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REVIEW

Predictors for unintentional medication reconciliation discrepancies in preadmission medication: a systematic review

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Abstract
Purpose Discrepancies in preadmission medication (PAM) are common and potentially harmful. Medication reconciliation is able to reduce the discrepancy rate, yet implementation is challenging. In order for reconciliation efforts to be more cost-effective, patients at high risk for reconciliation errors should be identified. The purpose of this systematic review is to identify predictors for unintentional discrepancies in PAM.
Methods Medline and Embase were searched systematically until June 2017. Only studies concerning adult subjects were retained. Quantitative studies were included if predictors for unintentional discrepancies in the PAM had been determined on hospital admission. Variables were divided into patient-, medication-, and setting-related predictors based on a thematic analysis. Studies on identification of predictors for discrepancies and potentially harmful discrepancies were handled separately.
Results Thirty-five studies were eligible, of which 5 studies focused on potentially harmful discrepancies. The following 16 significant variables were identified using multivariable prediction models: number of preadmission drugs, patient's age, availability of a drug list, patients' understanding of medication, usage of different outpatient pharmacies, number of high-risk drugs, discipline for which the patient is admitted, admitting physician's experience, number and type of consulted sources, patient's gender, type of care before admission, number of outpatient visits during the past year, class of medication, number of reimbursements, use of an electronic prescription system, and type of admission (elective vs emergency). The number of preadmission drugs was identified as a predictor in 20 studies. Potentially harmful discrepancies were ascertained in 5 studies with age found to have a predictive value in all 5 studies.
Conclusion Multiple suitable predictors for PAM-related discrepancies were identified of which higher age and polypharmacy were reported most frequently.

Keywords Medication reconciliation · Reconciliation discrepancies · Hospitalization · Risk stratification · High-risk patients · Predictors

Julie Hias and Lorenz Van der Linden shared first author.

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Background

Transitions of care, such as admission to and discharge from the hospital, have been associated with adverse drug events (ADEs). Part of these medication-related problems is due to inadequate communication between community care services and hospitals [1, 2]. Up to 27% of all hospital prescribing

errors can be attributed to discrepancies in medication histories at the time of admission [3]. Up to 67% of adult patients admitted to the hospital have at least one unintended medication discrepancy [3]. A recent systematic review showed that the median proportion of all potentially harmful discrepancies was 34% [2]. However, the causal impact of these discrepancies on clinical outcome (e.g., length of stay, readmission, and mortality) is less obvious [2, 4]. An inaccurate preadmission medication (PAM) list can lead to errors in drug treatment during admission as well as in discharge medication orders and can result in unintentional changes of the patient's chronic therapy [5, 6]. Obtaining a complete and accurate PAM list is essential in preventing avoidable medication errors during and after hospital stay [7].

Medication reconciliation during care transitions aims to reduce medication discrepancies, including those with a potential for harm, and has been mandated by health care accreditation organizations [1, 8–11]. Medication reconciliation should be performed in all patients during the initial 24 h after hospital admission. Usually, multiple sources are used to collect a best possible PAM list [12, 13]. In the study performed by Saint-Germain et al., the clinical pharmacist assessed on average 3.58 (±1.11) information sources to obtain the PAM list [13]. Up to 30 min might be spent on a structured reconciliation process [13–15]. Since different levels of expertise concerning reconciliation are available in the hospital setting, patients at higher risk for reconciliation errors should be interviewed preferentially by explicitly trained health care professionals, such as dedicated clinical pharmacists. Implementation of a structured medication reconciliation process can be a costly process in terms of human resources [16–18]. In order for reconciliation efforts to be more cost-effective and practically feasible, patients at high risk for reconciliation errors should be identified [1, 8, 19].

Aims

This systematic review was conducted in order to identify predictors of medication discrepancies. The aim was to identify those specific variables that are aligned with the highest risk for unintentional discrepancies in medication histories.

Methods

Data sources and searches

The PRISMA statement on how to conduct and report systematic reviews was followed in this review [20].

The used search string is summarized in Supplementary Table 1. The heuristic approach was applied to the bibliographic databases Medline and Embase. Additional relevant articles were identified through the snowball method.

Study selection

One reviewer (JH) selected the manuscripts; in case of doubt, manuscripts were retained if consensus was reached with two other researchers (LVdL and SDW). Initial assessment of the abstracts was performed for relevance; subsequently, full texts were examined for inclusion. Abstracts were included if the following criteria were met: medication reconciliation was mentioned in the study objectives, in particular gathering the best possible PAM list; studies had to include adult study subjects who were admitted to a hospital. Searches were limited to English, French, and Dutch articles published before June 2017. Only peer-reviewed investigative publications were retained.

The following criteria were used to further identify articles for inclusion. First, unintentional discrepancies had to be the primary objective of the studies. Unintentional discrepancies were defined as any difference between the best possible PAM list and the list gathered by usual care or involuntary differences between the best possible PAM list and admission orders. Second, predictors for the aforementioned discrepancies had to be described explicitly.

Data extraction and quality assessment

Data were extracted and compiled using a data collection form. The following information was extracted from the studies: author, country, study design, study population (sample size and target group), hospital setting, intervention (when, by whom, level of training, and type of intervention), type of drugs, type of discrepancies, severity of discrepancies, predictors (subdivided in three groups: patient-, medication-, and setting-related predictors), and statistical methods. If any of the previously mentioned criteria had not been described sufficiently, the author was contacted to acquire the necessary information. Only predictors that were available on hospital admission or shortly thereafter were retained for further analysis.

One researcher (JH) performed the quality assessment. The Newcastle-Ottawa Quality Assessment Scale (NOS) [21] for cohort studies was used to assess the quality of the included studies as recommended by the Cochrane Handbook for Systematic Reviews of Interventions [22]. Thresholds for converting the NOS scales to Agency for Healthcare Research and Quality standards (good, fair, and poor) were performed based on the following rules [23]:

- Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

- Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
- Poor quality: 0 or 1 star in selection domain OR 0 star in comparability domain OR 0 or 1 star in outcome/exposure domain

Data synthesis and analysis

A qualitative synthesis of the studies was performed based on a thematic analysis. Findings were summarized in patient-, medication-, and setting-related predictors. Predictors for potentially harmful discrepancies were reported separately. Results were adopted from the original manuscripts without further statistical analysis. In the summary of the results, a distinction was made between simple non-parametric statistical tests and prediction models.

Neither meta-analysis nor meta-regression was performed, because of the scarcity of data and the heterogeneity in methods, interventions, type of drugs, type of discrepancies, and reported outcomes, which precluded formal analysis.

Results

The search yielded 3615 articles; after removal of duplicates, 2977 abstracts were assessed of which 486 full articles were analyzed. A total of 35 cohort studies were used for analysis. The screening and selection progress is summarized in Fig. 1.

A detailed summary of the studies' characteristics and quality assessment is provided in Table 1. Tamblyn et al. and Glintborg et al. had the highest score according to the NOS [24, 25]. Thirteen studies were scored "good" [5, 7, 8, 24–33].

An overview of all studied variables and relevant statistical details of the included studies has been added in Supplementary Table 2.

Results described in more detail below were statistically significant, unless mentioned otherwise. A distinction was made between risk factors for overall discrepancies and potential harmful discrepancies and is described separately.

Twenty-three studies corrected for confounders by performing multivariable analyses [5–8, 12–14, 24–29, 31–33, 35, 38, 39, 43, 46–48]. Statistically significant results provided by multivariable analysis are summarized in Table 2 for both all and specifically potentially harmful unintentional discrepancies.

Risk factors for unintentional discrepancies

Table 3 summarizes all variables that were examined as risk factors for unintentional PAM-related discrepancies both statistically significant or not. A division was made between non-parametric tests and prediction models. Information on statistical analysis, as performed in the original studies, is provided in the legend. Variables for which potential correlation with unintentional discrepancies was tested in several studies and found at least once to be statistically associated are discussed in more detail in the following.

Patient-related predictors

Age was investigated in 24 studies [5–9, 12, 13, 15, 24, 25, 27, 31, 32, 34, 35, 38, 43, 45–51]; only 9 found a significant result. Gleason et al. demonstrated, in a univariable analysis, that patients older than 65 years were more likely to have a discrepancy in their medication history [27]. Mendez et al. found that the number of unintentional discrepancies was strongly correlated with age ($r = 0.67$) [15]. Five studies inferred that older age was a predictor for discrepancies; this was not retained after adjustment for confounders [5, 32, 35, 46, 47]. De Winter et al. identified increasing age as a predictor for discrepancies in a multivariable analysis [31]. Saint-Germain et al. showed in a geriatric population that an increasing age is correlated with less discrepancies, as detected through multivariable analysis [13].

Gender was tested in 24 studies [5–7, 9, 12, 13, 15, 24, 25, 27, 31, 32, 34, 38, 39, 42, 43, 45–51], of which 5 found that the female sex was associated with more discrepancies [27, 31, 39, 42, 50]. Of these 5 studies, only Balon et al. and De Winter et al. adjusted for confounders [31, 39].

Type of care service before admission was the subject of analysis in eight studies [6, 7, 12, 13, 31, 35, 44, 48]. Hellström et al. confirmed in a multivariable analysis that patients living at home before admission without community care service were at higher risk for PAM-related discrepancies, compared to patients who lived in a nursing home [7]. There was no significant difference in discrepancy rate for patients who lived at home with community care service, compared to patients who lived in a nursing home [7]. De Winter et al. included the type of care model provided before hospital admission in their prediction model [31]. Five studies [12, 46–48, 50] examined the difference between an elective admission and an emergency admission on the discrepancy rate. Patients who were admitted through the emergency department (ED) presented with more discrepancies than patients with scheduled admissions in the study performed by Pascual et al. The opposite was found by González-García et al., even after adjustment for confounders [46, 47].

Quélennec et al. detected, in a univariable analysis, that the proportion of patients with pneumonia was lower in the group of patients with discrepancies [9]. Nilsson et al. demonstrated that diabetic patients had a higher rate of discrepancies than non-diabetic patients; the association was no longer significant after adjusting for the number of treatments [51].

Table 1 Characteristics of included studies

Author	Study design	Population	Setting	Intervention	Type of drugs	Type of discrepancies	Severity of discrepancies	Quality assessment
		Sample size		Timing of intervention				Total[a]
		Target group		Who + level of training				
		Age		Type of intervention				
Tamblyn et al. [24]	Prospective cohort study	613	Emergency department Teaching hospital	Admission	Prescription drugs	Drug omission/commission	Not determined	8[a] = good; selection, 3[a]; comparability, 2[a]; outcome, 3[a]
		≥1 prescription medication with public drug insurance	Canada	Trained research assistants				
		18 years or older		Pharmacy records from 2 months before admission				
Chan et al. [34]	Prospective observational before-after study	580	General medical ward Teaching hospital	Within 24 h of admission	Prescription and non--prescription drugs	Drug omission/commission, discrepant dose/dosage	Determined, but not for risk analysis	4[a] = poor; selection, 2[a]; comparability, 0[a]; outcome, 2[a]
		≥5 drugs	New Zealand	Multidisciplinary team: final year pharmacy student, nurse, and clinical pharmacology resident				
		75 years or older		Structured interview				
Hellström et al. [7]	Prospective cohort study	670	Internal medicine ward Academic hospital	After admission	Prescription drugs	Drug omission/commission, discrepant dose/dosage	Not determined	7[a] = good; selection, 3[a]; comparability, 2[a]; outcome, 2[a]
			Sweden	Clinical pharmacist				
		Not specified (mean age 80 years)		Structured interview				
Salanitro et al. [35]	Cross-sectional analysis among intervention	423	All inpatient wards Academic hospitals	Admission	Not specified	Dose omission/commission, discrepant dose/dosage	Determined by pharmacists	6[a] = fair; selection, 2[a];

Table 1 (continued)

Author	Study design	Population	Setting	Intervention	Type of drugs	Type of discrepancies	Severity of discrepancies	Quality assessment
		patients of RCT of the PILL-CVD study [36]					based on clinical relevance	comparability, 2[a]; outcome, 2[a]
		Admitted with acute coronary syndromes or acute decompensated heart failure	Brigham and Boston	Pharmacist				
		18 years or older		Not specified				
Climente-Martí et al. [5]	Prospective observational study	120	Internal medicine ward Academic public tertiary-care hospital	Admission and discharge	Prescription drugs	Drug omission, discrepant dose/dosage/route of administration	Determined, but not for risk analysis	7[a] = good; selection, 3[a]; comparability, 2[a]; outcome, 2[a]
		With chronic preadmission treatment	Spain	Physician and pharmacist				
		Not specified (mean age 76 years)		Structured interview				
Unroe et al. [26]	Retrospective cohort	205	General medicine, cardiology and general surgery ward Academic, tertiary care hospital	Within 48 h of admission	Not specified	Drug omission/commission, discrepant dose/dosage	Determined by pharmacists based on clinical relevance	7[a], good; selection, 3[a]; comparability, 2[a]; outcome, 2[a]
			North Carolina	Clinical pharmacist trained with the hospitals medication reconciliation procedure				
		Not specified (mean age 60 years)		Structured interview				
Gleason et al. [27]	Prospective study	651–428 (with a completed risk factor interview)	General medicine patients Academic hospital	Within 24–48 h of admission	Prescription drugs	Drug omission/commission, discrepant dose/dosage/route of administration	Determined by pharmacists and physicians based on NCC MERP index	7[a] = good; selection, 3[a];

Table 1 (continued)

Author	Study design	Population	Setting	Intervention	Type of drugs	Type of discrepancies	Severity of discrepancies	Quality assessment
								comparability, 2[a]; outcome, 2[a]
		Patients with limited English proficiency were prioritized	Chicago	Study pharmacist				
		Adult patients		Structured interview				
Pippins et al. [29]	Prospective observational study	180	General medicine ward Academic hospitals	Admission and discharge	Not specified	Drug omission/commission, discrepant dose/dosage/route of administration	Determined by physicians based on the method described by Bates et al. [37]	7[a] = good; selection, 3[a]; comparability, 2[a]; outcome, 2[a]
			Massachusetts	Study pharmacist				
		Adult patients		Structured interview				
Glintborg et al. [25]	Prospective study	500	Acute medical emergency ward Academic hospital	Admission	Prescription drugs	Drug omission	Not determined	8[a] = good; selection, 3[a]; comparability, 2[a]; outcome, 3[a]
			Copenhagen	Not specified				
		17 years or older		Pharmacy records				
Feldman et al. [8]	Prospective study	563	General medicine wards Tertiary-care hospital	Within 24–48 h of admission and discharge	Not specified	Drug omission/commission, discrepant dose/dosage/route of administration	Determined, but not for risk analysis	7[a] = good; selection, 3[a]; comparability, 2[a]; outcome, 2[a]
			USA	Baccalaureate-prepared registered nurses				
		Adult patients		Structured interview				
Quélennec et al. [9]	Prospective observational study	256	Internal medicine ward University hospital	Within 24–48 h of admission	Prescription and non--prescription drugs	Drug omission/commission, discrepant dose/dosage	Determined, but not for risk analysis	4[a] = poor; selection, 2[a]; comparability, 0[a]; outcome, 0[a]

Table 1 (continued)

Author	Study design	Population	Setting	Intervention	Type of drugs	Type of discrepancies	Severity of discrepancies	Quality assessment
		Admitted through the emergency department	France	Study pharmacist including 3 students, 1 resident, and 1 senior. All trained to perform medication reconciliation				
		65 years or older		Structured interview				
Andersen et al. [38]	Prospective study	81	Acute internal medicine wards General hospitals	Within 24 h of admission	Prescription and non--prescription drugs	Drug omission	Determined, but not for risk analysis	6[a] = fair; selection, 2[a]; comparability, 2[a]; outcome, 2[a]
			Copenhagen	Pharmacist or physician				
		18 years or older		Structured interview and GP lists				
Balon et al. [39]	Prospective study	75	Medical and surgical wards Tertiary teaching hospital	Admission	Prescription and non--prescription drugs	Drug omission/commission, discrepant dose/dosage/route of administration	Not determined	6[a] = fair; selection, 2[a]; comparability, 2[a]; outcome, 2[a]
		≥1 prescription medication Patients form skilled nursing homes were excluded	Pennsylvania	Clinical pharmacist, pharmacy practice resident and advanced practice nurses				
		18 years or older		Structured interview				
Hatch et al. [28]	Retrospective medical record review	158	Medical and surgical ICU Academic hospital	Admission	Prescription and non--prescription drugs	Drug omission/commission, discrepant dose/dosage/formulation	Not determined	6[a] = good; selection, 3[a]; comparability, 1[a]; outcome, 2[a]
			Madison	Clinical pharmacists, pharmacy residents or pharmacy students				
		Not specified (mean age, 54 years)		Structured interview				
Knez et al. [40]		101	Medical ward	Admission				

Table 1 (continued)

Author	Study design	Population	Setting	Intervention	Type of drugs	Type of discrepancies	Severity of discrepancies	Quality assessment
	Prospective observational descriptive cross-sectional study		Teaching hospital		Prescription drugs	Drug omission/commission, discrepant dose/dosage/other	Determined, but not for risk analysis	4[a] = poor; selection, 2[a]; comparability, 0[a]; outcome, 2[a]
		≥1 drug Native speaking 18 years or older	Slovenia	Research pharmacist Structured interview				
Cornish et al. [41]	Prospective study	151	General internal medicine ward Tertiary-care teaching hospital	Admission	Prescription and non--prescription drugs	Drug omission/commission, discrepant dose/dosage	Determined, but not for risk analysis	4[a] = poor; selection, 2[a]; comparability, 0[a]; outcome, 2[a]
		≥4 regular prescription medication Not specified (mean age 77 years)	Toronto	Pharmacist, pharmacist student or medical student Structured interview				
Vargas et al. [42]	Prospective observational descriptive cross-sectional study	74	General and gastrointestinal surgery, infectious diseases, internal medicine, and orthopedics and orthopedic surgery wards Tertiary care	Admission	Prescription and non--prescription drugs	Drug omission/commission, discrepant dose/dosage/route of administration	Determined, but not for risk analysis	4[a] = poor; selection, 2[a]; comparability, 0[a]; outcome, 2[a]
		≥4 chronic drugs 66 years or older	Spain	Pharmacist Combination electronic and interview based medication reconciliation				
Beers et al. [43]	Prospective study	122	All inpatient wards, exclusive ICUs Academic hospital and community hospital	Within 48 h of admission	Prescription and non--prescription drugs	Drug omission/commission	Not determined	6[a] = fair; selection, 2[a]; comparability, 2[a]; outcome, 2[a]
		≥1 drug 66 years or older	Los Angeles	Trained research assistant Structured interview				

Table 1 (continued)

Author	Study design	Population	Setting	Intervention	Type of drugs	Type of discrepancies	Severity of discrepancies	Quality assessment
Steurbaut et al. [44]	Prospective observational study	197 ≥1 prescription drug 65 years or older	Geriatric ward University hospital Belgium	Within 48 h of admission Clinical pharmacist Structured interview	Prescription and non-prescription drugs	Drug omission	Determined, but not for risk analysis	4[a] = poor; selection, 2[a]; comparability, 0[a]; outcome, 2[a]
Belda-Rustarazo et al. [45]	Prospective observational study	814 ≥5 drugs >65 years	Internal medicine ward University hospital Spain	Within 24 h of admission or next working day Clinical pharmacist Electronic clinical records + structured interview	Prescriptions and non-prescription drugs	Drug omission/commission, discrepant dose/dosage	Determined, but not for risk analysis	4[a] = poor; selection, 2[a]; comparability, 0[a]; outcome, 2[a]
Damlien et al. [30]	Prospective observational study	276 Not specified (median age 69 years)	Emergency department Diakonhjemmet Hospital Norway	admission Clinical pharmacist or emergency nurse with adequate training and experience Structured interview	Not specified	Not specified	Determined by an expert panel (clinical pharmacist and chief physician) on clinical relevance	7[a] = good; selection, 3[a]; comparability, 2[a]; outcome, 2[a]
De Winter et al. [31]	Prospective observational study	3592 Patients awaiting admission ≥16 years	Emergency department Tertiary academic teaching hospital Belgium	Admission Clinical pharmacist or well-trained pharmacy technician Structured interview	Prescription and non-prescription drugs	Drug omission/commission, discrepant dose/dosage	Not determined	7[a] = good; selection, 3[a]; comparability, 2[a]; outcome, 2[a]

Table 1 (continued)

Author	Study design	Population	Setting	Intervention	Type of drugs	Type of discrepancies	Severity of discrepancies	Quality assessment
González-García et al. [46]	Prospective observational study	176	Department of Orthopedic Surgery and Traumatology of Department of Angiology and Vascular surgery	24–48 h after patient admission	Prescription and non--prescription drugs	Drug omission/commission, discrepant dose/dosage	Determined, but not for risk analysis	5[a] = fair; selection, 2[a]; comparability, 1[a]; outcome, 2[a]
		Hospitalization >2 days	Regional public hospital	Pharm graduate				
		>18 years	Spain	Electronic clinical record + structured interview				
Pascual et al. [47]	Cross-sectional observational study	164	Traumatology service	24–48 h after admission	Chronic drugs financed by the National Health Care System	Drug omission/commission, discrepant dose/dosage	Determined but not for risk analysis	7[a] = fair; selection, 2[a]; comparability, 2[a]; outcome, 3[a]
		Hospitalization >24 h	Tertiary hospital	Research team not specified				
		Chronic drug treatment						
		>18 years	Spain	electronic records				
Rodríguez Vargas et al. [48]	Prospective observational study	206	Internal medicine, infectious disease, orthopedic surgery, and general surgery units	Within 24 h after admission	Not specified	Drug omission/commission, discrepant dose/dosage	Determined, but not for risk analysis	6[a] = fair; selection, 2[a]; comparability, 2%; outcome, 2[a]
		≥5 preadmission medication	Tertiary-care teaching hospital	Hospital pharmacist specialist with 4 years of experience				
		>65 years	Spain	Structured interview				
Baena Parejo et al. [32]	Cross-sectional, descriptive, observational multicenter study	387	Emergency department	Within 24 h of admission	Prescription and non--prescription drugs	Drug omissions/commission, discrepant dose/dosage/route of administration	Not determined	7[a] = good; selection, 3[a]; comparability, 2[a]; outcome, 2[a]
			11 general hospitals	Pharmacist				
		>18 years	Spain	Structured interview				
Marinovic et al. [12]		411	Department of internal medicine	Within 24 h following hospital admission	Prescription and	Drug omission/commission, discrepant	Determined, but not for risk analysis	6[a] = fair; selection,

Table 1 (continued)

Author	Study design	Population	Setting	Intervention	Type of drugs	Type of discrepancies	Severity of discrepancies	Quality assessment
	Prospective observational study				non--prescription drugs	dose/dosage/route of administration		2[a]; comparability, 2[a]; outcome, 2[a]
		≥1 regular prescription medication	University hospital	Clinical pharmacist formally trained				
		≥18 years	Croatia	Structured interview				
Mendes et al. [15]	Randomized controlled trial (intervention group is of interest for this review)	39	General wards	Within 72 h of admission	Not specified	Drug omission/discrepant dose/dosage /route of administration	Not determined	4[a] = poor; selection, 2[a]; comparability, 0[a]; outcome, 2[a]
			University teaching hospital	Clinical pharmacist				
		>18 years	Brazil	Structured interview and pharmaceutical records				
Perehudoff et al. [49]	Observational study	78	non-geriatric internal wards or surgery wards	Within 36 h of admission	Not specified	Drug omission/commission, discrepant dose/dosage/route of administration/time of administration	Determined, but not for risk analysis	4[a] = poor; selection, 2[a]; comparability, 0[a]; outcome, 2[a]
		Consultation with the Geriatric Liaison Team was requested	University hospital	Hospital pharmacist				
		≥70 years	Belgium	Structured interview				
Spalla et al. [50]	Prospective observational study	79	Female and male medical clinic units	Within 48 h after admission	Not specified	Drug omission, discrepant dose	Determined, but not for risk analysis	5[a] = poor; selection, 3[a]; comparability, 0[a]; outcome, 2[a]
			University hospital	Pharmacist				
		≥18 years	Brazil	Structured interview				
Saint-Germain et al. [13]	Prospective study	200	Acute geriatric care ward	At admission	Not specified	Drug omission/commission, discrepant	Determined, but not for risk analysis	6[a] = fair; selection, 2[a];

Table 1 (continued)

Author	Study design	Population	Setting	Intervention	Type of drugs	Type of discrepancies	Severity of discrepancies	Quality assessment
						dose/dosage/-pharmaceutical form/substitution		comparability, 2[a]; outcome, 2[a]
			University hospital	Pharmacist				
		Geriatric inpatients (mean age 85 years)	France	Structured interview				
Lubowski et al. [33]	Prospective study	330	General medicine or general surgery service	Within 36 h of admission	Prescription and non--prescription drugs	Drug omission, discrepant dose/substitution	Determined, but not for risk analysis	6[a] = good; selection, 3[a]; comparability, 1[a]; outcome, 2[a]
			type of hospital not specified	Pharmacist students				
		>18 years	United States of America	Structured interview				
Cornu et al. [6]	Retrospective cohort study	199	Acute geriatric department	Admission	Not specified	Drug omission/commission, discrepant dose/brand/dosage	Not determined	5[a] = fair; selection, 2[a]; comparability, 1[a]; outcome, 2[a]
		≥1 prescription drug	University hospital	Pharmacist				
		≥65 years	Belgium	Structured interview				
Breuker et al. [14]	Prospective observational study	904	Endocrinology, diabetology, and nutrition department	Within 24 h of admission of first working day following admission	Prescription and non--prescription drugs	Drug omission/commission, discrepant dose/dosage/route of administration	Determined, but not for risk analysis	6[a] = fair; selection, 2[a]; comparability, 2[a]; outcome, 2[a]
			University hospital	Pharmacist: senior, resident and students				
		>18 years	France	Structured interview				
Nilsson et al. [51]	Prospective multicenter study	262	Geriatric, infection, nephrology and general internal medicine ward	Within 48 h after admission	Not specified	Drug omission/commission, discrepant dose/dosage/drug formulation	Determined, but not for risk analysis	5[a] = poor; selection, 3[a]; comparability, 0[a]; outcome, 2[a]
			5 hospitals					

Table 1 (continued)

Author	Study design	Population	Setting	Intervention	Type of drugs	Type of discrepancies	Severity of discrepancies	Quality assessment
				Clinical pharmacist with training in medication reconciliation				
		>18 years	Norway	Structured interview				

RCT randomized controlled trial, *PILL-CVD* Pharmacist Intervention for Low Literacy in Cardiovascular Disease, *NCC MERP* National Coordinating Council for Medication Error Reporting and Preventing Index for Categorizing Medication Errors, *pADEs* potential adverse drug events, *GP* general practitioner, *ICU* intensive care unit

[a] Score according to the Newcastle-Ottawa Quality Assessment Scale (NOS)

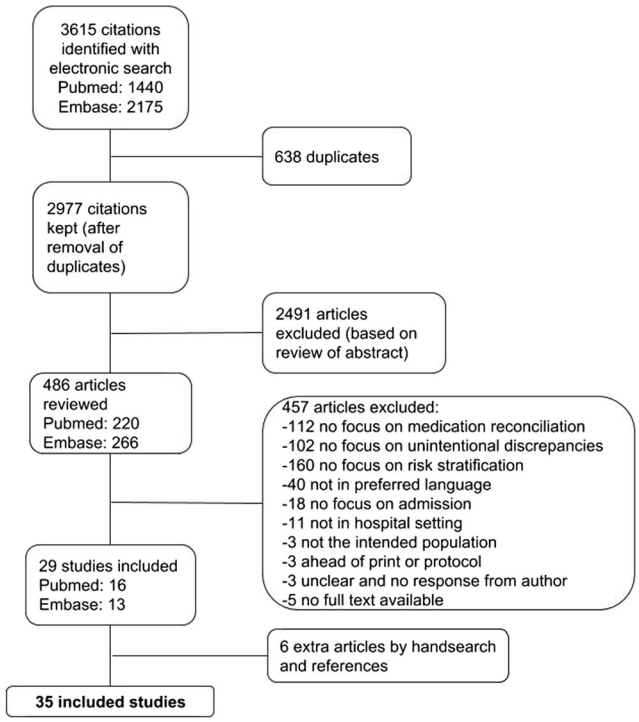

Fig. 1 Screening and selection process for study inclusion

Tamblyn et al. also demonstrated that subjects with more than two ED visits in the past year had more discrepancies than subjects with none or only one ED visit. Adjustment for confounders rendered this effect insignificant [24]. Baena Parejo et al. showed that patients with an episode in the previous 3 months had more discrepancies on admission; after adjustment for confounders, this effect disappeared [32].

Two research teams investigated the effect of patients' understanding of PAM on the number of discrepancies [12, 35]. Marinovic et al. found with a multivariable analysis that a low level of patients' understanding was associated with more discrepancies [12]. Level of education was tested as a predictor by three studies [8, 12, 46]. Patients with no or limited to a primary educational level experienced more discrepancies in a bivariate analysis, but not when adjusted for other variables [46].

Comorbidities were subject of analysis in seven studies [5, 12, 15, 32, 45, 48, 49]. According to the univariate analysis performed by Rodríguez Vargas et al., the number of comorbidities could predispose a patient to discrepancies [48]. Mendes et al. and Baena Parejo et al. found a correlation between the Charlson comorbidity index and unintentional discrepancies [15, 32].

Medication-related predictors

The number of PAM was analyzed as a predictor in 26 studies [5–8, 12, 13, 15, 24, 27, 31–35, 38, 40–43, 45–51]. Twenty-three studies [6–8, 12, 13, 15, 24, 27, 31–35, 40, 42, 43,

Table 2 Significant predictors from multivariable analysis for (potentially harmful) unintentional discrepancies in preadmission medication lists (unless otherwise stated)

Predictor	Author	Variables	Result	*p* value
Patients-related predictors				
Age	Salanitro et al. [35][a]	Age 55–64, 65+ vs <55	IRR 1.46 (95%CI 1.00–2.12)	$p < 0.05$
	Unroe et al. [26][a]	Age continuous, per 5 year increase	OR 1.16 (95%CI 1.01–1.33)	$p = 0.035$
	Gleason et al. [27][a]	Age ≥ 65 vs <45	OR 2.17 (95%CI 1.09–4.30)	$p \leq 0.05$
	Pippins et al. [29][a]	Age ≥85 vs <50	RR 0.34 (95%CI 0.16–0.73)	$p < 0.05$
	Saint-Germain et al. [13]	Age continuous	OR 0.93 (95%CI 0.88–0.99)	NR
Gender	Balon et al. [39]	Male vs female % accurate	OR 2.58 (95%CI 1.07–6.22)	NR
Type of care service before admission	Hellström et al. [7]	Own home, no care services vs care home	OR 1.58 (95%CI 1.02–2.45)	$p < 0.05$
Usage of different outpatient pharmacies	Tamblyn et al. [24]	≥2 pharmacies vs 1 pharmacy	OR 3.45 (95%CI 1.80–6.59)	$p = 0.0002$
	Gleason et al. [27][a]	≥2 pharmacies vs 1 pharmacy	OR 0.51 (95%CI 0.27–0.97)	$p \leq 0.05$
Availability of a drug list	Salanitro et al. [35]	Medication list available in EMR	IRR 0.60 (95%CI 0.43–0.84)	$p < 0.05$
	Salanitro et al. [35][a]	Medication list available in EMR	IRR 0.54 (95%CI 0.30–0.96)	$p < 0.05$
	Gleason et al. [27][a]	Medication list presented upon admission	OR 0.35 (95%CI 0.19–0.63)	$p \leq 0.05$
Patients' understanding of medication	Pippins et al. [29][a]	Medium or low vs high	RR 1.65 (95%CI 1.14–2.39)	$p < 0.05$
	Marinovic et al. [12]	Low vs high	OR 1.79 (95%CI 1.01–3.16)	$p = 0.046$
Number of outpatients visits past year	Pippins et al. [29][a]	≥13 vs 0–1	RR 1.75 (95%CI 1.16–2.65)	$p < 0.05$
Type of admission	González-García et al. [46]	Elective vs emergency	OR 4.450 (95%CI 2.046-9.688)	$p < 0.001$
Medication-related predictors				
Number of preadmission drugs	Tamblyn et al. [24]	7–12 drugs vs 2–6 drugs	OR 1.99 (95%CI 1.21–3.29)	$p = 0.007$
	Tamblyn et al. [24]	≥12 drugs vs 2–6 drugs	OR 2.92 (95%CI 1.71–4.97	$p < 0.0001$
	Hellström et al. [7]	Per additional medication	OR 1.10 (95%CI 1.06–1.14)	$p < 0.05$
	Salanitro et al. [35]	Per additional medication	IRR 1.12 (95%CI 1.08–1.16)	$p < 0.05$
	Salanitro et al. [35][a]	Per additional medication	IRR 1.17 (95%CI 1.10–1.25)	$p < 0.05$
	Beers et al. [43]	Number of medication	$R^2 = 0.32$	NR
	Feldman et al. [8]	Per additional medication	OR 1.087 (95%CI 1.044-1.132)	NR
	Gleason et al. [27][a]	Per additional medication	OR 1.21 (95%CI 1.14–1.29)	$p \leq 0.05$
	Pascual et al. [47]	Per additional medication	OR 1.333 (95%CI 1.143-1.555)	$p < 0.001$
	Gonzaléz-García et al. [46]	Per additional medication	OR 1.342 (95%CI 1.210-1.487)	$p < 0.001$
	Rodríguez Vargas et al. [48]	Per additional medication	OR 1.20 (95%CI 1.07–1.34)	$p = 0.002$
	Baena Parejo et al. [32]	Per additional medication	OR 1.313 (95%CI 1.180-1.460)	NR
	Marinovic et al. [12]	Per additional medication	OR 1.19 (95%CI 1.10–1.29)	$p < 0.001$
	Saint-Germain et al. [13]	Per additional medication	OR 1.22 (95%CI 1.07–1.39)	NR
	Cornu et al. [6]	Per additional medication	OR 1.47 (95%CI 1.24–1.74)	$p < 0.001$
	Lubowski et al. [33]	≥6 drugs	NR	$p < 0.05$
Class of medication	Glintborg et al. [25]	For reporting preadmission medication		
		Dermatologicals vs cardiovascular	OR 0.05 (95%CI 0.01–0.16)	$p < 0.005$
		Anti-infectives vs cardiovascular	OR 0.15 (95%CI 0.08–0.26)	$p < 0.005$
		Musculoskeletal vs cardiovascular	OR 0.18 (95%CI 0.09–0.35)	$p < 0.005$
		Sensory vs cardiovascular	OR 0.23 (95%CI 0.08–0.64)	$p < 0.005$
		Respiratory vs cardiovascular	OR 0.30 (95%CI 0.17–0.53)	$p < 0.005$

Table 2 (continued)

Predictor	Author	Variables	Result	*p* value
		Alimentary tract vs cardiovascular	OR 0.35 (95%CI 0.18–0.66)	$p < 0.005$
		Genitourinary vs cardiovascular	OR 0.37 (95%CI 0.14–0.96)	$p < 0.05$
		Nervous vs cardiovascular	OR 0.40 (95%CI 0.32–0.69)	$p < 0.005$
Number of reimbursements	Glintborg et al. [25]	For reporting preadmission medication		
		1 vs ≥5	OR 0.22 (95%CI 0.13–0.35)	$p < 0.005$
		2–4 vs ≥5	OR 0.62 (95%CI 0.4–0.98)	$p < 0.05$
Number of high-risk drugs	Pippins et al. [29][a]	≥4 vs 0 preadmission medication	RR 3.00 (95%CI 1.29–7.00)	$p < 0.05$
	Unroe et al. [26][a]	Presence of high-risk medication on admission	OR 76.68 (95%CI 9.13–643.76)	$p < 0.001$
Setting-related predictors				
Admitting service	Hatch et al. [28]	Trauma patients vs medical patients	More drug omissions in trauma patients	$p = 0.047$
		Trauma patients vs non-trauma surgical patients	More drug omissions in trauma patients	$p = 0.025$
		Non-trauma surgical patients vs medical patients	More dose omissions in non-trauma surgical patients	$p = 0.004$
		Non-trauma surgical patients vs medical patients	More frequency omissions in non-trauma surgical patients	$p = 0.007$
	Unroe et al. [26][a]	General surgery vs cardiology	OR 3.31 (95%CI 1.40–7.87)	$p < 0.007$
Admitting physicians' experience	Pippins et al. [29][a]	Resident vs intern	RR 0.51 (95%CI 0.31–0.82)	$p < 0.05$
	Rodríguez Vargas et al. [48]	Junior vs senior	OR 1.85 (95%CI 1.01–3.40)	$p = 0.047$
Source consulted	Pippins et al. [29][a]	Family member or caregiver yes vs no	RR 1.62 (95%CI 1.10–2.38)	$p < 0.05$
	Cornu et al. [6]	Per additional source consulted	OR 1.78 (95%CI 1.13–2.80)	$p = 0.01$
Use of CPOE system	Rodríguez Vargas et al. [48]	Yes vs no	OR 0.43 (95%CI 0.21–0.89)	$p = 0.023$

Type of performed statistical test in the original study: adjusted negative binominal logistic regression [35], multivariate logistic regression analyses [26], multiple logistic regression [27], multivariable binary logistic regression model [7], generalized estimating equations modeling [39], multivariable Poisson regression analysis [29], multivariate logistic regression [24], multivariate linear regression [43], logistic regression [8], model 2 multiple logistic regression analysis [25], negative binominal regression [28], multivariate logistic regression [46], multivariate logistic regression [47], forward stepwise logistic regression [48], multivariate logistic regression [32], multivariate logistic regression [12], multiple regression analysis [33], multivariate binary logistic regression analysis [6], and multivariate logistic regression [13]

IRR incidence rate ratio, *OR* odds ratio, *RR* relative risk, *CI* confidence interval, *EMR* electronic medical record, *NR* not reported, *CPOE* computerized physician order entry

[a] Result only applicable for potentially harmful discrepancies

45–51] found a significant effect, of which 13 [6–8, 12, 13, 24, 32, 33, 35, 43, 46–48] were able to show significance after adjustment for confounders; they demonstrated that a higher number of drugs was associated with a higher discrepancy rate.

In four studies, the link between specific drug classes and discrepancies was investigated [24, 25, 31, 34]. Tamblyn et al. concluded that therapeutic drug classes and the number of drugs correlated. Subsequently, only the number of drugs was included in the adjusted prediction model [24]. Chan et al. found that the PAM-related discrepancy rate for the "ear, nose, oropharynx, and eye," "skin," and "vitamins and mineral" classes was significantly higher than for the other classes in univariable analysis. Both prescription-only and over-the-counter (OTC) drugs were recorded, but dietary supplements and herbal or homeopathic products were excluded from the analysis as most of these products were not dispensed in the hospital [34]. Glintborg et al. furthermore showed that the type of Anatomical Therapeutic Chemical Classification, as defined by the WHO, was predictive for discrepancies upon admission in a multivariable analysis. Cardiovascular drugs were less likely to be omitted on admission [25]. De Winter et al. also found an association between specific drug classes and the number of discrepancies [31].

Setting-related predictors

The admitting service was tested as a predictor in four studies [28, 42, 46, 48]. Hatch et al. found that surgeons caring for trauma patients were likely to omit more medication

Table 3 Predictors for unintentional discrepancies in preadmission medication

Predictors for unintentional discrepancies	Non-parametric tests[a] Significant/total	Unadjusted predicting model[b] Significant/total	Adjusted predicting model[c] Significant/total
Patient-related predictors			
Age	6/13	3/5	2/11
Gender	4/13	0/4	2/8
Type of care service before admission	0/4	0/2	2/3
Usage of different outpatient pharmacies	–	1/1	1/1
No medication list available	–	0/1	1/1
Bottles brought on admission	1/1	–	–
Emergency department visits in past year	1/1	1/1	0/1
Clinical characteristics at admission	2/3	–	–
Final DRG weight	0/1	–	–
Severity of illness	–	–	0/1
Number of prescribing physicians	–	1/1	–
Communication barrier	0/2	0/2	0/2
Hospitalization in past year	–	0/2	0/3
Race	0/1	–	0/1
Health literacy	–	0/1	0/1
Patients' understanding of medication	–	0/1	1/2
Insurance type	–	0/1	0/1
Medication adherence	–	0/1	0/1
Directly admitted to ward	–	–	0/1
Level of education	–	1/1	0/2
Marital status	–	–	0/1
Primary payor	–	–	0/1
Barthel score/index	–	0/1	–
Number of comorbidities	3/5	0/1	0/2
ICU stay during hospitalization	0/1	–	–
Origin before admission	0/3	–	–
Type of admission (elective vs emergency)	1/3	1/1	1/2
Number of previous surgeries	1/1	–	0/1
Responsible for medication (patient vs caregiver)	0/2	–	–
History of ADEs	–	–	0/1
Triage risk screening tool	1/1	–	–
Drug delivered in multidose system	0/1	–	–
Medication-related predictors			
Number of preadmission drugs	13/15	4/5	13/15
Number of medication prescribed at hospital	0/1	–	–
Number of high-risk drugs	1/1	–	–
Class of medication	2/2	1/1	1/1
Route of administration	1/1	–	–
Number of reimbursements	–	–	1/1
Setting-related predictors			
Admitting service	0/2	0/1	1/1
Admitting discipline in the emergency department	1/1	–	–
Admitting physicians' experience	1/3	–	1/1
Hospitalist vs teaching service	0/1	–	–
Admission moment	0/5	–	–
Family member or caregiver as consulted source	1/2	–	–
Season	1/1	–	–

Table 3 (continued)

Predictors for unintentional discrepancies	Non-parametric tests[a] Significant/total	Unadjusted predicting model[b] Significant/total	Adjusted predicting model[c] Significant/total
Professional carrying out the reconciliation	1/1	–	0/1
Use of CPOE system	0/1	–	1/1
Primary care prescription list accessed	1/1	–	–
Number of clinical data sources	0/2	1/1	1/1

Some predictors were tested with different tests in the same study

ICU intensive care unit, *CPOE* computerized physician order entry system, *DRG* diagnosis-related group, *ADE* adverse drug event

[a] Performed tests by the original papers: Pearson correlation and ANOVA [34], chi-squared and *t* tests [27], chi-squared and *t* tests [9], Pearson correlation [40], *t* test [41], *t* test, chi-squared test, and Mann-Whitney *U* [42], Mann-Whitney *U* [44], chi-squared and *t* tests and ANOVA [45], Mann-Whitney *U* and Kruskal-Wallis test and Spearman's r [31], chi-squared and *t* tests and Mann-Whitney *U* test [47], chi-squared and *t* tests and Mann-Whitney *U* test [48], Student *t* test and Mann-Whitney *U* test and Pearson's chi-squared test and Fischer's exact test [32], Pearson correlation and Spearman correlation [15], Pearson chi-squared and independent sample *t* tests [49], chi-squared and Student's *t* tests [13], Mann-Whitney *U* and Student *t* test [14], independent sample *t* test, and Pearson's chi-squared test [51]

[b] Performed test by the original papers: univariate association [24], negative binomial logistic regression [35], univariate logistic regression [5], logistic regression [46], and univariate binary logistic regression [6]

[c] Performed tests by the original papers: multivariate logistic regression [24], logistic regression [8], multivariable binary logistic regression [7], negative binominal logistic regression [35], multivariate logistic regression [5], multiple logistic regression analysis [25], multiple logistic regression model: variables eliminated backwards [38], GEE modeling [39], negative binominal regression [28], multivariable linear regression analysis [43], multivariate logistic regression [46], multivariate logistic regression [47], multivariate logistic regression [32], multivariate logistic regression [12], multivariate logistic regression [13], multiple regression analysis [33], and multivariate binary logistic regression [6]

compared to physicians caring for medical and non-trauma surgical patients [28].

Three studies examined whether the clinical experience of the admitting physicians had an influence on the discrepancy rate [31, 34, 48]. Rodríguez Vargas et al. found after adjustment for confounders that junior physicians had a higher risk on discrepancies than senior physicians [48].

Belda-Rustarao et al. and Baena Parejo et al. studied the effect of consulted sources on the discrepancy rate [32, 45]. Baena Parejo et al. found more discrepancies when the caregiver was interviewed as opposed to other sources [32].

Three studies investigated whether the number of consulted sources for the collection at the best possible PAM list was associated with more discrepancies [6, 13, 15]. Cornu et al. identified the number of information sources consulted as a risk factor for the presence of at least one discrepancy after adjustment for confounders [6].

Risk factors for potentially harmful unintentional discrepancies

Five studies focused on clinically relevant PAM-related errors [26, 27, 29, 30, 35]. In all these studies, the potential for patient harm of the PAM-related discrepancies was ascertained. In two studies, a systematic classification was used [27, 29], while in the other studies, assigning potential harm was based on expert opinion [26, 30, 35]. Adjustment for confounders was performed in four studies [26, 27, 29, 35]. The variables analyzed as risk factors for potentially harmful unintentional discrepancies are summarized in Table 4. Both statistically significant and insignificant results are shown in Table 4. A distinction was made between univariable and multivariable analyses as performed by the included studies.

Variables for which potential correlation with unintentional discrepancies was tested in several studies and found at least once to be statistically associated are discussed in more detail in the following.

Patient-related predictors

For each study, it was investigated whether age was a predictor for potentially harmful discrepancies [26, 27, 29, 30, 35]. In four studies, it was shown that older patients had a higher risk for clinically relevant discrepancies [26, 27, 30, 35]. In contrast, Pippins et al. concluded that patients older than 85 years had significantly less clinically relevant discrepancies compared to those younger than 50 years [29].

Three studies examined if gender was associated with more discrepancies [26, 27, 30]. Only Damlien et al. found that woman had more discrepancies than men [30].

Salanitro et al., Gleason et al., and Damlien et al. showed that patients with a medication list (available in the EMR (within 90 days prior to admission) or presented on admission) had less discrepancies with a potential for harm [27, 30, 35].

Patients' understanding of their medication was scrutinized in two studies [29, 35]. Pippins et al. showed that patients with medium or low understanding of their medication had a higher risk for potentially harmful PAM-related discrepancies than patients with a high understanding of their medication [29].

Table 4 Predictors for potentially harmful unintentional discrepancies in preadmission medication

Predictors for potentially harmful unintentional discrepancies	Non-parametric tests[a] Significant/total	Unadjusted predicting model[b] Significant/total	Adjusted predicting model[c] Significant/total
Patient-related predictors			
Age	1/1	1/2	4/4
No medication list available	1/1	0/1	2/2
Patients understanding of medication	–	0/1	1/2
Usage of different outpatient pharmacies	–	–	1/1
Number of outpatients visits past year	–	–	1/1
Health literacy	–	1/1	0/1
Type of care service before admission	–	0/1	0/2
Communication barrier	–	0/1	0/2
Gender	1/1	0/1	0/1
Insurance type	–	0/1	0/1
Medication adherence	–	0/1	0/1
Race	–	0/1	0/1
ICU stay during hospitalization	–	–	0/1
Bottles brought on admission	–	–	0/1
Partners PCP	–	–	0/1
Hospitalization past month	–	–	0/1
Hospitalization past year	1/1	–	–
Number of prescribing physicians	–	–	0/1
Final DRG weight	–	–	0/1
Number of comorbidities	1/1	0/1	/
Cause of admission	0/1	–	–
Medication handling	0/1	–	–
Medication-related predictors			
Number of preadmission medication	1/1	1/2	2/3
High-risk medication	–	1/1	2/2
Change in therapy in the last year	–	–	0/1
Setting-related predictors			
Admitting service	–	1/1	1/1
Admitting physician experience	–	–	1/1
Family member or caregiver as consulted source	–	–	1/1
Hospitalist vs teaching service	–	–	0/1

Some predictors were tested with different tests in the same study

ICU intensive care unit, *PCP* primary care physician, *DRG* diagnosis-related group

[a] Performed test by the original papers: Pearson's chi-squared test [30]

[b] Performed tests by the original papers: negative binominal logistic regression [35] and univariate logistic regression [26]

[c] Performed tests by the original papers: multiple logistic regression analyses [27], multivariable Poisson regression [29], negative binominal logistic regression [35], and multivariate logistic regression [26]

Unroe et al. and Damlien et al. analyzed if the number of comorbidities was a potential predictor [26, 30]. Only Damlien et al. found that patients with more than three comorbidities had more discrepancies [30].

Medication-related predictors

Although it was investigated in each of the five abovementioned studies, if the total number of PAM was associated with potentially harmful discrepancies, only Salanitro et al., Damlien et al., and Gleason et al. showed that the risk for discrepancies increased per additional drug [27, 30, 35]. Pippins et al. found that five drug classes, which included gout medication, muscle relaxants, lipid-lowering agents, anti-depressants, and respiratory medication, were most frequently involved in the occurrence of potentially harmful discrepancies. They established that the intake of at least four of these drug classes increased the discrepancy rate [29]. Unroe et al. also found that

the presence of high-risk medication, as defined by the authors as medication included on the Institute of Safe Medication Practice high-alert list or the North Carolina Narrow Therapeutic Index list, on admission was associated with a higher proportion of patients with PAM-related discrepancies [26].

Setting-related predictors

Unroe et al. showed that patients admitted to the general surgery ward were more likely to have a PAM-related discrepancy than those admitted to the cardiology ward [26].

Discussion

We found and assessed 56 potential predictors, of which 19 were significantly associated with discrepancies. The following 16 significant variables were identified using multivariable prediction models; they are listed hereafter according to the number of articles in which there was a statistically significant association: number of preadmission drugs, patient's age, availability of a drug list, patients' understanding of medication, usage of different outpatient pharmacies, number of high-risk drugs, discipline for which the patient is admitted, admitting physician's experience, number and type of consulted sources, patient's gender, type of care before admission, number of outpatient visits during the past year, class of medication, number of reimbursements, use of an electronic prescription system, and type of admission (elective vs emergency).

Some variables appeared contradictory. Four studies [26, 27, 30, 35] indicated that an increase in age increased the risk for potentially harmful discrepancies, in contrast to Pippins et al. [29], who found that patients older than 85 years had significantly less potentially harmful discrepancies than patients younger than 50. The latter was also seen by Saint-Germain et al., where in a geriatric population, a higher age was protective for all unintentional discrepancies [13]. This conflicting result could be explained by the possible difference in the degree of medical and social support between very old patients and other adults [29], signifying an inversion of the relation between age and discrepancy risk in the very old. As shown by Hellström et al., patients who lived in their own home with no care services had a higher risk for discrepancies than patients coming from a nursing home [7]. Remarkably, in contrast to Tamblyn et al. [24], Gleason et al. [27] found that patients visiting multiple community pharmacies were seen to have less PAM-related discrepancies. Pascual et al. [47] found that patients admitted trough the emergency department had more discrepancies than the ones with a scheduled admission; on the other hand, González-García [46] et al. found the opposite, while three other studies found no significant difference between an elective admission and an emergency admission [12, 48, 50].

Strengths and limitations

To our knowledge, this systematic review was the first attempt to identify predictors for unintentional discrepancies in medication histories, including patient-, medication-, and setting-related predictors. A portion of these predictors can be collected as part of patient care and are available upon hospital admission, such as age, gender, type of care before admission, and availability of a drug list. Other variables are possibly available shortly after admission or after the gathering of a PAM list by usual care, such as the number of preadmission drugs as reported by the admitting physician, the admitting service, and the admitting physician's experience. These predictors could then be incorporated in clinical decision rules or care pathways to target high-risk patients in the medication reconciliation process on admission, especially when resources are limited.

Several of these factors were investigated in the majority of the assessed studies (e.g., age, number of preadmission drugs), while other predictors (e.g., availability of a drug list, health literacy, changes in therapy in the past year) were only subjected to analysis in few studies.

The methodological heterogeneity is characterized by the lack of uniform definitions or very diverse statistical analyses and subsequent reporting precluded meta-analysis. Furthermore, some of these methodological dissimilarities could explain the observed differences in (statistically significant) predictors.

No uniform type for a discrepancy was used in the selected manuscripts. This varied from drug therapy omissions as compared to the PAM list [25, 38, 44] or a combination of omissions and commissions (added therapy) [24, 43] to also including differences in dose, dosage, or route of administration [5, 8, 12, 14, 15, 27, 29, 32, 39, 42]. Two different types of intervention were used: a structured interview or one based on community pharmacy records. Another factor that might explain why some found a specific predictor to be significant while others did not is the sample size calculation or lack thereof. Sample sizes varied from 39 to 3592, which could imply that some studies lacked power to detect a statistically significant result. In this review, significant results were presented, but there was no focus on effect size. Some variables had a barely significant result, shown by a p value close to 0.05 (e.g., the effect of patients' understanding of medication on discrepancies reported by Marinovic et al. [12]) (OR 1.79 (95%CI 1.01–3.16), $p = 0.046$)). Some odds ratios were furthermore characterized by a very broad 95% confidence interval (e.g., number of high-risk medication (OR 76.68 (95%CI 9.13–643.76) [26]). Differences in study settings could also have contributed to the ambiguity described above; e.g., wards

with predominantly unplanned admissions might detect more inadequate medication histories than wards with more elective admissions [28]. Although several studies included patients from different wards [14, 15, 26–28, 33, 39, 42, 43, 46, 48–51], only six studies [26–28, 42, 46, 48] considered the specific type of admission ward as a predictor. The level of communication between community care services and hospitals is likely to vary between settings and countries and could therefore influence the discrepancy rate and the associated variables. The included subjects differed among the gathered studies: in some, only elderly [6, 9, 13, 34, 42, 43, 45, 48, 49] were included; in others, patients taking less than four types of drugs [34, 41, 42, 45, 48] were excluded. Since some researchers concluded that age and the number of PAM could be predictive for unintentional discrepancies, the variables polypharmacy and age could already be biased due to the inclusion criteria of certain studies. Also, some research groups looked selectively at prescription-only drugs [5, 7, 24, 25, 27, 40]. The possible difference in the exact point in time of the reconciliation process might also prove to be of relevance, as certain variables only become available later on during hospital stay. Three research groups did not distinguish between predictors for discrepancies on admission and at discharge [5, 8, 29]. Choice of statistical tests differed as well; it varied from non-parametric tests to predictive models which were whether or not corrected for confounders. Besides, not all researchers used the same variables to correct for in their multivariable analysis. Adjustment for confounders is desirable, on account of a possible interaction between multiple predictors such as a possible interaction between high age and polypharmacy.

The search was restricted to two databases. Since there was a substantial number of additional manuscripts retrieved from the second database, some manuscripts within the scope of this review may have been missed; however, the selected databases are large and widely used for systematic literature reviews. Furthermore, the database results were complemented with the snowball method. This review was intentionally limited to medication reconciliation in the hospital setting, so our results should be carefully interpreted as regard to their application to the ambulatory setting. It was also limited to hospital admission, since, in our opinion, identification of reconciliation discrepancies should be carried out as early as possible to prevent downstream potential drug-related problems. Only one reviewer performed the selection of the articles and the quality assessment. Yet a stringent method was used for both. Also, two other reviewers evaluated articles in case of any uncertainty. There were multiple meetings to ensure the quality of this review, and agreement was established between the three reviewers. Due to a lack of a single quality scale for this variety of non-randomized controlled trials, the NOS for cohort studies was used as proposed by the Cochrane Handbook for Systematic Reviews of Interventions [21, 22]. Because of the typical design of the included studies—studies without control group and lack of follow-up period—only few criteria were considered appropriate for actual grading (e.g., representativeness, assessment of outcome, adjustment for confounders) and could be used to discriminate between the different studies. In addition, the scale did not inquire whether studies were sufficiently powered to identify predictors. Future research is necessary to develop a quality assessment tool allowing proper evaluation of this type of studies.

Of the 35 selected articles, the relation between the number of discrepancies and the incidence of new and potentially avoidable adverse events was only explored in five studies [26, 27, 29, 30, 35]. Pippins et al., Damlien et al., and Gleason et al. rated with an independent team the discrepancies' potential for harm, including the presumed severity [27, 29]. Gleason et al. classified the harm according to an adjusted National Coordinating Council for Medication Error Reporting and Prevention Index [27]. Pippins et al. rated the supposed severity of the discrepancies according to a previously worked out classification of Bates et al. [29, 37]. In our opinion, the pursuit of predictors for clinically relevant discrepancies is important, as the prevention and early resolution of these discrepancies might eventually help in preventing avoidable adverse events altogether. Additional studies are needed to identify patients at risk for clinically significant discrepancies potentially causing harm and resulting in actual harm [2].

Additional prospective studies focusing on potentially harmful discrepancies with none or few exclusion criteria so that the results can be generalizable are necessary. The predictors should be clearly defined (e.g., ED triage acuity scale [52]) and limited to those that are readily available upon admission (or very shortly thereafter) (e.g., age). Afterwards, these predictors could be implemented in clinical decision rules or care pathways to predict patients with a high risk for unintentional discrepancies. Prospective validation of these prediction models including aforementioned predictors should be the next step to render these models useable in practice. In a subgroup analysis, Schnipper et al. advocated the use of a potential adverse drug event (PADE) risk score to identify those high-risk patients in whom medication reconciliation should be performed in order to effectively prevent PADE [10]. This risk score was developed by Pippins et al. [29]. At the time of this review, the validation study of the Medication Reconciliation Quality Improvement Study risk stratification tool was still ongoing, which included a risk stratification tool based on expert consensus. It aims to demonstrate a reduction in PAM-related discrepancies and an improvement in patient outcomes [53, 54]. Furthermore, more research is necessary to facilitate the medication reconciliation process by providing access to all health care providers pre- and post admission to all dispensed medications. Relying on electronic prescribing

registers as the only source of drug record may potentially jeopardize patient care, as shown by Engqvist et al. [55] Electronic prescribing registers can provide accurate information at the moment of drug dispensation, but is not necessarily correct and complete at time of hospital admission. Hence, a structured medication reconciliation process based on multiple sources will still be of importance for some high-risk patients.

Conclusion

This systematic review has identified several predictors for (potentially harmful) discrepancies in medication histories upon hospital admission, including patient, medication-, and setting-related predictors. A high number of preadmission drugs were found to be a significant predictor for unintentional discrepancies. Also, age had a predictive value for potentially harmful discrepancies. These variables should be validated in risk prediction models and evaluated to improve their performance in a more generalizable population.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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