BMJ Open

Methodological approaches for medication error analyses in patient safety and pharmacovigilance reporting systems: a scoping review protocol

Olga Tchijevitch [iD],[1] Sebrina Maj-Britt Hansen,[2] Søren Bie Bogh [iD],[1] Jesper Hallas,[3] Søren Birkeland [iD] [1]

¹OPEN - Open Patient data Explorative Network, Department of Clinical Research, University of Southern Denmark, Odense, Denmark
²University Library of Southern Denmark, University of Southern Denmark, Odense, Denmark
³Clinical Pharmacology, Pharmacy, and Environmental Medicine, Department of Public Health, University of Southern Denmark, Odense, Denmark

Correspondence to
Ms Olga Tchijevitch;
otchijevitch@health.sdu.dk

ABSTRACT

Introduction Medication errors (MEs) are associated with patient harm and high economic costs. Healthcare authorities and pharmacovigilance organisations in many countries routinely collect data on MEs via reporting systems to improve patient safety and for learning purposes. Different approaches have been developed and used for the ME analysis, but an overview of the scope of available methods currently is lacking. This scoping review aimed to identify, explore and map available literature on methods used to analyse MEs in reporting systems.

Methods and analyses This protocol describes a scoping review, based on the Joanna Briggs Institute methodological framework. A systematic search will be performed in MEDLINE (Ovid), Embase (Ovid), Cinahl (EBSCOhost), Cochrane Central, Google Scholar, websites of the major pharmacovigilance centres and national healthcare safety agencies, and citation search in Scopus in August 2022. All retrieved records are to be independently screened by two researchers on title, abstract and full text, involving a third researcher in case of disagreement. Data will be extracted and presented in descriptive and tabular form. The extraction will be based on information about methods of ME analyses, type of reporting system and information on MEs (medication name, ATC codes, ME type, medication–event categories and harm categories).

Ethics and dissemination Ethical approval is not required. The results will be disseminated via publication in peer-reviewed journals, scientific networks and relevant conferences.

INTRODUCTION

A medication error (ME) is an error in the medication treatment process which may occur during all stages of medication use from ordering, through dispensing and administration, to monitoring.[1] MEs constitute a major challenge to patient safety[2] and are associated with patient harm and increasing national expenses.[3–5] The prevalence of preventable medication harm has been estimated to be 3% in adult patients in primary and secondary healthcare settings on average, with higher rates

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This scoping review, based on an established scoping review methodology, will be the first to identify and map existing publications on methods used to analyse medication errors (MEs) in reporting systems.

⇒ The systematic search strategy is developed in collaboration with an experienced information specialist, and study selection and data extraction are to be performed by independent reviewers.

⇒ No formal quality assessment on the included publications will be done, as the review aimed to map publications on methodology of ME analyses in reporting systems.

⇒ The search strategy may result in a large number of publications that may require refinement of eligibility criteria.

in elderly (11%) and intensive care patients (7%).[6] For example, in the UK, error-related harm is estimated to contribute to more than 1700 deaths per year, costing £98.5 million (€114.6 million) for hospital admissions and extended hospital stay.[7] In European healthcare, the estimated yearly cost range from €4.5 to €21.8 billion,[8] and worldwide, it adds up to about €35 billion.[2]

MEs and harm associated with MEs have been a challenge to safety for decades.[9 10] Consequently, patient safety reporting systems (PSRS) have been introduced to and adopted by many countries. The PSRS are based on reports of incidents that resulted in harm or might have caused harm. The main intention of the PSRS is to learn and thereby prevent forthcoming injuries.[11] The PSRS are organised on different levels (national, regional, institutional, etc). Some are voluntary; others are mandatory; some only include MEs, while others may include other hazardous healthcare incidents. The share of ME reports is remarkably high, corresponding to 11% of nearly 1 200 000 annual incident

reports in England and Wales, and 56% of 222 289 annual incident reports in Denmark.[11 12]

In pharmacovigilance, spontaneous reporting systems (SRS) were initially applied when monitoring *adverse drug reactions* (ADR), but recently, SRS play a more dominant role when monitoring MEs, quite in accordance with the recommendations from WHO and EU for collaboration between safety organisations in healthcare.[8 13] The European database for ADR (EudraVigilance) and the US Adverse Events Reporting System collected 147 824 ME reports in 2002–2015 and more than 100 000 reports in 2015.[14 15] The number of reported incidents has increased rapidly, reaching an overwhelming volume of reports.[11 12 14] Analysing the large amount of data, collected via reporting systems by national safety authorities and pharmacovigilance centres, is costly and challenging.[16 17] Inefficiently analysed data may ultimately impede the learning potential of ME reports and, at the end, may compromise patient safety. Moreover, healthcare systems may choose to deprioritise or even phase out parts of the mandatory reporting, thereby taking patient safety a great step backwards.[18] Various approaches to ME analyses have been developed to address challenges, ranging from traditional manual reviewing and arithmetical counting to advanced computerised methods such as natural language processing and data mining methods. However, knowledge of the current scope of methodological approaches and the frequency of their use is limited. There is therefore a need to provide an up-to-date overview of the knowledge to understand and make recommendations for necessary developments. A preliminary search in PubMed has not identified systematic or scoping reviews on this topic. In this scoping review, we aimed to identify, explore and map the existing publications/scientific literature on methods of ME analysis in reporting systems.

METHODS

The proposed scoping review will be based on Joanna Briggs Institute methodological framework,[19] initially developed by Arksey and O'Malley.[20] This method is based on five stages: (1) identifying the research question; (2) identifying relevant studies; (3) study selection; (4) charting the data, and (5) collating, summarising and reporting the results.

The proposed review is to be reported according to Preferred Reporting Items for Systematic Review and Meta-Analyses Extension for Scoping Reviews.[21]

The definition of terms is presented in table 1.

Identifying the research question

The research question emerged from knowledge gaps identified by the authors. As the availability of methodological approaches and new technologies used to analyse large databases is rapidly growing, the following question was formulated: 'What is known from the literature about ME methods

Table 1	Definitions of terms
ME	'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 healthcare professional, patient, or consumer. Such events may be related to professional practice, healthcare products, procedures, and systems, including prescribing, order communication, product labelling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use'.[25] MEs can be classified according to their severity in nine categories from 'no harm' to 'death', according to the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) classification index.[26] Other definitions on MEs might be applicable and will be labelled during the extraction.
ADEs	'Injuries resulting from medical interventions related to a drug. ADE may result from medication errors or from adverse drug reactions (ADR) in which there were no error'.[27] ADEs can be preventable and non-preventable. Preventable ADE is always a result of an error. Non-preventable ADE is ADR, an injury without an error.[27]
ADR	'A response to a medicine which is noxious and unintended, and which occurs at doses normally used in man'.[28] In this study we intend to focus exclusively on preventable ADE.
SRS and pharmacovigilance	A system, that relies on 'an unsolicited communication by a healthcare professional or consumer to a company, regulatory authority or other organization(…), that describes one or more adverse drug reactions in a patient who was given one or more medicinal products and that does not derive from a study or any organized data collection scheme'.[29] SRS are administered by pharmacovigilance centres, operated at national or international levels, and might be referred to as 'post marketing spontaneous reports', 'post marketing surveillance' or 'adverse events reaction systems'. Pharmacovigilance is defined as 'the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine/vaccine related problem'.[30] Pharmacovigilance is dealing with patient safety issuers and all drug-related problems, resulting in ADEs.[31]
PSRS	Systems for reporting of incidents in healthcare that 'cause an injury to the patient or pose a risk of harm.[32] The fundamental role of a PSRS is to enhance patient safety by learning from failures of the healthcare system'.[13] PSRS are usually administered by the local or national healthcare authorities (both private and governmental) and might be referred to as 'patient incident reporting', 'safety database' or 'event reporting system'.

ADE, adverse drug event; ADR, adverse drug reaction; ME, medication error; PSRS, patient safety reporting systems; SRS, spontaneous reporting systems.

of analyses in reporting systems?' The intention of the review is to help researchers and organisations engaged with medication safety to get an overview over current methods for ME analyses and to support authorities when considering alternative or supplementary methods for ME analyses.

Identifying relevant studies

The search strategy is developed in cooperation with the research team and an information specialist (SM-BH) using a search guide developed by Bramer et al.[22] First, we identified elements from the research question: 'MEs' and 'system analyses'. Second, we collected subject-specific headings and key words and their synonyms accordingly. The search was initially performed in Embase (Ovid) and translated to MEDLINE (Ovid), Cinahl (EBSCOhost) and Cochrane Central (online supplemental appendix 1).

Google Scholar, major national healthcare safety agencies and pharmacovigilance centres' websites will be searched for relevant publications. The final search will be made in August 2022. We will review the reference lists of the included studies and use the citation search in Scopus for each reference. Additionally, we will contact authors of publications for further information, if necessary. All searches will be limited to 2005 onwards. From this point in time, many countries started to introduce national PSRS.[23 24]

Study selection

All retrieved records from the literature search will be imported and managed in Covidence. Two researchers (OT) and (SM-BH) are independently to screen at title/abstract level and second at full-text level according to the inclusion and exclusion criteria listed further. In case of disagreement, the third researcher (SB) will be involved to achieve consensus.

All publications with titles and abstracts available in English or Scandinavian languages will be mapped without further language restrictions. However, the data extraction will be possible only for publications published in full in English or Scandinavian languages.

Inclusion criteria

► Publications targeting MEs or AEs related to MEs that have occurred to persons of any age and gender.
► Publications that describe methodologies used to identify and analyse MEs.
► Publications from all healthcare institutions or organisations that use reporting systems as a source, including SRS or PSRS on national, regional or local levels.
► Publications reporting on ADE and ADR will be considered only if a described association exists between these two and MEs.

Exclusion criteria

► Review articles, editorials and publications that do not provide information on medication involved or ME's category.
► Publications exploring herbal or traditional medicines.

Data extraction

Two researchers (OT) and (SB) will independently extract data using a charting table, developed by the research team. A priori pilot testing will be performed on two or three sources to ensure that all relevant results are extracted, iteratively updating a data-charting form.[19]

General characteristics are to be extracted from the selected publications: author(s), year of publication, source of origin/country of origin, study design, settings and population. Thereafter, the following information is to be extracted: methods used for MEs' detection and analysis, the type of the reporting system used, the frequency and characteristics of MEs revealed by the analysis: the most frequent medications involved in MEs (their generic name and ATC code), medication–event combinations, based either on stages of medication process (prescribing, transcribing, dispensing/preparation, administering/documenting and monitoring) or ME category (such as wrong medication, wrong patient, wrong dose, wrong route, wrong time, omission error, etc (online supplemental appendix 2), or on patient demographic characteristics, such as age and gender, categories of medication-related harm and the reporting organisation. Additionally, limitations/biases, such as the quality of data and funding sources, will be noted.

The outcome of ME analyses may vary from study to study. In some studies focus may be on adverse events/patient harm; in other studies, focus may be on hazardous medication–event situations. Likewise, differences may occur as some studies may, for example, investigate only prescribing or administration errors or MEs connected to a particular drug of interest. In contrast, other studies may explore MEs more generally.

Data summary

The primary aim of the scoping review is to provide an overview of the methods used for MEs' analysis; these methods will be seen in connection with the type of the reporting system and detailed information on MEs, their types and frequency.

The results will be summarised and presented in descriptive and tabular form.

Patient and public involvement

This protocol is developed without patient or public involvement.

Study status

The scoping review protocol was submitted on 26 September 2021 and was last updated on 4 May 2022. The study is to start immediately after the publication of the protocol. We plan to fulfil the study by January 2023.

ETHICS AND DISSEMINATION

The review does not require approval from the ethics committee as it is a literature study. Dissemination of the results will take place via publication in peer-reviewed journals and presentations for the stakeholders that

work on patient safety, as well as scientific networks and conferences.

ORCID iDs
Olga Tchijevitch http://orcid.org/0000-0002-2356-8366
Søren Bie Bogh http://orcid.org/0000-0002-6207-0501
Søren Birkeland http://orcid.org/0000-0001-7857-3181

REFERENCES

1. Lisby M, Nielsen LP, Brock B, *et al*. How should medication errors be defined? Development and test of a definition. *Scand J Public Health* 2012;40:203–10.
2. World Health Organization. The third WHO global patient safety challenge: medication without harm [online]. Available: http://www.who.int/patientsafety/medication-safety/en/ [Accessed 17 Feb 2021].
3. Hoonhout LHF, de Bruijne MC, Wagner C, *et al*. Nature, occurrence and consequences of medication-related adverse events during hospitalization: a retrospective chart review in the Netherlands. *Drug Saf* 2010;33:853–64.
4. Kjellberg J, Wolf RT, Kruse M, *et al*. Costs associated with adverse events among acute patients. *BMC Health Serv Res* 2017;17:651.
5. de Vries EN, Ramrattan MA, Smorenburg SM, *et al*. The incidence and nature of in-hospital adverse events: a systematic review. *Qual Saf Health Care* 2008;17:216–23.
6. Hodkinson A, Tyler N, Ashcroft DM, *et al*. Preventable medication harm across health care settings: a systematic review and meta-analysis. *BMC Med* 2020;18:313.
7. Elliott RA, Camacho E, Jankovic D, *et al*. Economic analysis of the prevalence and clinical and economic burden of medication error in England. *BMJ Qual Saf* 2021;30:96–105.
8. Goedecke T, Ord K, Newbould V, *et al*. Medication errors: new EU good practice guide on risk minimisation and error prevention. *Drug Saf* 2016;39:491–500.
9. Leape LL, Brennan TA, Laird N, *et al*. The nature of adverse events in hospitalized patients. Results of the Harvard medical practice study II. *N Engl J Med* 1991;324:377–84.
10. To Err is human: building a safer health system [online]. Washington, DC: National Academies Press, 2000. Available: http://www.nap.edu/catalog/9728 [Accessed 23 Feb 2021].
11. Cousins DH, Gerrett D, Warner B. A review of medication incidents reported to the National reporting and learning system in England and Wales over 6 years (2005-2010). *Br J Clin Pharmacol* 2012;74:597–604.
12. Styrelsen for Patientsikkerhed. Dansk Patientsikkerhedsdatabase. Årsberetning 2019 [online]. Available: https://stps.dk/da/udgivelser/2020/aarsberetning-for-dansk-patientsikkerhedsdatabase-2019/~/media/01707469F7F9446FB3D3FD4EAB99CD6E.ashx [Accessed 18 Feb 2021].
13. World Health Organization. Reporting and learning systems for medication errors [online]. Available: http://www.who.int/medicines/areas/quality_safety/safety_efficacy/emp_mes/en/ [Accessed 23 Feb 2021].
14. Newbould V, Le Meur S, Goedecke T, *et al*. Medication errors: a characterisation of spontaneously reported cases in EudraVigilance. *Drug Saf* 2017;40:1241–8.
15. Carnovale C, Mazhar F, Pozzi M, *et al*. A characterization and disproportionality analysis of medication error related adverse events reported to the FAERS database. *Expert Opin Drug Saf* 2018;17:1161–9.
16. Bate A, Evans SJW. Quantitative signal detection using spontaneous ADR reporting. *Pharmacoepidemiol Drug Saf* 2009;18:427–36.
17. Ventola CL. Big data and pharmacovigilance: data mining for adverse drug events and interactions. *P T* 2018;43:340–51.
18. Rigsrevisionen 2014. Beretning til Statsrevisorerne om problemerne med at udvikle og implementere Fælles Medicinkort. [Internet]. Available: http://www.rigsrevisionen.dk/media/1999813/problemerne-med-at-udvikle-og-implementere-faelles-medicinkort.pdf
19. Peters M, Godfrey C, McInerney P. *Chapter 11: Scoping Reviews. In: Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis [Internet]. JBI*, 2020. https://wiki.jbi.global/display/MANUAL/Chapter+11%3A+Scoping+reviews
20. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;8:19–32.
21. Tricco AC, Lillie E, Zarin W, *et al*. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018;169:467–73.
22. Bramer WM, de Jonge GB, Rethlefsen ML, *et al*. A systematic approach to searching: an efficient and complete method to develop literature searches. *J Med Libr Assoc* 2018;106:531–41.
23. NHS England » Introducing our new system for patient safety learning [Internet]. Available: https://www.england.nhs.uk/blog/introducing-our-new-system-for-patient-safety-learning/ [Accessed 21 Sep 2021].
24. Bjørn B, Anhøj J, Lilja B. [Reporting of patient safety incidents: experience from five years with a national reporting system]. *Ugeskr Laeger* 2009;171:1677–80.
25. NCC MERP. About Medication Errors [Internet]. 2014 [cited 2021 Feb 17]. Available: https://www.nccmerp.org/about-medication-errors
26. indexColor2001-06-12.pdf [Internet]. [cited 2021 Feb 23]. Available: https://www.nccmerp.org/sites/default/files/indexColor2001-06-12.pdf
27. Bates DW, Boyle DL, Vander Vliet MB, *et al*. Relationship between medication errors and adverse drug events. *J Gen Intern Med* 1995;10:199–205.
28. safety-of-medicines--adverse-drug-reactions-jun18.pdf [Internet]. [cited 2021 Feb 22]. Available: https://www.who.int/docs/default-source/medicines/safety-of-medicines--adverse-drug-reactions-jun18.pdf?sfvrsn=4fcaf40_2
29. 2006 - E 2 D Post Approval Safety Data Management.pdf [Internet]. [cited 2021 May 31]. Available: https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-12.pdf
30. Pharmacovigilance [Internet]. [cited 2022 Apr 8]. Available: https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance
31. Clinical Pharmacy Education, Practice and Research : Clinical Pharmacy, Drug Information, Pharmacovigilance, Pharmacoeconomics and Clinical Research [Internet]. [cited 2022 Apr 8]. Available: https://web-s-ebscohost-com.proxy1-bib.sdu.dk/ehost/ebookviewer/ebook/bmxlYmtfXzE4NzAwNDRfX0FOO?sid=6f9200dc-99cf-46d1-b942-794bbbacd6d9@redis&vid=0&format=EB&lpid=lp_201&rid=0
32. WHO-EIP-SPO-QPS-05.3-eng.pdf [Internet]. [cited 2021 May 31]. Available: https://apps.who.int/iris/bitstream/handle/10665/69797/WHO-EIP-SPO-QPS-05.3-eng.pdf?sequence=1&isAllowed=y