Drug Safety (2020) 43:517–537
https://doi.org/10.1007/s40264-020-00918-3

SYSTEMATIC REVIEW

# Prevalence and Nature of Medication Errors and Medication-Related Harm Following Discharge from Hospital to Community Settings: A Systematic Review

Fatema A. Alqenae[1] · Douglas Steinke[1] · Richard N. Keers[1,2]

Published online: 3 March 2020


## Abstract

**Background** Little is known about the epidemiology of medication errors and medication-related harm following transition from secondary to primary care. This systematic review aims to identify and critically evaluate the available evidence on the prevalence and nature of medication errors and medication-related harm following hospital discharge.

**Methods** Studies published between January 1990 and March 2019 were searched across ten electronic databases and the grey literature. No restrictions were applied with publication language or patient population studied. Studies were included if they contained data concerning the rate of medication errors, unintentional medication discrepancies, or adverse drug events. Two authors independently extracted study data.

**Results** Fifty-four studies were included, most of which were rated as moderate (39/54) or high (7/54) quality. For adult patients, the median rate of medication errors and unintentional medication discrepancies following discharge was 53% [interquartile range 33–60.5] ($n=5$ studies) and 50% [interquartile range 39–76] ($n=11$), respectively. Five studies reported adverse drug reaction rates with a median of 27% [interquartile range 18–40.5] and seven studies reported adverse drug event rates with a median of 19% [interquartile range 16–24]. For paediatric patients, one study reported a medication error rate of 66.3% and another an adverse drug event rate of 9%. Almost a quarter of studies (13/54, 24%) utilised a follow-up period post-discharge of 1 month (range 2–180 days). Drug classes most commonly implicated with adverse drug events were antibiotics, antidiabetics, analgesics and cardiovascular drugs.

**Conclusions** This is the first systematic review to explore the prevalence and nature of medication errors and adverse drug events following hospital discharge. Targets for future work have been identified.

## Key Points

Studies found that the median rate of medication error ($n=5$) or unintentional medication discrepancy ($n=11$) was nearly 50% in adult and elderly patients after hospital discharge.

Nearly 20% of adult and elderly patients in studies ($n=7$) were reported to be affected by adverse drug events (ADEs) after hospital discharge.

Drug classes most commonly reported with ADEs post-hospital discharge were antibiotics, antidiabetics, analgesics and cardiovascular drugs.

Further research is needed to examine the burden of medication errors, preventable ADEs and ADEs post-hospital discharge in all populations, in particular paediatric populations.

Prior publication: This project has been presented as a poster at the Prescribing and Research In Medicines Management (PRIMM) UK and Ireland 30th Annual Scientific Meeting (14 December, 2018, London, UK), "A Systematic Review of Medication Errors and Medication Related Harm Post Hospital Discharge". An abstract of this submission is published in *Pharmacoepidemiology and Drug Safety*, Volume 28, Issue S1. In addition, this project was presented as a poster at the HSJ Patient Safety Congress in Manchester, UK on 2–3 July, 2019, "How Common are Medication Errors and Medication Related Harm After Hospital Discharge? A Systematic Review".

**Electronic supplementary material** The online version of this article (https://doi.org/10.1007/s40264-020-00918-3) contains supplementary material, which is available to authorized users.

✉ Fatema A. Alqenae
Fatema.alqenae@postgrad.manchester.ac.uk

Extended author information available on the last page of the article

## 1 Introduction

Transitions of care can be defined as "changes in the level, location, or providers of care as patients move within the healthcare system" [1]. Whilst they are intended to be seamless and safe, care transitions are known to place patients at risk of adverse outcomes including medication errors (MEs), missed test results and adverse events including hospital readmission [2].

As healthcare providers may be poorly affiliated across care boundaries, miscommunication during handoff makes the transition of care a fertile ground for MEs and preventable harm [3]. In March 2017, the burden of risk associated with medication safety at the transfer of care was brought to the global attention with the publication of the World Health Organization (WHO) Third Global Patient Safety Challenge: Medication Without Harm, where transitions featured as one of three priorities for action [4].

Medication safety challenges at the point of hospital admission have been well documented [5, 6] but these issues may also occur shortly after hospital discharge. The time period immediately following hospital discharge can be a challenging time for patients, both in terms of safety but also socially and emotionally, when patients may be anxious and suffer with functional impairment [7]. This in turn may have an impact on medication adherence, and may increase the risk of adverse drug events (ADEs) (see Sect. 2.2 for the terminology of medication safety terms) [8, 9]. Medication regimes are often known to undergo significant changes during hospitalisation, where medications may be stopped, replaced, and undergo changes in doses or frequency and new medications may be initiated [10]. Communication gaps may compound the risk and include delayed/lack of discharge letters, insufficient monitoring plans [3, 11] and incomplete or poor-quality discharge summaries [12, 13]. Recent evidence indicates that adverse drug reaction (ADR)-related hospital readmissions occur with a median rate of 20% of patients [interquartile range (IQR) 7–23] ($n=4$), and ADE-related hospital readmissions with a rate of 13% ($n=1$) [14]. Unjustified medication at hospital discharge may not only affect patient safety but may also be associated with a high financial burden [15].

There is an emerging body of literature that reports on the prevalence and nature of MEs and ADEs [16] as well as medication discrepancies [17–19] at the point of hospital discharge (i.e. before patients return home). In contrast, our collective understanding from available studies investigating the burden of MEs and ADEs in the period following hospital discharge to the community is limited, owing in part to there being no up-to-date published systematic reviews on this topic across all patient groups. One previous systematic review of drug-related problems occurring post-hospital discharge in elderly populations was published almost 10 years ago [20] and another from 2018 focused on medication-related harm also in elderly populations [21]. Given the level of interest in this stage of the patient journey amongst health leaders [22] and as new studies emerge in the field [23, 24], there is a need to identify and collectively appraise global evidence on the burden and nature of MEs/ADEs post-hospital discharge across populations to best inform the development of remedial interventions and advance the WHO patient safety agenda. This systematic review therefore aimed to identify and critically appraise the available international evidence on the prevalence and nature of MEs and ADEs following transition of care from hospital to community settings.

## 2 Methods

This systematic review follows the criteria specified in the "Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA)", 2015 statement [25]. A PRISMA checklist is included in Appendix 1 of the Electronic Supplementary Material (ESM).

### 2.1 Search Strategy

Ten electronic databases were searched: MEDLINE, EMBASE, International Pharmaceutical Abstracts (IPA), Health Management Information Consortium (HMIC), PsycINFO, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Web of Science [26, 27]. A grey literature search was completed using Open Grey via the website http://www.opengrey.eu that is based on the "System for Information on Grey Literature in Europe" (SIGLE) database. The grey literature includes unpublished research (e.g. dissertations or theses), published non-research literature (e.g. government reports or newsletters), studies in progress and recently published studies pending to be referenced in databases [28].

The search was limited to between January 1990 and March 2019. The search strategy was developed using terms related to three categories; epidemiology, process and outcomes. The search included the following keywords and their synonyms: ('rate' OR 'prevalen*') AND ('hospital discharge*' OR 'care transition*') AND ('medication error*' OR 'adverse drug event*'). Search terms underwent minor modification to suit different databases. An example of the search strategy is included in Appendix 2 of the ESM.

## 2.2 Definitions

Studies that reported events broadly meeting our adapted outcome definitions (see Table 1) were included. Unintentional medication discrepancies (UMDs) were considered MEs but were reported separately. Studies reporting prescribing errors and medication administration errors were considered MEs. Studies evaluating drug-related problems were included if they explicitly reported distinct ME or drug-related harm data and rates were able to be subsequently extracted. Studies evaluating medication adherence were not included as our focus was on iatrogenic complications. The patient populations were considered to be/include the elderly if studies predominantly included patients with chronological age ≥ 60 years, or if studies said/implied they were studying elderly patients [29, 30].

## 2.3 Inclusion Criteria

Quantitative studies that reported a rate of MEs, UMDs, and/or medication-related harm including ADRs and/or ADEs identified during the time period following hospital discharge to community settings (or provided enough data to calculate a rate manually) were sought. Studies were included if data were collected after discharge to community settings including the patients' own home, care/nursing homes, rehabilitation/intermediate care facilities and other long-term care facilities. Interventional studies were only included if they provided baseline data on outcome rates. Grey literature and all original peer-reviewed research except review and editorial articles were included. The reference lists of relevant reviews/editorials were screened for additional studies. Conference abstracts were included only if they provided suitable data regarding ME/UMD or drug-related harm rates (or enough data to calculate these). No restrictions were applied to the age or groups of patient populations included. No language restriction was applied.

## 2.4 Exclusion Criteria

Studies that reported an estimated denominator or those that did not use empirically collected data (data gathered by experimentation or observation) were excluded. Studies restricted to measuring non-adherence, or potentially inappropriate prescribing were excluded. Studies that measured outcomes of interest arising from interviews and questionnaires, or used data from incident reporting systems alone were also ineligible because of reporting and hindsight bias [37]. Studies that reported outcome rates for a specialised ward(s)/ward group(s)/hospital(s) [e.g. oncology, cardiac], a single disease, single drug class, single drug or pre-defined drug class were excluded, as the review intended to produce generalisable findings. Studies that reported outcome rate data limited to events arising from new or altered medication regimes during hospitalisation or at discharge were excluded. Finally, studies were excluded if they predominantly focused on patients discharged home from the emergency department or those with regular planned admissions.

## 2.5 Screening Process

The study screening process was completed by the lead researcher based on the inclusion and exclusion criteria. Initially, duplicate titles were removed followed by the title screening stage and then an abstract screening stage [38]. This was followed by full-text screening along with

**Table 1** Definitions

| Term | Definition |
|---|---|
| Adverse drug reactions (ADRs) | "A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function" [31] |
| Adverse drug events (ADEs) | "An injury resulting from medical intervention related to drug" [32] |
| Preventable adverse drug events (pADEs) | "Harm caused by the use of a drug as a result of an error" [33] |
| Medication errors (MEs) | "A medication error is any preventable event 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. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labelling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use" [34] |
| Unintentional medication discrepancies (UMD) | ''Difference between medications taken by a patient prior to admission and medications ordered in the hospital" [35]. Pippins [35] stated that discrepancies are either intentional (not an error, either documented or not) or unintentional (medication error). For our study we included only unintentional medication discrepancies, using an adapted definition by Mueller et al. [36] "unexplained differences in documented medication regimens across different cite of care" |

the identification of additional studies from the reference lists of included studies and relevant review articles. Titles, abstracts and full texts that were considered unclear for inclusion were discussed with the review team and consensus reached.

Papers published in non-English language had their English abstract screened for inclusion. The abstract mentioning discharge and medication had their full paper translated into English by Google Translate® for inclusion. Google Translate® was found to be around 90% accurate in a recent study by Jackson et al. [39]. If the study was deemed potentially relevant and considered for a full-text review, a medically trained native speaker would be sought to translate the paper [40]. However, no non-English language papers were found relevant for a full-text review.

### 2.6 Data Extraction

Data extraction for each included study was carried out independently by two reviewers using a standardised tool in Appendix 3 of the ESM. The data extraction tool contents were imported into Microsoft Excel®, 2010 (Microsoft, Redmond, WA, USA) for analysis, where each row represented one publication. The reviewers then met to discuss the results and resolve any discrepancies.

Published study authors were contacted for missing or unclear information. Authors of conference abstracts were contacted to determine if a full-text publication was available. Each author was contacted a maximum of three times, over 8 weeks; if no answer was provided, then the paper was excluded [41]. For all screened papers and the cohort of included papers, the author response rate following contact attempts was 55% (76/139) and 61.5% (24/39), respectively.

### 2.7 Quality Assessment

Prior to inclusion, exclusion criteria were applied to ensure included studies presented empirically collected data with a suitable denominator [42]. The second stage of quality assessment was completed by the lead researcher using an adapted, validated quality appraisal framework for medication safety studies established by Allan and Barker [43]. The framework used to assess the quality of included studies was originally made to assess ME studies; however, we have adapted the tool to assess the quality of ME and ADE studies. This framework has been successfully applied in other systematic reviews of MEs and ADEs [44–47]. The framework appraises study internal validity by assessing the quality of outcome reporting.

### 2.8 Data Synthesis

Outcome event rates including ME, UMD, ADE and ADR rates were calculated as either the denominator value affected by at least one event (numerator) per total denominator value (e.g. patients affected by at least one ME over total number of included patients), or as the total number of events per total denominator value (e.g. total number of MEs per total number of patients). Denominator values were either discharged patients, doses administered, individual prescribed medications or whole prescriptions. Only studies that provided the outcome rate using the denominator value affected by at least one event (numerator) were used in median (IQR) calculations to avoid inflating outcome rates if more than one event could be counted per denominator value.

The degree of heterogeneity of the included studies meant that a meta-analysis of the data was not possible. Instead, median outcome rates for different medication safety outcome denominators and studies focusing on particular age groups were calculated along with interquartile ranges (IQRs). Comparisons were drawn between studies and basic descriptive statistics provided for the country/year of origin, method of data collection, definitions of outcome events, severity of outcome events and medication types/classes involved. Medication classes implicated with events were considered ‘common’ if they were reported at least in four studies as being within the top three most common medications involved in safety events.

## 3 Results

### 3.1 Overview of Included Studies

The total number of citations identified was 22,082. After removing duplicates, this number fell to 16,571. The PRISMA flow diagram (Fig. 1) illustrates the citation review stages. All included studies are summarised in one table in Appendix 4 of the ESM, followed by tables in Appendixes 5–8 of the ESM, which summarise these studies based on the medication safety measure (ME, ADE, ADR, UMD).

In total, 54 studies were included in the systematic review, including 20,895 hospital discharges across 26 countries. The included studies consisted of 41 published papers [23, 24, 48–86] and 13 conference abstracts [87–99]. One of the included conference abstracts [88] was combined with one letter to the editor [100]. All included studies were published in English.

The majority of included studies were conducted in the United States of America (USA) (17/54, 31.5%) [52, 54–57, 61, 70, 74, 76, 78, 79, 82, 89, 90, 94, 96, 97], followed by

the United Kingdom (UK) (7/54, 13%) [24, 49, 50, 59, 87, 95, 98]. Forty-three (79.6%) studies were published from the year 2010 onwards [23, 24, 51–53, 56–61, 64–70, 72, 73, 75–82, 84, 85, 87–99]. Of the 54 studies, 28 (51.8%) included adult patients, 18 (33.3%) focused specifically on elderly patients. Three studies (5.5%) were exclusively conducted in paediatric patients [75, 86, 95]. Most studies (85.2%, 46/54) were prospective in design [23, 24, 48–52, 54, 55, 57–60, 63–78, 80, 81, 83, 85, 86, 89–93, 95–99].

Seventy six percent of studies (41/54) included patients who were discharged home [24, 49–54, 56–59, 61, 62, 64, 65, 67–72, 74–82, 85–88, 92, 94–99], with three (5.5%) including patients discharged to nursing homes [60, 66, 98]. The most frequent data collection method was screening case summaries [e.g. discharge medical record and discharge summary] (43/54, 79.6%), followed by telephone follow-up interviews with the patient (25/54, 46.2%). Data collectors were mostly pharmacists (27/54, 50%). Almost a quarter of included studies (13/54, 24%) utilised a follow-up period post-discharge of 1 month, with the next most common time period being 1 week (7/54, 12.9%). The shortest follow-up period was 2 days and the longest was 180 days. Table 2 summarises key study characteristics.

### 3.2 Quality Assessment of Included Studies

A summary of the quality assessment of included studies is provided in Table 3. The quality assessment score was low (score = 1–4) in 14.8% of studies (8/54), moderate (score = 5–8) in 72.2% (39/54) and high (score = 9–12) in 12.9% (7/54). The aim and objectives were clearly described in all but one paper [96] and the outcome definition was clearly mentioned in 27 papers [24, 49, 50, 53, 54, 56, 58–62, 64, 68–70, 72, 75, 76, 79–86, 88]. In studies that measured drug-related problems (DRPs) but also reported data on MEs/ADEs, reported definitions of DRPs were accepted. The definition of a DRP was provided in six studies [53, 56, 58, 76, 79, 81] out of the cohort of 27 studies that mentioned outcome definitions. Error categories were mentioned in 14 studies [23, 24, 60, 61, 65, 70–72, 75, 81, 85, 87, 90, 97] but were only defined in five studies [60, 72, 75, 85, 87]. The outcome denominator was clearly defined in all papers and the data collection method was described clearly in all but one study [91]. The study setting was clearly described in all but six studies [73, 80, 90, 91, 93, 98]. Validity measures, to assess if independent personnel or an expert panel evaluated the event other than the data collector, were applied in 29 studies [23, 24, 48, 50, 54–59, 61, 62, 64–67, 69, 70, 72, 74, 77–80, 83, 84, 86, 94, 95] to confirm the occurrence of medication safety outcomes. Reliability measures to evaluate if a formal test/evaluation (e.g. Kappa test or consensus) was completed to assess inter-rater reliability were applied in 12 studies [24, 50, 54, 61, 65, 66, 70, 74, 78–80, 83]. Nearly two thirds of the included papers reported their limitations with 16 papers (including 11 conference abstracts [49, 58, 67, 68, 86, 89–99]) not reporting this information. Only nine studies [24, 59, 60, 63, 75, 80, 81, 83, 98] calculated sample size, with five studies [60, 75, 77, 83, 98] describing any assumptions made.

### 3.3 Medication Error Studies

In total, 12 studies [23, 65, 71, 72, 75, 85, 87, 89, 90, 96, 97, 99] reported data concerning the frequency of MEs. Six studies used established definitions of MEs [23, 71, 72, 75, 85, 87], with one study developing their own definition [90], and five not reporting any definition [65, 89, 96, 97, 99]. Five studies [71, 72, 87, 90, 97] reported data specifically concerning prescribing errors, of which two [72, 87] used the prescribing error definition proposed by Dean et al. [101].

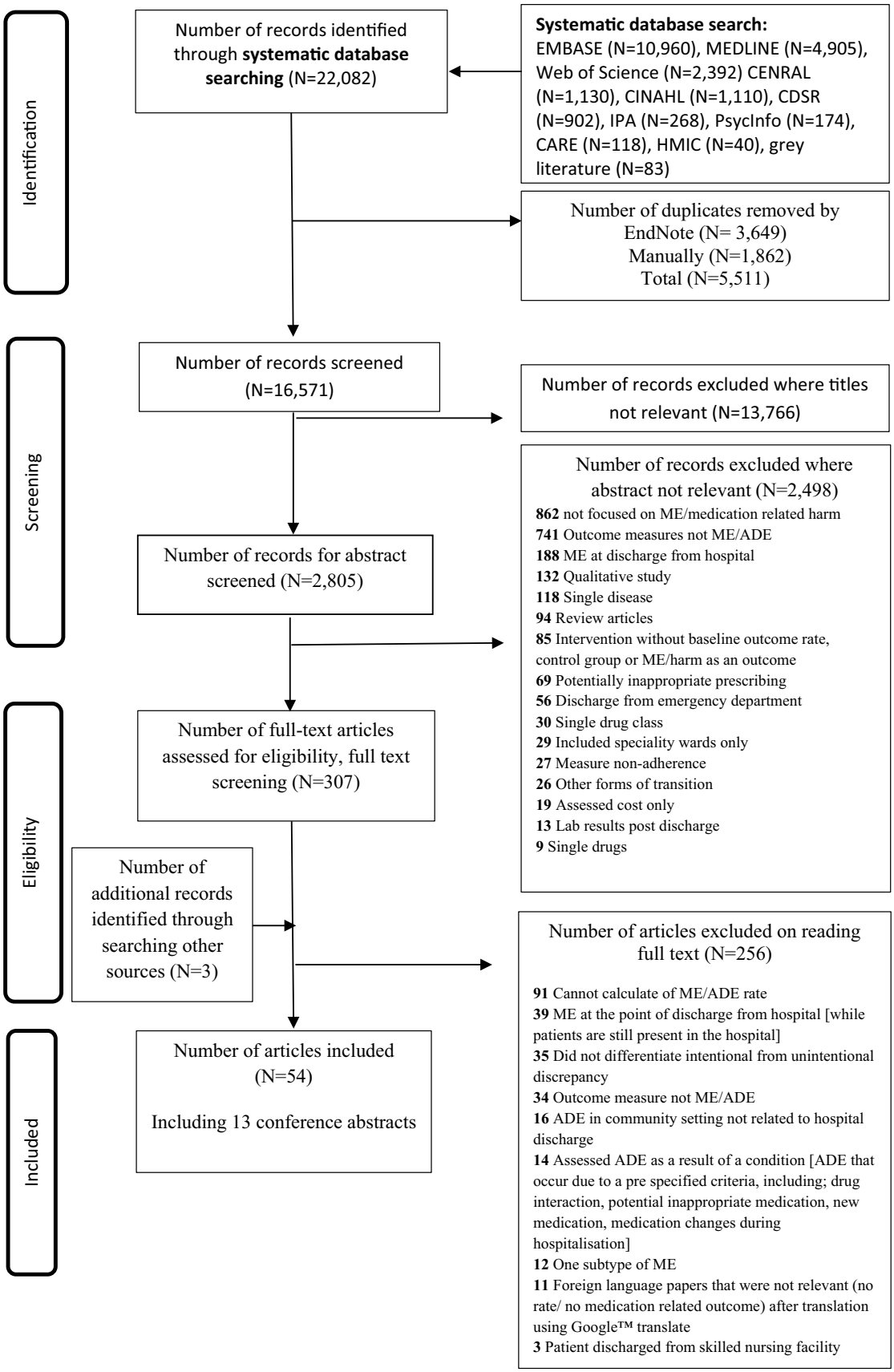
All studies explicitly used the number of discharged patients as their denominator. Seven studies that used patients affected by at least one ME as their numerator are summarised below [23, 72, 75, 87, 89, 96, 99]. Across five studies from three settings that reported ME rates per discharged patient [23, 87, 89, 96, 99], a median of 53% [IQR 33–60.5%] of adult and elderly patients experienced MEs post-discharge. Two prospective studies [96, 99] out of these five reported ME rates for patients discharged home as 47–53% of discharged patients. A range of 19–53% of elderly discharged patients ($n = 2$) experienced at least one ME post-discharge [23, 96].

One study [72] reported that one or more prescribing errors affected 43% of discharged patients. Another study [87] reported that 3.5% of discharge medications were affected by at least one monitoring error post-discharge. One study [61] reported ME and medication administration error rates for infants as 66.3% and 54.0% of discharged patients, respectively.

### 3.4 Unintentional Medication Discrepancy Studies

In total, 14 studies reported data concerning the frequency of UMDs [49, 50, 57, 59, 60, 66, 70, 74, 83, 84, 88, 93, 95, 98]. Three studies [83, 84, 93] used an established UMD definition, seven [49, 50, 59, 60, 70, 74, 95] developed their own and four [57, 66, 88, 98] did not report any definition.

The majority of included studies explicitly used the number of discharged patients affected by at least one event as their numerator, except two studies that used the number of


Identification
Screening
Eligibility
Included
Number of records identified through **systematic database searching** (N=22,082)
**Systematic database search:** EMBASE (N=10,960), MEDLINE (N=4,905), Web of Science (N=2,392) CENRAL (N=1,130), CINAHL (N=1,110), CDSR (N=902), IPA (N=268), PsycInfo (N=174), CARE (N=118), HMIC (N=40), grey literature (N=83)
Number of duplicates removed by EndNote (N= 3,649) Manually (N=1,862) Total (N=5,511)
Number of records screened (N=16,571)
Number of records excluded where titles not relevant (N=13,766)
Number of records for abstract screened (N=2,805)
Number of records excluded where abstract not relevant (N=2,498)
**862** not focused on ME/medication related harm
**741** Outcome measures not ME/ADE
**188** ME at discharge from hospital
**132** Qualitative study
**118** Single disease
**94** Review articles
**85** Intervention without baseline outcome rate, control group or ME/harm as an outcome
**69** Potentially inappropriate prescribing
**56** Discharge from emergency department
**30** Single drug class
**29** Included speciality wards only
**27** Measure non-adherence
**26** Other forms of transition
**19** Assessed cost only
**13** Lab results post discharge
**9** Single drugs
Number of full-text articles assessed for eligibility, full text screening (N=307)
Number of additional records identified through searching other sources (N=3)
Number of articles excluded on reading full text (N=256)
**91** Cannot calculate of ME/ADE rate
**39** ME at the point of discharge from hospital [while patients are still present in the hospital]
**35** Did not differentiate intentional from unintentional discrepancy
**34** Outcome measure not ME/ADE
**16** ADE in community setting not related to hospital discharge
**14** Assessed ADE as a result of a condition [ADE that occur due to a pre specified criteria, including; drug interaction, potential inappropriate medication, new medication, medication changes during hospitalisation]
**12** One subtype of ME
**11** Foreign language papers that were not relevant (no rate/ no medication related outcome) after translation using Google™ translate
**3** Patient discharged from skilled nursing facility
Number of articles included (N=54)
Including 13 conference abstracts

◂**Fig. 1** Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram. *ADE* adverse drug event, *CDSR* Cochrane Database of Systematic Reviews, *CENTRAL* Cochrane Central Register of Controlled Trials, *CINAHL* Cumulative Index to Nursing and Allied Health Literature, *DARE* Database of Abstracts of Reviews of Effects, *HMIC* Health Management Information Consortium, *IPA* International Pharmaceutical Abstracts, *ME* medication error

discharge medications affected by one or more UMDs [49, 50]. These latter studies [49, 50] reported that 11–52.7% of individual prescribed medications had at least one UMD post-discharge. One study [95] reported that at least one UMD affected 12% of discharged paediatric patients. Across 11 studies [57, 59, 60, 66, 70, 74, 83, 84, 88, 93, 98], a median rate of 50% (IQR 39–76) of adult and elderly patients experienced at least one UMD post-discharge (range 14–93.5%). Four studies [59, 70, 74, 93] that used a telephone follow-up among data collection methods, and five studies using case note screening [60, 66, 83, 84, 98] reported the rate of UMD to be 65–93.5% and 14–76%, respectively, per adult and elderly patient discharged. A range of 36.5–93.5% of discharged elderly patients ($n=5$) experienced UMDs post-discharge [60, 66, 83, 88, 93].

## 3.5 Adverse Drug Events

Seventeen studies [24, 48, 54–56, 61, 67, 69, 70, 74, 78, 80, 82, 86, 92, 94, 97] reported ADE rates post-hospital discharge, 17 studies [24, 51–53, 58, 62–64, 68, 71, 73, 76, 77, 79, 81, 82, 91] reported non-preventable ADE rates (ADRs) post-discharge, one study [24] reported both.

### 3.5.1 Non-preventable Adverse Drug Events (Adverse Drug Reactions)

Three studies [62, 64, 68] used the ADR definition proposed by the WHO in 1972, nine studies [51, 53, 58, 63, 71, 76, 79, 81, 82] used a broader DRP definition that included ADRs, and three [52, 77, 91] did not state a definition.

All studies explicitly used the number of discharged patients as their denominator. Across five studies [24, 58, 64, 73, 91] that used patients affected by events as their numerator, a median of 27% (IQR 18–40.5) of adult and elderly patients experienced one or more ADRs post-hospital discharge. Two studies [24, 73] that used a telephone follow-up as the most common data collection method reported the rate of ADRs post-discharge to be 20.4–27% of discharged patients. A range of 27–51% of elderly discharged patients ($n=3$) experienced ADRs post-discharge [24, 58, 64].

### 3.5.2 Adverse Drug Events

Four studies [61, 74, 80, 86] used the ADE definition proposed by Bates et al. [32]. Seven studies [48, 55, 67, 78, 92, 94, 97] did not formally define ADEs. All studies explicitly used the number of discharged patients as their denominator. One study [86] reported the rate of post-discharge ADEs as 9% of paediatric patient hospital discharges. One study [82] reported the mean number of ADEs per discharged patient as 3. Across seven studies [24, 54, 55, 61, 69, 74, 94] that used patients affected by at least one event as their numerator, the median ADE rate was found to be 19% [IQR 16–24%] of adult and elderly patients experiencing one or more ADEs post-discharge. Two studies [74, 80] reported that between 11 and 16% of discharged patients experienced one or more preventable ADEs.

Five studies [24, 54, 55, 69, 74] that used telephone follow-up interviews among data collection methods reported 11–37% (median 20.3%, IQR 13.5–30.5) of adult and elderly patients discharged experienced one or more ADEs. Two studies [61, 94] that used case note screening among data collection methods reported that 18.7–18.9% of discharged patients were affected by ADEs post-hospital discharge. Two studies [54, 78] that adapted Bates definition of ADEs and used the same data collection method reported that 11–16% of adult and elderly patients had at least one ADE after hospital discharge. The highest reported ADE rate was 37% of patients using a telephone interview method in one study [24] in the UK. A range of 18.7–37% of elderly discharged patients ($n=4$) experienced ADEs post-discharge [24, 55, 61, 94]. Table 4 summarises outcome rates of the included studies per patient population.

## 3.6 Severity of Events

Eighteen [24, 54–56, 59, 61, 62, 64, 66, 69, 70, 72, 78, 80, 88, 91, 94, 95] (18/54, 33.3%) studies reported severity data of identified outcome measures, including one ME study [72], three ADR studies [62, 64, 91], nine ADE studies [24, 54–56, 61, 69, 78, 80, 94] and five UMD studies [59, 66, 70, 88, 95]. Seven studies [54, 61, 62, 64, 72, 78, 80] reported severity assessment based on existing rating scales published in the literature. Of these, three studies [54, 61, 78] used the severity rating proposed by Bates et al. [32], with various other scales being used by remaining studies.

Comparability of the severity of events was limited because of heterogeneity across studies in presenting severity of event data (e.g. number of patients affected by one or more serious incidents, or number of serious incidents), severity rating scale, and the small number of included studies particularly when divided across patient populations. One study reported that 86% of adult patients affected by MEs were considered to be moderate harm events [72]. Among

**Table 2** Characteristics of included studies

| Characteristics | Number of studies ($n=54$) | % | References |
|---|---|---|---|
| Country | | | |
| USA | 17 | 31.5 | [52, 54–57, 61, 70, 74, 76, 78, 79, 82, 89, 90, 94, 96, 97] |
| UK | 7 | 13 | [24, 49, 50, 59, 87, 95, 98] |
| Norway | 4 | 7.4 | [60, 65, 81, 86] |
| Canada | 3 | 5.5 | [53, 63, 92] |
| The Netherlands | 2 | 3.7 | [58, 88] |
| Australia | 2 | 3.7 | [48, 77] |
| France | 2 | 3.7 | [62, 99] |
| Sweden | 2 | 3.7 | [66, 83] |
| Switzerland | 2 | 3.7 | [23, 51] |
| India | 2 | 3.7 | [68, 75] |
| Italy | 1 | 1.8 | [84] |
| New Zealand | 1 | 1.8 | [85] |
| Belgium | 1 | 1.8 | [93] |
| Croatia | 1 | 1.8 | [64] |
| Ireland | 1 | 1.8 | [72] |
| Egypt | 1 | 1.8 | [67] |
| Europe[a] | 1 | 1.8 | [71] |
| Jordan | 1 | 1.8 | [73] |
| Oman | 1 | 1.8 | [80] |
| Sri Lanka | 1 | 1.8 | [91] |
| Saudi Arabia | 1 | 1.8 | [69] |
| Publication year | | | |
| 1990–9 | 3 | 5.5 | [49, 50, 55] |
| 2000–9 | 8 | 14.8 | [48, 54, 62, 63, 71, 74, 83, 86] |
| 2010–19 | 43 | 79.6 | [23, 24, 51–53, 56–61, 64–70, 72, 73, 75–82, 84, 85, 87–99] |
| Patient demographics | | | |
| Adults | 28 | 51.8 | [49–52, 54, 56, 57, 59, 60, 67, 69–74, 76–82, 84, 87, 91, 98, 99] |
| Elderly[b] | 18 | 33.3 | [23, 24, 48, 53, 55, 58, 61, 63–66, 68, 83, 88, 90, 93, 94, 96] |
| Paediatric | 3 | 5.5 | [75, 86, 95] |
| All age groups | 1 | 1.8 | [62] |
| Not specified | 4 | 7.4 | [85, 89, 92, 97] |
| Study design | | | |
| Prospective | 46 | 85.2 | [23, 24, 48–52, 54, 55, 57–60, 62–78, 80, 81, 83, 85, 86, 88–93, 95–99] |
| Retrospective | 8 | 14.8 | [53, 56, 61, 79, 82, 84, 87, 94] |
| Study setting[f] | | | |
| Home | 41 | 75.9 | [24, 49–54, 56–59, 61, 62, 64, 65, 67–72, 74–82, 85–88, 92, 94–99] |
| Home care[c] | 5 | 9.2 | [23, 24, 55, 60, 66] |
| Nursing home | 3 | 5.5 | [60, 66, 98] |
| Other[d] | 5 | 9.2 | [48, 63, 83, 84, 89] |
| Not specified | 3 | 5.5 | [90, 91, 93] |
| Study focus[g] | | | |
| ME | 12 | 21.8 | [23, 65, 71, 72, 75, 85, 87, 89, 90, 96, 97, 99] |
| UMD | 14 | 25.9 | [49, 50, 57, 59, 60, 66, 70, 74, 83, 84, 88, 93, 95, 98] |
| ADR | 17 | 30.9 | [24, 51–53, 58, 62–64, 68, 71, 73, 76, 77, 79, 81, 82, 91] |
| ADE | 17 | 30.9 | [24, 48, 54–56, 61, 67, 69, 70, 74, 78, 80, 82, 86, 92, 94, 97] |
| Data collection method[h] | | | |
| Screen case note | 43 | 79.6 | [23, 24, 48–52, 54, 56–61, 63–72, 74–87, 89, 93–95, 98] |
| Telephone follow-up | 25 | 46.2 | [24, 52, 54, 55, 59, 63, 65, 67–74, 76, 78–80, 90, 93, 95, 97, 99] |

**Table 2** (continued)

| Characteristics | Number of studies ($n=54$) | % | References |
|---|---|---|---|
| Home visit | 12 | 22.2 | [49, 50, 53, 58, 63, 64, 71, 81, 88, 92, 95, 96] |
| Other[e] | 16 | 29.6 | [23, 56–58, 62, 64, 71, 75–77, 82, 86, 87, 90, 92, 96] |
| Not specified | 1 | 1.8 | [91] |
| Profession of data collector[i] | | | |
| Pharmacist | 27 | 50 | [24, 52, 53, 56, 60, 61, 63, 66, 69, 71, 73, 76, 77, 79, 81–83, 85–87, 89, 90, 92, 94, 97–99] |
| Physician | 6 | 11.1 | [54, 62, 64, 70, 84, 88] |
| Nurse | 5 | 9.2 | [23, 70, 78, 84, 96] |
| Research assistant | 7 | 12.9 | [55, 58, 59, 65, 67, 74, 80] |
| Pharmacy student | 1 | 1.8 | [51] |
| Not specified | 10 | 18.5 | [48–50, 57, 68, 72, 75, 91, 93, 95] |
| Follow-up period, days[j] | | | |
| 1–15 | 20 | 37 | [23, 49, 50, 53, 57, 60, 66, 69, 71, 72, 76, 82, 85, 86, 88, 90, 92, 93, 97, 99] |
| 16–30 | 19 | 35.1 | [52, 54–56, 58, 59, 62–64, 67, 70, 73, 74, 79, 80, 83, 95, 96] |
| 31–180 | 11 | 20.3 | [24, 48, 61, 68, 77, 78, 81, 87, 91, 94, 98] |
| Not specified | 4 | 7.4 | [51, 75, 84, 89] |

*ADE* adverse drug event, *ADR* adverse drug reaction, *ME* medication error, *UMD* unintentional medication discrepancy

[a]One study included data from six countries in Europe including; Austria, Germany, Denmark, Spain, The Netherlands and Portugal

[b]Among the 18 studies, nine studies included patients aged ≥ 65 years [21, 53, 55, 61, 64–66, 83, 94], one study included patients aged ≥ 64 years [23], three studies included patients aged ≥ 60 years [58, 63, 68] and five studies did not mention a cut-off age [48, 88, 90, 93, 96]. Among the five studies that did not mentioned the cut-off age, two studies mentioned the mean age and referred to patients as older adults [48, 88], one study included patients discharged from a geriatric ward [93], one study included veteran geriatric patients [96] and one study included Medicare Advantage patients [90]

[c]Providing care at patient home

[d]Long-term care facility, local care settings, local care home programme, outpatient rehabilitation facility, community healthcare

[e]Follow-up visit at hospital/clinic, medication reconciliation post discharge, general practitioner database, reporting of incident, questionnaire, interview at community pharmacy, medication reconciliation (via secure messaging at home), reporting of incident

[f]Studies could have patient discharged to more than one location

[g]Study focus could be more than one outcome

[h]Studies could have more than one data collection method

[i]Studies data collectors could be from more than one profession

[j]Follow-up period for the outcome of interest

patients affected by ADRs, three studies reported that serious ADRs affected 6.9%, 47% and 60% of elderly, adult and all age groups patients, respectively [62, 64, 91]. Among patients affected by ADEs post-hospital discharge, serious ADEs were reported to affect 13.3% of adult patients, and 81% of elderly patients in two studies [24, 54]. Four studies reported that the median rate of serious ADEs was found to be 29% (IQR 21–38.5%) of adult and elderly patients experiencing one or more ADEs post-discharge [61, 69, 80, 94]. Among patients affected by UMDs, three studies reported that between 25 and 34% of elderly patients [66, 88], and 63.3% of paediatric patients were affected by moderate harm events [95]. Two studies reported that 33–38% of UMDs identified post-hospital discharge as associated with a high potential of harm in adult patients [59, 70]. Appendix 9 of the ESM includes a summary of severity data of the included studies.

### 3.7 Medication Involved in Unintentional Medication Discrepancies/Adverse Drug Events

Fourteen studies [24, 53–56, 61, 62, 64, 70, 71, 78, 79, 82, 91] reported data regarding individual medications or drug classes associated with UMDs ($n=1$) and ADEs ($n=14$). Studies evaluating MEs did not report data regarding medications involved. The most common drug classes that were reported to lead to post-discharge ADEs across 14 studies [24, 53–56, 61, 62, 64, 70, 71, 78, 79, 82, 91] were antibiotics, antidiabetics, analgesics and cardiovascular drugs (common subclasses were anti-hypertensive and anticoagulant medications). Only one study [64] reported a

**Table 3** Quality assessment

| Study ID (first author, year) | Aim/ objective | ME/ADE definition | Error categories specified | Error categories defined | Denominator clearly defined | Data collection method described clearly | Study setting clearly described | Validity measure applied to confirm the occurrence of error | Reliability measure applied | Listed of study limitation | Calculation of sample size described | Mentioned of any assumption made | Total score of criteria achieved (out of 12) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ahmad, 2014 [58] | √ | √ DRP | | | √ | √ | √ | √ | | | | | 6 |
| Al-Ghamdi, 2012 [69] | √ | √ | | | √ | √ | √ | √ | | √ | | | 7 |
| Al-Hashar, 2018 [80] | √ | √ | | | √ | √ | | √ | √[a] | √ | √ | | 8 |
| Alldred, 2010 [87] | √ | | √ | √ | √ | √ | √ | | | √ | | | 7 |
| Armor, 2016 [82] | √ | √ | | | √ | √ | √ | | | √ | | | 6 |
| Bergkvist, 2009 [83] | √ | √ | | | √ | √ | √ | √ | √[a] | √ | √ | √ | 10 |
| Bonaudo, 2018 [84] | √ | √ UMD | | | √ | √ | √ | √ | | √ | | | 7 |
| Braund, 2014 [85] | √ | √ | √ | √ | √ | √ | √ | | | √ | | | 8 |
| Buajordet, 2002 [86] | √ | √ | | | √ | √ | √ | √ | | | | | 6 |
| Cameron, 2010 [92] | √ | | | | √ | √ | √ | | | | | | 4 |
| Claeys, 2013 [93] | √ | | | | √ | √ | | | | | | | 3 |
| Crotty, 2004 [48] | √ | | | | √ | √ | √ | √ | | √ | | | 6 |
| Donovan, 2012 [94] | √ | | | | √ | √ | √ | √ | | | | | 5 |
| Duggan, 1996 [49] | √ | √ | | | √ | √ | √ | | | | | | 5 |
| Duggan, 1998 [50] | √ | √ | | | √ | √ | √ | √ | √ | √ | | | 8 |
| Eichenberger, 2010 [51] | √ | | | | √ | √ | √ | | | √ | | | 5 |
| Falangan, 2010 [53] | √ | √ DRP | | | √ | √ | √ | | | √ | | | 6 |

**Table 3** (continued)

| Study ID (first author, year) | Aim/ objective | ME/ADE definition | Error categories specified | Error categories defined | Denominator clearly defined | Data collection method described clearly | Study setting clearly described | Validity measure applied to confirm the occurrence of error | Reliability measure applied | Listed of study limitation | Calculation of sample size described | Mentioned of any assumption made | Total score of criteria achieved (out of 12) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Fanizza, 2018 [52] | √ | | | | √ | √ | √ | | | √ | | | 5 |
| Forster, 2005 [54] | √ | √ | | | √ | √ | √ | √ | √ | √ | | | 8 |
| Gray, 1999 [55] | √ | | | | √ | √ | √ | √ | | √ | | | 6 |
| Hawes, 2018 [56] | √ | √ DRP | | | √ | √ | √ | √ | | √ | | | 7 |
| Heyworth, 2014 [57] | √ | | | | √ | √ | √ | √ | | √ | | | 6 |
| Hockly, 2018 [59] | √ | √ | | | √ | √ | √ | √ | | √ | √ | | 8 |
| Holdhus, 2019 [60] | √ | √ UMD | √ UMD | √ UMD | √ | √ | √ | | | √ | √ | √ | 10 |
| Huynh, 2013 [95] | √ | | | | √ | √ | √ | √ | | | | | 5 |
| Kannan, 2013 [61] | √ | √ | √ | | √ | √ | √ | √ | √ | √ | | | 9 |
| Leland, 2012 [96] | | | | | √ | √ | √ | | | | | | 3 |
| Letrilliart, 2001 [62] | √ | √ | | | √ | √ | √ | √ | | √ | | | 7 |
| MacAulay, 2008 [63] | √ | | | | √ | √ | √ | | | √ | √ | | 6 |
| Marusic, 2014 [64] | √ | √ | | | √ | √ | √ | √ | | √ | | | 7 |
| Mesteig, 2010 [65] | √ | | √ | | √ | √ | √ | √ | √[a] | √ | | | 8 |
| Meyer-Massetti, 2018 [23] | √ | | √ | | √ | √ | √ | √ | | √ | | | 7 |
| Midlov, 2012 [66] | √ | | | | √ | √ | √ | √ | √[a] | √ | | | 7 |
| Ibrahim, 2012 [67] | √ | | | | √ | √ | √ | √ | | | | | 5 |

**Table 3** (continued)

| Study ID (first author, year) | Aim/ objective | ME/ADE definition | Error categories specified | Error categories defined | Denominator clearly defined | Data collection method described clearly | Study setting clearly described | Validity measure applied to confirm the occurrence of error | Reliability measure applied | Listed of study limitation | Calculation of sample size described | Mentioned of any assumption made | Total score of criteria achieved (out of 12) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mohammad, 2011 [97] | √ | | √ | | √ | √ | √ | | | | | | 5 |
| Nagaraju, 2015 [68] | √ | √ | | | √ | √ | √ | | | | | | 5 |
| Osorio, 2014 [70] | √ | √ UMD | √ UMD | | √ | √ | √ | √ | √[a] | √ | | | 9 |
| Parekh, 2018 [24] | √ | √ | √ | | √ | √ | √ | √ | √[a] | √ | √ | | 10 |
| Patel, 2011 [98] | √ | | | | √ | √ | | | | | √ | √ | 5 |
| Paulino, 2004 [71] | √ | | √ | | √ | √ | √ | | | √ | | | 6 |
| Pourrat, 2017 [99] | √ | | | | √ | √ | √ | | | | | | 4 |
| Riordan, 2016 [72] | √ | √ | √ | √ | √ | √ | √ | √ | | √ | | | 9 |
| Salameh, 2019 [73] | √ | | | | √ | √ | | | | √ | | | 4 |
| Schnipper, 2006 [74] | √ | | | | √ | √ | √ | √ | √ | √ | | | 7 |
| Sittambalam, 2015 [89] | √ | | | | √ | √ | √ | | | | | | 4 |
| Solanki, 2017 [75] | √ | √ | √ | √ | √ | √ | √ | | | √ | √ | √ | 10 |
| Tantipin-ichwong, 2017 [90] | √ | | √ | | √ | √ | | | | | | | 4 |
| Tetuan, 2018 [76] | √ | √ DRP | | | √ | √ | √ | | | √ | | | 6 |
| Tong, 2015 [77] | √ | | | | √ | √ | √ | √ | | √ | | √ | 7 |
| Tsilimingras, 2015 [78] | √ | | | | √ | √ | √ | √ | √ | √ | | | 7 |

**Table 3** (continued)

| Study ID (first author, year) | Aim/ objective | ME/ADE definition | Error categories specified | Error categories defined | Denominator clearly defined | Data collection method described clearly | Study setting clearly described | Validity measure applied to confirm the occurrence of error | Reliability measure applied | Listed of study limitation | Calculation of sample size described | Mentioned of any assumption made | Total score of criteria achieved (out of 12) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Westberg, 2017 [79] | √ | √ DRP | | | √ | √ | √ | √ | √[a] | √ | | | 7 |
| Wijekoon, 2017 [91] | √ | | | | √ | | | | | | | | 2 |
| Willoch, 2012 [81] | √ | √ DRP | √ | | √ | √ | √ | | | √ | √ | | 8 |
| Wilting, 2012 [88][b] | √ | √ | | | √ | √ | √ | | | √ | | | 6 |

*ADE* adverse drug event, *DRP* drug-related problem, *ID* identifier, *ME* medication error, *UMD* unintentional medication discrepancy

[a]Consensus meeting

[b]Information mentioned in the letter to the editor [100] was used in the quality assessment

statistical method to formally associate the prescription of warfarin with ADEs. Appendix 10 of the ESM summarises medications and medication classes that were reported to be involved in UMDs/ADEs, classified according to the British National Formulary system [102].

## 4 Discussion

### 4.1 Main Findings

This is the first systematic review of published international evidence concerning the epidemiology of MEs and ADEs post-hospital discharge across population groups. We have identified that medication poses a frequent and enduring risk to patient safety following discharge from hospital, which reinforces care transfer being a WHO Global Patient Safety Challenge priority for action. We found across included studies that a median of one in two adult and elderly patients are affected by at least one ME post-hospital discharge, one in two affected by one or more UMD, and one in five affected by one or more ADEs (the median rate of MEs, UMDs and ADEs post-hospital discharge was 53% [IQR 33–60.5] ($n=5$), 50% [IQR 39–76] ($n=11$) and 19% [IQR 16–24] ($n=7$), respectively). We also reported emerging evidence of the nature of these risks, with a median of nearly one third of adult and elderly patients affected by clinically serious ADEs post-hospital discharge and medication classes most commonly reported with ADEs as antibiotics, antidiabetics, analgesics and cardiovascular drugs.

The focus of this review was on both process measures such as MEs and outcome measures such as ADEs [103]. Medication errors that occur irrespective of harm are an important window into the safety of healthcare systems. This helps understand what can turn errors into ADEs where risks may lie dormant and what patterns emerge that may support learning to prevent harmful events occurring in the future.

This review has revealed that similar median rates of ADEs and/or UMDs occur post-hospital discharge to those reported on hospital admission [104], during inpatient stay [105] and whilst residing in ambulatory care [106]. This indicates that the transition of care from hospital to home should be considered an equal priority to other stages of the patient journey by researchers and healthcare policy makers. Evidence indicates that hospital discharge has been the subject of attention in patient safety policy documents [13, 22, 107–109], where these documents are translating into action on the ground in the form of new initiatives [110].

We have observed that research has been accelerating in the field of medication safety post-hospital discharge since the year 2010. A previous review published in 2010 [20] found that ADEs post-hospital discharge affected 20% of elderly patients ($n=1$) [55], while our review updates and

**Table 4** Outcome rate summary

| Patient group | Error and discrepancy | | Harm | |
|---|---|---|---|---|
| | ME ($n=12$) | UMD ($n=14$) | ADR ($n=17$) | ADE ($n=17$) |
| Paediatric | 66.3% of discharged patients ($n=1$) [75]<br>54.2% of discharged patients [administration error] ($n=1$) [75] | 12% of discharged patients ($n=1$) [95] | NA | 9% of discharged patients ($n=1$) [86] |
| Adults and elderly | 19–63% of discharged patients, median rate 53% [IQR 33–60.5] ($n=5$) [23, 87, 89, 96, 99]<br>43% of discharged patients [prescribing error] ($n=1$) [72]<br>3.5% of medications in discharge prescriptions [monitoring error] ($n=1$) [87] | Range 11–52.7% of medications in discharge prescriptions ($n=2$) [49, 50]<br>Range 14–93.5% of discharged patients, median rate 50% [IQR 39–76] ($n=11$) [57, 59, 60, 66, 70, 74, 83, 84, 88, 93, 98] | Range 15.7–51% of discharged patients [median 27%, IQR 18–40.5] ($n=5$) [24, 58, 64, 73, 91] | Range 11–37% of discharged patients, median rate 19% [IQR 16–24] ($n=7$) [24, 54, 55, 61, 69, 74, 94] |
| Adults (excluding elderly) | 43% of discharged adult patients [prescribing error] ($n=1$) [65]<br>3.5% of medications in discharge prescription [monitoring error] ($n=1$) [80] | Range 11–52.7% of medications in discharge prescriptions ($n=2$) [42, 43]<br>Range 14–82% of discharged patient median rate 57.5% [IQR 35–76.7] ($n=6$) [57, 59, 70, 74, 84, 98] | Range 15.7–20.4% of discharged patients ($n=2$) [73, 91] | Range 11–24% of discharged patients ($n=3$) [54, 69, 74] |
| Elderly | 19–53% of discharged patients ($n=2$) [23, 96] | Range 36.5–93.5% of discharged patients ($n=5$) [60, 66, 83, 88, 93] | Range 27–51% of discharged patients ($n=3$) [24, 58, 64] | Range 18.7–37% of discharged patients ($n=4$) [24, 55, 61, 94] |
| All age groups | NA | NA | 0.4% of discharged patient ($n=1$) [62] | NA |

*ADE* adverse drug event, *ADR* adverse drug reaction, *IQR* interquartile range, *ME* medication error, *NA* Not Available, *UMD* unintentional medication discrepancy

strengthens this evidence with a rate of 18.7–37% of discharged elderly ($n=4$) [24, 55, 61, 94]. Our review found that the median rate of MEs and ADEs is higher in the elderly population. While two previous systematic reviews of medication safety incidents post-hospital discharge in the elderly were informative [20, 21], they examined the elderly in isolation whereas our review compared this patient group with other populations to help determine priorities. Older patients may be a high-risk group to experience MEs and ADEs owing to factors including pharmacodynamic/pharmacokinetics differences, additional co-morbidities and polypharmacy [111–115]. It also reinforces the recent WHO Medication Safety in Transitions of Care—Technical Report, which recommend targeting medication reconciliation interventions to high-risk areas [116].

Many studies included in this review report MEs and medication discrepancies following the evaluation and comparison of medication lists in hospital case notes and discharge prescriptions to data obtained from interviewing patients in the community setting following hospital discharge. However, these studies often omitted data from primary care records post-hospital discharge, which may have led to inaccurate ME/UMD rates being reported, instead relying primarily on patient-reported data [59].

### 4.2 Implications of Findings

Our systematic review identifies that the burden of MEs and ADEs following hospital discharge is comparatively under-researched in paediatric and nursing/care home settings. This is important as evidence indicates that medication safety challenges for these patient groups exist both during hospitalisation [46] and at the point of discharge from hospital [117]. Further work to explore the burden and causes of medication safety challenges following transfer to nursing and care homes is also required as unique factors have been reported to complicate these care transitions, including the older age of patients and their elevated severity of illness/care needs [118], as well as apparent challenges with accountability and communication among staff [119, 120].

The majority of studies (47/54, 87%) included in this review originated from developed nations (in particular, the USA and UK) and there was limited evidence from developing countries (e.g. Africa and South America, $n=1$ study) [121]. Low levels of patient support post-hospital discharge as a result of underdeveloped primary care services have been reported in such nations [122]. In addition, with the exception of the USA, nations that have multiple studies included in our review rarely contained data across all our outcome measures, which limits a global assessment of risk.

Studying preventable ADEs is important as they are amendable to intervention (unlike many ADRs) [123] and may better inform the design of system improvements alongside an understanding of other preventable events such as MEs and UMDs. A recent systematic review and meta-analysis of preventable harm in healthcare worldwide reported a pooled prevalence of 6%, with medications a chief contributor to this harm [123]. In this review, only two studies measured preventable ADEs to be between 11 and 16% of discharged patients. Further exploration of the burden and causes of preventable ADEs would further the WHO Third Global Patient Safety Challenge: Medication Without Harm agenda, which aims to reduce severe avoidable patient harm by 50% and names care transitions as a key area to address [4].

This systematic review found that medication classes most implicated in harm post-hospital discharge were cardiovascular, analgesic, antibiotic, and antidiabetic medications. Similar findings have been reported by other literature [106, 124, 125] investigating medication-related harm in ambulatory settings and medication-related causes for hospital admission. These medication groups may become a focus of attention by researchers and healthcare staff as potential targets for remedial action that could improve patient outcomes [126]. Our review can be used to inform the development and update a medication-related harm prediction tools that focus on post-discharge risk [127], as well as to update and reinforce prescribing and monitoring quality indicators in primary care settings [128–130]. Elsewhere these findings could also inform ongoing use of the national health services (National Health Service) New Medicines Service in community pharmacies in the UK [131], which involves counselling the patient starting new medications for chronic diseases including diabetes mellitus and hypertension and for those starting new anticoagulant medications. Our findings suggest that longer term analgesic medications could be considered for inclusion in the New Medicines Service.

Our ability to make direct comparisons between included studies was limited because of the observed heterogeneity in country of origin, patient groups studied, data collection methods and outcome definitions. Other systematic reviews of MEs [46, 132, 133] and ADEs [45, 106, 134] also report similar limitations with this body of literature. For example, we observed no pattern in included studies with regard to the follow-up period post-discharge and the outcome rate or their definitions. There is currently no consensus regarding the specific time point to stop collecting data [135]. There is also wide variation and disagreement in time frame definitions used in research concerning hospital readmission [1, 136, 137]. This suggests that greater consistency and standardisation of methods (for example, standardisation of the outcome definition via the Delphi technique [138]) are required between studies investigating transfer of care to enhance comparability of results and ultimately the development of remedial interventions. Aside from standardisation of methods, there is also a need to improve the quality

of reporting in studies of care transitions as few studies reported outcome definitions and other essential information. A similar deficit in the quality of reporting of medication safety studies [47] and observational epidemiological studies have been noted previously [139], where standard tools for reporting to a higher standard were proposed. However, most studies were rated as moderate or high quality.

It is anticipated from our identified rate of error/harm that the cost of "no action taken" is high in terms of a patient's subsequent use of the healthcare services post-hospital discharge. A number of reviews have been published that evaluated interventions (including medication reconciliation, community pharmacy involvement and electronic communication interventions) to reduce MEs and ADEs post-discharge [140–146]. However, none have reported consistent reductions in these outcomes. Understanding the epidemiology and nature of medication safety challenges post-hospital discharge paves the way for research to examine the causes, where in-depth study of aetiology in this area could support the development of interventions [147, 148]. Studies have been limited to incident report analysis [13, 149] and staff surveys that report that communication deficits have been implicated in ME/ADEs post-discharge [19]. In addition, attention has recently been drawn to the patient's experience of hospital discharge, where patients reported pressured discharges, the complicated nature of discharge, communication issues and healthcare system fragmentation (e.g. lack of shared electronic records across care boundaries affected their medication management post-discharge [9, 137, 150, 151]). Indeed, recent research has included the valuable patient perspective on discharge and how they may manage their medication effectively [8, 150–155]. This research should be used by academics, policymakers and healthcare staff alongside the findings of this review and explorations of the causes of MEs/ADEs post-discharge from the health provider perspective to connect patients and health systems together to reduce medication safety risks from a more holistic perspective.

### 4.3 Strengths and Limitations

A comprehensive search strategy was conducted across the grey literature and ten electronic databases covering the modern healthcare era, with search criteria involving no restrictions on language, study country or patient demographics. We also presented a transparent review methodology with reporting following the PRISMA approach, and an author contact section [156] to reduce reporting bias. We also performed a quality assessment of included studies to help frame our findings in context.

However, this study has a number of limitations that affected the internal validity including no independent quality assessment, and single author screening of citations, which could have led to the omission of relevant studies (though uncertain cases were discussed amongst the research team) [157]. A meta-analysis of outcome rate data was also not possible because of heterogeneity of included data.

## 5 Conclusions

This is the first known comprehensive systematic review of the burden and nature of MEs and medication-related harm following hospital discharge across general populations, and informs global efforts directed toward understanding and addressing medication-related morbidity associated with care transitions. Medication errors and ADEs have been found to be common following hospital discharge, but a detailed comparison between studies was limited because of differences in the design of included studies. Despite this, a number of important targets were identified for future study that could guide the development of successful remedial interventions and move forward the global safety agenda.

**Acknowledgements** We are thankful to Ghadah H. Alshehri for her help with creating the systematic review protocol.

**Author Contributions** All authors contributed to the study conception and design. Systematic review planning, data extraction and data analysis were led and performed by FAA, and supported by RNK and DS. Citation screening and identification were completed by FAA. The first draft of the manuscript was written by FAA and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

**Data Availability** All data generated and analysed during this study are included in this published article and its supplementary information files.

## Compliance with Ethical Standards

**Funding** Fatema A. Alqenae gratefully acknowledges the Kuwait Civil Service Commission for funding her PhD programme at the University of Manchester. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Conflict of interest** Fatema A. Alqenae, Douglas Steinke and Richard N. Keers have no conflicts of interest that are directly relevant to the content of this study.

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## Affiliations

**Fatema A. Alqenae[1] · Douglas Steinke[1] · Richard N. Keers[1,2]**

[1] Division of Pharmacy and Optometry, School of Health Sciences, Centre for Pharmacoepidemiology and Drug Safety, University of Manchester, Oxford Road, Manchester M13 9PT, UK

[2] Pharmacy Department, Greater Manchester Mental Health NHS Foundation Trust, Manchester, UK