance of drug interactions in pediatrics. J Pharmacol Pharmacotherapeutics. 2012;3(4):304.
24. Zheng WY, Richardson L, Li L, Day R, Westbrook J, Baysari M. Drug-drug interactions and their harmful effects in hospitalised patients: a systematic review and meta-analysis. Eur J Clin Pharmacol. 2018;74:15–27.
25. Steinman MA. Polypharmacy and the balance of medication benefits and risks. Am J Geriatr Pharmacother. 2007;5(4):314–6.
26. Becker ML, Kallewaard M, Caspers PW, Visser LE, Leufkens HG, Stricker BH. Hospitalisations and emergency department visits due to drug–drug interactions: a literature review. Pharmacoepidemiol Drug Saf. 2007;16(6):641–51.
27. Rosas-Carrasco Ó, García-Peña C, Sánchez-García S, Vargas-Alarcón G, Gutiérrez-Robledo LM, Juárez-Cedillo T. The relationship between potential drug-drug interactions and mortality rate of elderly hospitalized patients. Rev Invest Clin. 2011;63(6):564–73.
28. Riechelmann RP, Del Giglio A. Drug interactions in oncology: how common are they? Ann Oncol. 2009;20(12):1907–12.
29. Kovačević M, Vezmar Kovačević S, Miljković B, Radovanović S, Stevanović P. The prevalence and preventability of potentially relevant drug-drug interactions in patients admitted for cardiovascular diseases: A cross-sectional study. Int J Clin Pract. 2017;71(10):e13005.
30. Kothari N, Ganguly B. Potential drug-drug interactions among medications prescribed to hypertensive patients. J Clin Diagn Research: JCDR. 2014;8(11):HC01.
31. Moura CS, Prado NM, Belo NO, Acurcio FA. Evaluation of drug–drug interaction screening software combined with pharmacist intervention. Int J Clin Pharm. 2012;34:547–52.
32. Nasuhara Y, Sakushima K, Endoh A, Umeki R, Oki H, Yamada T, et al. Physicians' responses to computerized drug interaction alerts with password overrides. BMC Med Inf Decis Mak. 2015;15:1–6.
33. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg. 2021;88:105906.
34. Zeng X, Zhang Y, Kwong JS, Zhang C, Li S, Sun F, et al. The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review. J evidence-based Med. 2015;8(1):2–10.
35. Adem L, Tegegne GT. Medication appropriateness, polypharmacy, and drug-drug interactions in ambulatory elderly patients with cardiovascular diseases at Tikur Anbessa specialized hospital, Ethiopia. Clin Interv Aging. 2022;509:17.
36. Assefa YA, Kedir A, Kahaliw W. Survey on polypharmacy and drug-drug interactions among elderly people with cardiovascular diseases at Yekatit 12 hospital, Addis Ababa, Ethiopia. Integr Pharm Res Pract. 2020:1–9.
37. Dagnew SB, Tadesse TY, Zeleke MM, Yiblet TG, Addis GT, Mekonnen GB, et al. Drug–drug interactions among hospitalized elderly in patients at medical wards of Northwest Ethiopia's comprehensive specialized hospitals: A multicenter observational study. SAGE Open Med. 2022;10:20503121221135874.
38. Teni FS, Gedif T. Prevalence and predictors of inappropriate medications prescribing among elderly outpatients at a university hospital in Northwestern Ethiopia: a retrospective cross-sectional study. Ethiop Pharm J. 2015;30(2):124–32.
39. Bhagavathula AS, Seid MA, Adane A, Gebreyohannes EA, Brkic J, Fialová D. Prevalence and determinants of Multimorbidity, polypharmacy, and potentially inappropriate medication use in the older outpatients: findings from EuroAgeism H2020 ESR7 project in Ethiopia. Pharmaceuticals. 2021;14(9):844.
40. Dagnew SB, Binega Mekonnen G, Gebeye Zeleke E, Agegnew Wondm S, Yimer Tadesse T. Clinical pharmacist intervention on drug-related problems among elderly patients admitted to medical wards of Northwest Ethiopia comprehensive specialized hospitals: a multicenter prospective, observational study. Biomed Res Int. 2022;2022(1):8742998.
41. Fadare JO, Ajayi AE, Adeoti AO, Desalu OO, Obimakinde AM, Agboola SM. Potential drug-drug interactions among elderly patients on anti-hypertensive medications in two tertiary healthcare facilities in Ekiti State, South-West Nigeria. Sahel Med J. 2016;19(1):32–7.
42. Abdu N, Teweldemedhin S, Mosazghi A, Asfaha L, Teshale M, Kibreab M et al. Non-steroidal anti-inflammatory drugs: Usage and co-prescription with other potentially interacting drugs in elderly: a cross-sectional study. 2019.
43. Saka SA, Yusuf AA. Drug therapy problem in elderly outpatients with benign prostatic hyperplasia. West Afr J Pharm. 2021;32(1):33–44.
44. Dube SO. Prevalence of over the counter (OTC) medicine use and the potential of drug-drug interactions with concomitant prescription medicine use at an old age home in Johannesburg. 2023.
45. Teka F, Teklay G, Ayalew E, Teshome T. Potential drug–drug interactions among elderly patients admitted to medical ward of ayder referral hospital, Northern Ethiopia: a cross sectional study. BMC Res Notes. 2016;9:1–8.
46. Van Heerden JA. Assessment of potentially inappropriate medicine prescribing for elderly patients in the South African private health sector. North-West University (South Africa), Potchefstroom Campus; 2016.
47. Fitzmaurice MG, Wong A, Akerberg H, Avramovska S, Smithburger PL, Buckley MS, et al. Evaluation of potential drug–drug interactions in adults in the intensive care unit: a systematic review and meta-analysis. Drug Saf. 2019;42:1035–44.
48. Harasani K, Xhafaj D, Begolli A, Olvera-Porcel MC. Prevalence of potentially inappropriate prescriptions in primary care and correlates with mild cognitive impairment. Pharm Pract (Granada). 2020;18(3).
49. Roughead EE, Kalisch LM, Barratt JD, Gilbert AL. Prevalence of potentially hazardous drug interactions amongst Australian veterans. Br J Clin Pharmacol. 2010;70(2):252–7.
50. Patel R, Zhu L, Sohal D, Lenkova E, Koshki N, Woelfel J, et al. Use of 2015 beers criteria medications by older medicare beneficiaries. Consultant Pharmacist®. 2018;33(1):48–54.
51. Naples JG, Marcum ZA, Perera S, Newman AB, Greenspan SL, Gray SL, et al. Impact of drug–drug and drug–disease interactions on gait speed in community-dwelling older adults. Drugs Aging. 2016;33:411–8.
52. Ayenew W, Asmamaw G, Issa A. Prevalence of potential drug-drug interactions and associated factors among outpatients and inpatients in Ethiopian hospitals: a systematic review and meta-analysis of observational studies. BMC Pharmacol Toxicol. 2020;21:1–13.
53. Bacic-Vrca V, Marusic S, Erdeljic V, Falamic S, Gojo-Tomic N, Rahelic D. The incidence of potential drug–drug interactions in elderly patients with arterial hypertension. Pharm World Sci. 2010;32:815–21.
54. Bories M, Bouzillé G, Cuggia M, Le Corre P. Drug–drug interactions in elderly patients with potentially inappropriate medications in primary care, nursing home and hospital settings: a systematic review and a preliminary study. Pharmaceutics. 2021;13(2):266.
55. Roblek T, Vaupotic T, Mrhar A, Lainscak M. Drug-drug interaction software in clinical practice: a systematic review. Eur J Clin Pharmacol. 2015;71:131–42.
56. Kongsholm GG, Nielsen AKT, Damkier P. Drug interaction databases in medical literature: transparency of ownership, funding, classification algorithms, level of documentation, and staff qualifications. A systematic review. Eur J Clin Pharmacol. 2015;71:1397–402.
57. Hines LE, Murphy JE. Potentially harmful drug–drug interactions in the elderly: a review. Am J Geriatr Pharmacother. 2011;9(6):364–77.
58. Roblek T, Trobec K, Mrhar A, Lainscak M. Potential drug-drug interactions in hospitalized patients with chronic heart failure and chronic obstructive pulmonary disease. Archives Med Sci. 2014;10(5):920–32.
59. Kheshti R, Aalipour M, Namazi S. A comparison of five common drug–drug interaction software programs regarding accuracy and comprehensiveness. J Res Pharm Pract. 2016;5(4):257–63.
60. Riechelmann RP, Tannock IF, Wang L, Saad ED, Taback NA, Krzyzanowska MK. Potential drug interactions and duplicate prescriptions among cancer patients. J Natl Cancer Inst. 2007;99(8):592–600.
61. Leikola S. Development and application of comprehensive medication review procedure to community-dwelling elderly. [dissertation]. Helsinki: Dissertationes Biocentri Viikki Universitatis Helsingiensis, Helsinki University Printing House; 2012;48:65.
62. Mousavi S, Ghanbari G. Potential drug-drug interactions among hospitalized patients in a developing country. Caspian J Intern Med. 2017;8(4):282.

63. Cruciol-Souza JM, Thomson JC. Prevalence of potential drug-drug interactions and its associated factors in a Brazilian teaching hospital. J Pharm Pharm Sci. 2006;9(3):427–33.
64. Kashyap M, D'Cruz S, Sachdev A, Tiwari P. Drug-drug interactions and their predictors: results from Indian elderly inpatients. Pharm Pract. 2013;11(4):191.
65. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. Exp Opin Drug Saf. 2014;13(1):57–65.
66. Ismail M, Aziz S, Noor S, Haider I, Shams F, Haq I, et al. Potential drug-drug interactions in pediatric patients admitted to intensive care unit of Khyber teaching hospital, Peshawar, Pakistan: A cross-sectional study. J Crit Care. 2017;40:243–50.
67. Zwart-van Rijkom JE, Uijtendaal EV, Ten Berg MJ, Van Solinge WW, Egberts AC. Frequency and nature of drug–drug interactions in a Dutch university hospital. Br J Clin Pharmacol. 2009;68(2):187–93.
68. Trevisan DD, Silva JB, Póvoa VC, Araujo CP, Oliveira HC, Araújo EP, et al. Prevalence and clinical significance of potential drug-drug interactions in diabetic patients attended in a tertiary care outpatient center. Brazil Int J Diabetes Developing Ctries. 2016;36:283–9.
69. Subramanian A, Adhimoolam M, Kannan S. Study of drug–Drug interactions among the hypertensive patients in a tertiary care teaching hospital. Perspect Clin Res. 2018;9(1):9–14.
70. Ren W, Liu Y, Jiang H, Lv X, Zhang N. Epidemiology of potential drug-drug interactions in hospitalized patients with type 2 diabetes mellitus in China: a retrospective study. Front Endocrinol. 2024;15:1387242.
71. Kameswaran R, Praveen M, Krishnaveni K, Sambathkumar R. An assessment of potential Drug-Drug interactions in hypertensive patients in A tertiary care hospital. Age. 2019;255(3560):6439.
72. Perić A, Udilović A, Dobrić S, Vezmar Kovačević S. The impact of treatment choices on potential drug–drug interactions in hypertensive patients. Br J Clin Pharmacol. 2022;88(5):2340–8.

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