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SYSTEMATIC REVIEW

Economic Evaluations of Medication Safety Interventions in Primary and Long-Term Care: A Systematic Review

Sneha T. Amritlal[1,2] · Rosalyn Chandler[1,2] · Alireza Mahboub-Ahari[1,2] · Luke Paterson[1,3] · Anthony J. Avery[2,4] · Darren M. Ashcroft[2,5] · Antony Chuter[2] · Rachel A. Elliott[1,2]

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Abstract

Objectives Most medication errors occur in primary and long-term care, and a wide range of medication safety interventions have been implemented, but these are often expensive, with little evidence around cost-effectiveness. We report a systematic review of economic evaluations of these interventions within primary and long-term healthcare settings.

Methods A comprehensive search was conducted in databases (Medline, Embase, Econlit and PsycINFO) for full economic evaluations of primary care interventions targeting all errors in the medication use process (January 2004 to September 2025). Methodological and reporting qualities were assessed using standard tools.

Results From 8523 records, 44 studies evaluating interventions in general/family practice (22), community pharmacy (11) and nursing/care/residential homes (11) met the inclusion criteria, 24 of which were either pharmacy led (19) or multidisciplinary medication reviews (5). All but one study looked at prescribing or monitoring interventions only. A total of 12 studies included all patients, with 24 focusing on older adults (> 65 years) and 3 focusing on condition-specific groups. Most studies only included costs from a healthcare perspective (39). Outcomes ranged from prescribing errors (9), hospital utilisation (13) and health-related quality of life (15) to falls (6) and adverse drug events (6). In total, 21 studies carried out an incremental cost-effectiveness analysis (16 including the incremental cost per quality-adjusted life year gained), and 14 reported the intervention cost-effectiveness. Remaining studies were cost–consequence (18) and cost–benefit analyses (5). Study reporting quality varied considerably, with lack of transparency in the design of the decision-analytic model, varied reporting of costs, little consideration of indirect costs or the impact of loss of trust on future use of healthcare, limitations in handling of uncertainty or discounting and very little patient involvement around targeting patients or designing interventions. Of the ten studies using decision models, all scored poorly for model validation. The quality of studies has not improved over time.

Conclusions While some interventions demonstrated cost-effectiveness, study quality was variable, with generally poorly validated models. Study heterogeneity precluded meaningful direct comparison between studies. Significant research gaps remain as studies focused mainly on prescribing and monitoring errors, there was little or no investigation of technology-based interventions and there was inadequate targeting of patients most vulnerable to harm.

1 Introduction

Medications are the most common intervention in any healthcare system. The safe use of medicines can effectively treat medical conditions by providing cure, relieving symptoms and preventing (or delaying) serious illness. However, medicines can sometimes cause more harm than good, particularly where risks and potential benefits are finely balanced or when the prescriber does not take full account of the risks. A medication error can be defined as '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…including prescribing, order communication, product labelling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use' [1].

Globally, the cost of medication errors has been estimated at US $42 billion annually [2]. In England, an estimated 237 million medication errors occur annually, leading to 1700 deaths, imposing an avoidable economic burden of £98 million [3]. Given the substantial impact of medication errors, the World Health Organization (WHO) launched the 'Medications without Harm' challenge in March 2017, aiming to reduce medication-related harm by 50% in 5 years [2]. In

Extended author information available on the last page of the article

Key Points

Most economic evaluations of medicine safety interventions in primary and long-term care focus on prescribing and monitoring medicines in adults in general/family practice and community pharmacy, and many report that the intervention is cost-effective.

The quality of many studies was not very good, especially around clearly describing economic modelling methods or incorporating the patient perspective in the study design.

Other than some studies looking at people over 65 years old, studies do not seem to be clearly targeting patients or settings most vulnerable to harm from medication errors. There is also little work on the impact of system or technology advances on medication safety.

earlier work looking at medication errors, we concluded that the largest number of all medication errors and specifically clinically important prescribing errors happen in primary and long-term care owing to the sheer quantity of prescribing [3]. Our further work has identified high numbers of medication errors, and associated burden, at care-setting transitions, primarily between primary/long-term care and acute hospital care, [4] and this has been highlighted as a specific challenge by the WHO [5].

Clearly, there is a pressing need for interventions to reduce prescribing errors in primary and long-term care. In response to this, a wide range of medication safety interventions have been implemented in primary and long-term care, including computerised medication safety alerts, electronic audit and feedback (often paired with a pharmacist intervention) and structured medication reviews conducted by healthcare professionals, often pharmacists. The effectiveness and consistency of these interventions are influenced by growing but unevenly adopted digital platforms and policy efforts to improve medicines information interoperability across care settings.

Strategies and initiatives to reduce medication errors are often expensive, with little evidence on their cost-effectiveness [6]. Most economic evidence focuses on hospital-based interventions, despite the fact that most medication use and errors occur in primary care and long-term care, including nursing and care homes. To achieve maximum benefit, resources need to be directed to the most cost-effective interventions in areas with the greatest unmet need, embracing recent technological and system advancements.

There are currently no systematic reviews of economic evaluations of medication safety interventions in primary and long-term care, so this literature review aimed to address this gap. By doing so, we aimed to highlight key unmet needs to steer future research and support decision-makers in allocating limited resources efficiently to areas with the greatest potential for impact on avoidable costs and harm.

2 Materials and Methods

Medication safety interventions were defined as those that (1) explicitly stated that their aim was to improve medication safety and measured either safety-relevant process indicators (e.g. medication errors) or safety-relevant patient outcomes (e.g. hospitalisations); (2) did not explicitly state that their aim was to improve medication safety but measured either safety-relevant process indicators or safety-relevant patient outcomes.

These interventions include professional, organisational, structural or patient-mediated measures that target medication errors occurring in primary (general/family practice and community pharmacy) and long-term care (nursing/care/residential homes) settings leading to hospital admissions, emergency department visits and mortality in adults.

Professional interventions include quality assurance tools providing educational interventions for practitioners or participants, such as training GPs in the use of structured assessments. Organisational interventions include activities led by specific healthcare professionals (e.g. nurse- or pharmacist-led chronic disease clinics and nurse prescribing) and/or clinical multidisciplinary teams, such as pharmacist-managed medication reviews. Structural interventions include the organisation of quality monitoring services, such as implementation of an electronic health record (EHS) system. Patient-mediated interventions aim to change healthcare professional performance through patient interactions or information provided by, or to, patients [7].

This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 guidelines [8]. The protocol for this review is registered on the PROSPERO website (registration no. CRD42024527371) [9].

2.1 Search Strategy

A repeatable search strategy (Online Supplementary Material 1) was developed for the electronic databases. On 8 May 2024, the following databases were searched: Econlit, OVID MEDLINE (R), Ovid MEDLINE (R) Daily Update, APA PsycInfo and Embase. The search strategy utilised both natural language and controlled vocabulary terms. The initial search covered studies from January 2004 to April 2024 and was further updated on 18 September 2025 to include studies published between January 2004 and September 2025. The search drew upon an existing Cochrane review

that examined the benefits of professional, organisational and structural interventions to reduce medication errors in primary care up to 2016 [10] and was further updated in a more recent version extending coverage to 2024 [11]. Additional Medical Subject Heading (MeSH) terms related to care transitions were incorporated into our search strategy to ensure broader coverage of relevant studies. The search terms relevant to care transitions were drawn from a published literature review [12].

2.2 Inclusion and Exclusion Criteria

The detailed inclusion and exclusion criteria for the review are presented in Table 1.

2.3 Study Selection

Two review authors (L.P. and R.A.E.) independently screened the titles and abstracts to assess studies against the inclusion criteria. Studies that did not meet the inclusion criteria or met exclusion criteria were removed from the review. Studies identified as systematic reviews were reviewed to identify potentially relevant studies not captured otherwise. Full-text copies of all potentially relevant studies were obtained, with first authors contacted for any clarifications and/or access to supplementary appendices. One research author (R.A.E.) independently screened the full-text articles with disagreements resolved between the review authors.

2.4 Data Extraction

Two review authors (R.C. and S.A.) independently completed data extraction, with discrepancies resolved by discussion between all review authors. Studies were grouped together on the basis of similar interventions and common outcomes.

The following data were extracted: name of the first author, date of publication, publisher, country, region, article title, study design, time horizon, perspective, population/sample size, intervention, comparator, primary outcome(s), secondary outcome(s), type of economic evaluation, decision model type (if applicable), software used, resource use, source of unit cost, currency, price year, discounting of costs and effects, primary economic outcome, clinical effectiveness estimates, source of effectiveness, health benefit measure, source of benefit, intervention cost, downstream healthcare costs, total cost difference, statistical method to derive cost difference, primary outcome findings, health benefit findings, incremental cost-effectiveness ratio (if reported), methods to handle uncertainty, sensitivity, scenario, subgroup analysis findings and value of information (if conducted).

2.5 Assessment of Reporting Quality

Reporting quality was assessed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist 2022 [14]. The CHEERS checklist consists of 24 items categorised into seven sections: (1) title,

Table 1 Study inclusion and exclusion criteria

Category	Inclusion and exclusion criteria
Study design	Include if study is an economic evaluation as defined in Drummond et al. (2015): cost-effectiveness analysis, cost–utility analysis, cost–consequence analysis, cost-minimisation analysis or cost–benefit analysis [13]
Intervention	Include if study reports a medication intervention that aims to improve patient safety
Setting	Include if the study is conducted in primary or long-term care settings, including family/general practice[a], nursing/care/residential home[b] or community pharmacies[c]. Include transfer-of-care interventions if they are conducted in one of these settings
Patient outcomes	Include if the study reports any of the following patient or patient-relevant process outcomes: medication or prescribing errors, adverse drug events, hospitalisations resulting from medication errors or relevant disease-specific outcomes such as gastrointestinal bleeding, falls or other clinically significant events
Date range	Include if study was published between 2004 and 2025
Article type	Exclude if study is a commentary, editorial, abstract, thesis or expert opinion paper
Intervention	Exclude if study reports a pharmacogenetic intervention[d]
Language	Exclude if manuscript is not available in English

[a]General/family practice where medical services are provided on an outpatient basis, without admission to a hospital or other inpatient facility

[b]Nursing/care/residential home setting refers to residential facility providing long-term care to individuals, often older people

[c]Community pharmacy setting refers to directly accessible pharmacy services, often found on high streets, supermarkets and health centres

[d]Pharmacogenetic interventions excluded to ensure the review remains focused on improving the medication safety process in primary care settings rather than personalised medicine approaches

(2) abstract, (3) introduction, (4) methods, (5) results, (6) discussion and (7) other relevant information (e.g. sources of funding and conflict of interest).

For studies conducting an economic evaluation within a randomised controlled trial (RCT), reporting quality of the RCT was assessed using the Consolidated Standards of Reporting Trials (CONSORT) checklist [15]. The CONSORT checklist consists of 25 items, grouped into similar categories as in the CHEERS checklist.

In both cases, each item was independently assigned 'yes' for reported, 'no' for not reported, 'partial' for not adequately reported and 'not applicable' for non-relevant items by the review authors (R.C. and S.A.), with discrepancies resolved with the team.

2.6 Assessment of Methodological Quality

Methodological quality was assessed using the Quality of Health Economic Studies (QHES) checklist [16]. The QHES checklist is a validated instrument consisting of 16 'yes' or 'no' response criteria that are used to derive a quantitative score of study quality [17]. Each response criterion is weighted between 1 and 9 points. The total score, aggregated across all the criteria, can range from 0 (lowest quality) to 100 (highest quality). The studies were categorised as extremely poor (QHES scores, 0–25), poor (QHES scores, 25.1–50), moderate (QHES scores, 50.1–75) or high (QHES scores, 75.1–100) quality [18].

For economic evaluations using decision modelling approaches, methodological quality was assessed using the Assessment of the Validation Status of Health-Economic decision models (ADViSHE) checklist [19]. The ADViSHE checklist has 13 items divided into: (1) validation of the conceptual model, (2) input data validation, (3) validation of the computerised model, (4) operational validation and (5) other validation techniques. While the ADViSHE checklist does not provide a validity score like the QHES checklist, it does provide an assessment of the quality of decision-analytic models. Each item was assigned 'yes' for completed, 'no' for not completed, 'partial' for not adequately completed and 'not applicable' for non-relevant items. One point was assigned for studies completely reporting an item, 0.5 points for partially reported items and 0 points for non-reported items. Both quality assessments were independently completed by R.C. and S.A., with discrepancies resolved by the team.

3 Results

3.1 Study Selection

We identified 8523 studies through bibliographic database searches. After removal of duplicates, there were 7393 publications eligible for title and abstract screening. After screening titles and abstract for inclusion and exclusion criteria, 7294 publications were excluded. Google Scholar searches yielded a further two relevant systematic reviews for screening. Full texts were sought for the 101 studies, of which 19 were systematic reviews and 82 were primary studies. We identified 12 additional primary studies through a review of the systematic reviews. Afterwards, full-text screening was conducted for the eligibility of the 94 primary studies, of which 50 were excluded. A total of 44 publications was included in this systematic review (Fig. 1).

3.2 Study Characteristics

The characteristics of the included studies are presented in Table 2. The detailed summary of included studies, including results, is presented in Online Supplementary Material 2, Table 1. Of the 44 included studies, most were conducted in the USA ($n = 13$) [20–32], followed by the UK ($n = 11$) [33–43].

3.2.1 Intervention and Control

Most of the studies focused on pharmacist-led interventions, primarily various types of medication reviews ($n = 19$) [20, 21, 27, 28, 32, 37–39, 41–43, 46, 49, 51–54, 57, 60]. A medication review is the process of evaluating the patient's medication and chronic conditions aiming to reduce polypharmacy and thereby optimising the patient outcomes [20]. A few studies included multi-professional medication reviews (MPMR), involving a multidisciplinary team of physicians, pharmacists, nurses and other healthcare professionals ($n = 5$) [35, 44, 50, 61, 62]. Nine studies focused on deprescribing interventions, [25, 36, 47, 48, 55, 56, 58, 59, 63] and four studies used disease management interventions [26, 30, 31, 40]. In addition, four studies focused on transfer-of-care (TOC) interventions [22–24, 29], and one study had general practitioner (GP)-delivered medication review [45].

Two studies used the PINCER intervention, which utilises information technology to identify and prevent specific medication errors [33, 34]. In this programme, pharmacists worked within general practices to identify existing errors and implement measures to prevent future problems. Two other studies also targeted specific medication errors [38, 40]. Patterson et al. [38] evaluated the appropriateness of psychoactive prescribing in nursing home residents, while Willis et al. [40] assessed the proportion of patients meeting at least one of nine indicators related to high-risk prescribing of non-steroidal anti-inflammatory drugs (NSAIDs) and anti-platelet agents.

In most studies, the control arm received usual care. One study had medication discrepancies identified by nurses as the control group [24]. In the studies by Avery et al. (2012)

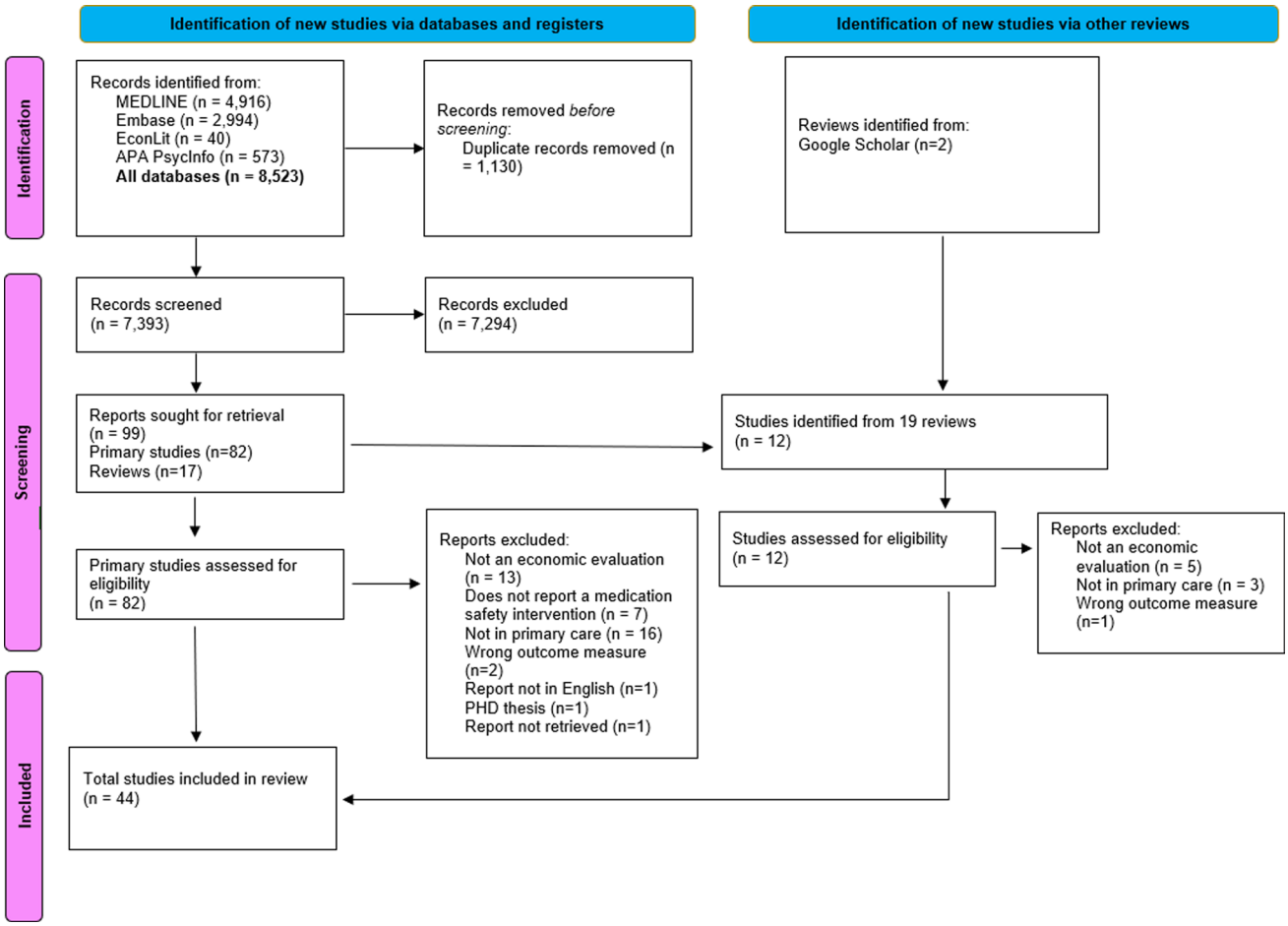

Fig. 1 PRISMA 2020 flow diagram for updated systematic reviews which included searches of databases, registers and other sources

and Elliott et al. (2014), the PINCER intervention was compared with feedback (of patients with medication errors) rather than usual care because of ethical considerations [33, 34]. Since the intervention identified patients at risk, keeping this information from practices was deemed unethical. Similarly, in the study by Gillespie et al. (2017), control practices received simple patient-level potentially inappropriate prescribing (PIP) postal feedback [44].

3.2.2 Resource Use and Cost

Costs were mostly included only from a healthcare perspective ($n = 39$) [20–29, 31–34, 37–39, 41–53, 55–63]. In trial-based analyses, resources mainly came from trial data. Resources were also sourced from routine and national databases, published literature and expert elicitation. Three studies took the societal perspective, of which one study estimated the opportunity cost of events by calculating the national mean charges for the most relevant diagnosis-related group (DRG) or diseases (International Classification of Diseases, Ninth Revision [ICD-9]) code [30]. One study included cost associated with the use of informal care such as help from family, friends and neighbours [54]. Jungo et al. [62] primarily adopted a healthcare-system perspective but also had a secondary analysis to approximate the societal perspective.

3.2.3 Clinical Outcome Measure

In 13 studies, the primary clinical outcome measures were related to hospital utilisation, including hospital readmissions rates and emergency room visits [22, 23, 25, 26, 29, 37, 46, 48–51, 56, 60]. Fifteen studies also estimated the health-related quality of life [30, 31, 34, 36, 39, 42, 44, 48, 50–53, 56, 60, 62]. Few studies estimated medication-management related outcomes, including potentially inappropriate medications (PIPs) [38, 40, 43–45, 48, 59, 60, 62], adverse drug events (ADE) [20, 25, 47, 50, 55, 61], drug-related problems (DRPs) [27, 28, 54, 57, 63], medication adherence (proportion days covered [PDC]) [21, 42], medication discrepancies [24] and changes in medication/polypharmacy events [32, 41]. Other outcome measures were fall rates [35, 42, 48, 56,

Table 2 Study characteristics

Criterion	Category	*N* of studies	References
Country	USA	13	[20–32]
	UK	11	[33–43]
	Ireland	5	[44–48]
	Australia	2	[49, 50]
	Spain	2	[51, 52]
	Netherlands	2	[53, 54]
	Canada	2	[55, 56]
	Sri Lanka	1	[57]
	Singapore	1	[58]
	Egypt	1	[59]
	Israel	1	[60]
	France	1	[61]
	Switzerland	1	[62]
	United Arab Emirates	1	[63]
Type of economic evaluation	Cost–consequence analysis	18	[21, 23–29, 32, 41, 43, 48, 57–61, 63]
	Cost–utility analysis	16	[30, 31, 34, 36, 37, 39, 40, 42, 44, 45, 50, 51, 53, 55, 56, 62]
	Cost-effectiveness analysis[a]	5	[20, 33, 35, 38, 54]
	Cost–benefit analysis	5	[22, 46, 47, 49, 52]
Setting	General/family practice care setting	22	[22–26, 30–34, 36, 37, 39, 40, 43–46, 49, 50, 57, 62]
	Community pharmacy setting	11	[20, 21, 42, 51–56, 59, 63]
	Nursing/care home setting	11	[27–29, 35, 38, 41, 47, 48, 58, 60, 61]
Perspective	Healthcare	39	[20–29, 31–34, 37–39, 41–53, 55–63]
	Health and social care[b]	3	[35, 36, 40]
	Societal[c]	3	[30, 54, 62]
Time horizon	< 1 year	15	[23, 25, 27, 28, 33, 37, 41, 45, 48, 50–53, 59, 63]
	1 year	19	[20, 21, 26, 29, 35, 38, 39, 42–44, 47, 49, 54–56, 58, 60–62]
	> 1 year (2 years to lifetime)	7	[22, 30, 31, 34, 36, 40, 46]
	Not reported	3	[24, 32, 57]
Decision model type	Decision tree	4	[20, 31, 33, 61]
	Decision tree + Markov-type state-transition model	3	[34, 55, 56]
	Markov-type state-transition models	3	[30, 36, 40]
Population	Adult patients		
	≥ 18 years	3	[23, 32, 57]
	≥ 50 years	2	[24, 43]
	Older adults (≥ 65 years)	24	[25, 27–30, 35–39, 41, 42, 45, 47, 48, 51, 52, 54–56, 58, 60–62]
	Patients in general/family care practices	8	[22, 33, 34, 40, 44, 46, 49, 50]
	Medicare beneficiaries	1	[20]
	Community pharmacy patients	3	[21, 59, 63]
	Condition-specific groups:		
	People with Parkinson disease	1	[53]
	People prescribed renin–angiotensin system (RAS) agents)	1	[31]
	People receiving warfarin	1	[26]

Table 2 (continued)

Criterion	Category	*N* of studies	References
Intervention	Medication review by pharmacists	19	[20, 21, 27, 28, 32, 37–39, 41–43, 46, 49, 51–54, 57, 60]
	Deprescribing[d]	9	[25, 36, 47, 48, 55, 56, 58, 59, 63]
	Multi-professional medication review	5	[35, 44, 50, 61, 62]
	Disease management	4	[26, 30, 31, 40]
	Transfer-of-care	4	[22–24, 29]
	IT-supported error identification	2	[33, 34]
	Medication review by general practitioner	1	[45]
Targeted-medication-use stage	Monitoring	16	[20, 22–24, 26–31, 37, 43, 47, 48, 54, 63]
	Prescribing and monitoring	15	[25, 32–34, 36, 38–40, 45, 55, 56, 58–60, 62]
	Prescribing	12	[35, 41, 42, 44, 46, 49–53, 57, 61]
	Dispensing	1	[21]
Economic outcome measure	Cost–consequence analysis	22	[21–29, 32, 39, 41, 43, 46, 48, 49, 52, 57–61, 63]
	Incremental analysis	21	[20, 30, 31, 33–40, 42, 44, 45, 50, 51, 53–56, 62]
	Benefit–cost ratio	4	[22, 47, 49, 52]
Clinical outcome measure	Medication management-related outcomes[e]	27	[20, 21, 24, 25, 27, 28, 32, 38, 40–45, 47, 48, 50, 54, 55, 57, 59–63]
	Hospital utilisation-related outcomes[f]	13	[22, 23, 25, 26, 29, 37, 46, 48–51, 56, 60]
	Health-related quality of life	15	[30, 31, 34, 36, 39, 42, 44, 48, 50–53, 56, 60, 62]
	Fall rates	6	[35, 42, 48, 56, 58, 60]

[a]The measures of health outcome/effect used in the studies were error avoided, probability of avoiding a preventable adverse drug reactions (ADE), fall ratio, proportion of residents receiving inappropriate psychoactive medication and difference in drug-related problems (DRPs)

[b]Costs included provision of personal social care services such as home care support

[c]Jungo et al. [62] primarily adopted a healthcare system perspective but also had a secondary analysis to approximate the societal perspective

[d]Deprescribing is a specific type of medication review/disease management that focuses on reducing the numbers of medicines prescribed to people, particularly those on multiple medicines for long-term conditions

[e]Includes potentially inappropriate medications (PIPs), adverse drug events (ADE), drug-related problems (DRPs), medication adherence, medication discrepancies and changes in medication

[f]Includes hospital readmissions and emergency room visits

58, 60], identified/reduction in error rates [33, 34], relative risk of systolic blood pressure control [36] and occurrence of strokes and systemic embolic events [30].

3.2.4 Incremental Analysis Results

In total, 21 studies reported incremental cost-effectiveness ratios (ICER) as the economic output. ICER is calculated by dividing the incremental cost by incremental effect to provide a ratio of 'extra cost per extra unit of health effect' for the alternative interventions [64]. Out of the 21 studies, 16 included the incremental cost per quality-adjusted life year (QALY) gained [30, 31, 34, 36, 37, 39, 40, 42, 44, 45, 50, 51, 53, 55, 56, 62]. The measure of health outcome/effect used in other studies was error avoided [33], probability of avoiding a preventable ADE, [20] fall ratio, [35] proportion of residents receiving inappropriate psychoactive medication [38] and difference in DRPs [54].

Collectively, 14 out of the 21 studies that conducted an incremental analysis found the intervention to be cost-effective [30, 33, 34, 38–40, 42, 44, 45, 50, 51, 55, 56, 62]. Amongst them, three UK-based studies used a willingness-to-pay threshold of US $25,400–$38,100 (£20,000–£30,000) per QALYs gained, consistent with the National Institute for Health and Care Excellence (NICE) guidelines [34, 39, 42]. Two Canadian studies used a threshold of US $35,430 and $70,860 (CA $50,000 and CA $100,000) per QALY [55, 56]. In addition, three European studies reported thresholds of US $48,825 per QALY [44], US $23,000–$52,300 per QALY [45] and US $32,550–$48,825 per QALY [51], respectively. Patterson et al. (2011) reported a 93% probability that an intervention would be cost-effective if society was willing to pay US $2,000 per resident per year to eliminate inappropriate psychoactive medication use [38]. However, no justification was provided for the selection of this threshold. Similarly, a UK study by Twigg et al. (2015)

estimated the 12-month ICER to be US $15,972 (£11,885), with the probability of the intervention being cost-effective at US $25,400 and US $38,100 being 81.0% and 90.5%, respectively [42]. None of the remaining studies reported whether thresholds were used.

Six studies reported that the interventions were not cost-effective [20, 35–37, 53, 54]. Desborough et al. (2020) found that the intervention was dominated by usual care (the intervention group had both higher costs and a higher fall rate) [35]. This was mainly attributed to the population, which consisted of older adults living in care homes with higher-than-expected losses to follow-up, primarily due to mortality. In addition, the multi-factorial nature of falls may have also contributed to the results, as a single medication-focused intervention might not significantly impact overall fall rates. Similarly, the study by Jowett et al. [36] suggests that anti-hypertensive deprescribing was not cost-effective in older patients aged ≥ 80 years and, therefore, should not be routinely attempted in patients with well-controlled systolic blood pressure. Chinthammit et al. [20] estimated the cost-effectiveness of comprehensive medication reviews (CMR) versus non-comprehensive medication review (non-CMR) and found the non-CMR interventions to be more effective and less costly than CMRs.

Smith et al. [31] conducted an economic evaluation of a laboratory monitoring program for renin–angiotensin system agents and found that intervening in all patients or those with diabetes was not cost-effective. However, targeting patients with chronic kidney disease was cost-effective at least 95% of the time (at both willingness to pay thresholds of US $10,000 and US $30,000 per QALY) in the base case.

3.2.5 Cost Consequence and Cost–Benefit Analysis Results

In total, 18 studies conducted cost–consequence analyses to estimate the economic impact of the interventions [21, 23–29, 32, 41, 43, 48, 57–61, 63], and five studies utilised a cost–benefit analysis [22, 46, 47, 49, 52]. Twenty studies found the intervention to be cost-saving and supports the economic case for investment in medication safety interventions by demonstrating a substantial return on investment [21–24, 26–29, 32, 43, 46, 47, 49, 52, 57–61, 63]. However, three studies found no significant cost differences in the intervention group [25, 41, 48].

Rashid et al. [25] evaluated the effectiveness, safety and economic impact of pharmacist-led deprescribing of NSAIDs and found no significant NSAID prescription-cost savings from deprescribing, possibly attributable to varied patient usage patterns. However, potential cost benefits may arise from reduced acute care use related to lower rates of pain exacerbation. Similarly, Zermansky et al. [41] assessed the impact of pharmacist-led clinical medication reviews among elderly care home residents and found no significant difference in the number and cost of drugs per patient in the intervention group. This is because the pharmacist recommended nearly as many starts of new medicines as discontinuations. Hurley et al. [48] utilised a pharmacist-led STOPPFrail-based deprescribing intervention and found significant improvements in most of the clinical outcomes, except for mean monthly medication costs. Since the population in the study was older adults, the cost trends may be influenced by changes in patient needs over time, especially for managing end-of-life symptoms.

3.2.6 Handling of Uncertainty

Collectively, 27 studies conducted sensitivity analyses to address uncertainty surrounding their findings [20, 22, 27, 30, 31, 33–40, 44–47, 49–51, 53, 54, 56, 61, 62, 65, 66]. The analyses included probabilistic sensitivity analyses [20, 30, 31, 33, 34, 36, 37, 39, 40, 44, 45, 56, 61, 66], one-way deterministic sensitivity analyses [20, 22, 30, 36, 38, 40, 44, 45, 47, 50, 61, 62, 65] and scenario analyses [34, 36–39, 44, 46, 49, 50, 56, 65, 66]. In addition, eight studies used bootstrapping to estimate uncertainty [33, 34, 38, 46, 51, 53, 54, 62] and another used a covariate-adjusted sensitivity analysis [35]. One used non-parametric statistical testing to assess skewness [27].

3.3 Reporting Quality

3.3.1 Reporting Standards in Economic Evaluations

The reporting quality of the included studies assessed against CHEERS criteria [14] is presented in Online Supplementary Material 3, Table 2. Figure 2 shows the percentage of responses (yes, no, partial or N/A) for each CHEERS item. Of the 28 items, 14 achieved a mean score above 75%, indicating good reporting quality, with 7 items (items 5, 6, 7, 11, 12, 23 and 26) scoring ≥ 90%. Six items had a mean score less than 20% indicating very poor reporting quality. The items were item 4 (health economics plan), item 10 (discount rate), item 16 (rationale and description of model), item 19 (characterising distributional effects), item 21 (approach to engagement with patients and others affected by the study) and item 25 (effect of engagement with patients and others affected by the study). Notably, some of these items, including items 4, 19, 21 and 25, are recent additions to the CHEERS checklist, which explains the limited reporting observed. Only a few studies were model based, and among them, some did not clearly specify the rationale for selecting the specific model or whether it was publicly available. This helps to explain the low score for item 16.

3.3.2 Reporting Quality of Randomised Controlled Trials

A total of 25 studies [22, 33–41, 44, 45, 49–56, 58–60, 62, 63] were included in the CONSORT quality appraisal [15], as they used specific RCTs for their effectiveness estimates. The assessment of the reporting quality of the included studies against CONSORT items is presented in Online Supplementary Material 3, Table 3. Figure 3 shows the percentage of responses (yes, no, partial or N/A) for each CONSORT item. The CONSORT checklist contains 25 items [15], out of which 14 items performed well. Background and objectives were clearly reported in almost all the studies. Trial design description, eligibility criteria for participants, settings and location where the data were collected, details of the interventions, primary and secondary outcomes, methodology for sample size determination and statistical methods used to compare outcomes between groups were some of the items that had good reporting quality.

Key methodological elements, including the implementation of random allocation sequence, information about who generated the sequence and concealment methods were inadequately reported in most studies. Blinding received low mean scores across the included studies. However, in most cases, blinding of healthcare professionals such as pharmacists, physicians and nurses was not feasible owing to their active role in delivering the intervention. Patients and GPs were typically not blinded to group allocation, as the nature of interventions such as medication reviews made it impractical. However, outcome assessors were blinded in most studies, helping to avoid the risk of detection bias. Most studies also did not explicitly report whether any additional analyses, such as subgroup and adjusted analyses, were conducted. Furthermore, potential sources of bias were largely unreported in most studies.

3.4 Methodological Quality

3.4.1 Methodological Quality of Included Economic Evaluations

The QHES instrument contains 16 dimensions [16]. An outline of the dimensions, along with the mean score for each dimension, is shown in Fig. 4. The total score for each of the included papers is shown in Fig. 5. A total of 14 studies (32%) scored above the threshold of being 'good' studies (score ≥ 75) [30, 33–36, 44–47, 51, 52, 55, 56, 62]. None of the studies achieved a perfect 100 score. The three studies with the highest QHES scores had totals of 95, 89.5 and 87.5, respectively [33, 34, 55].

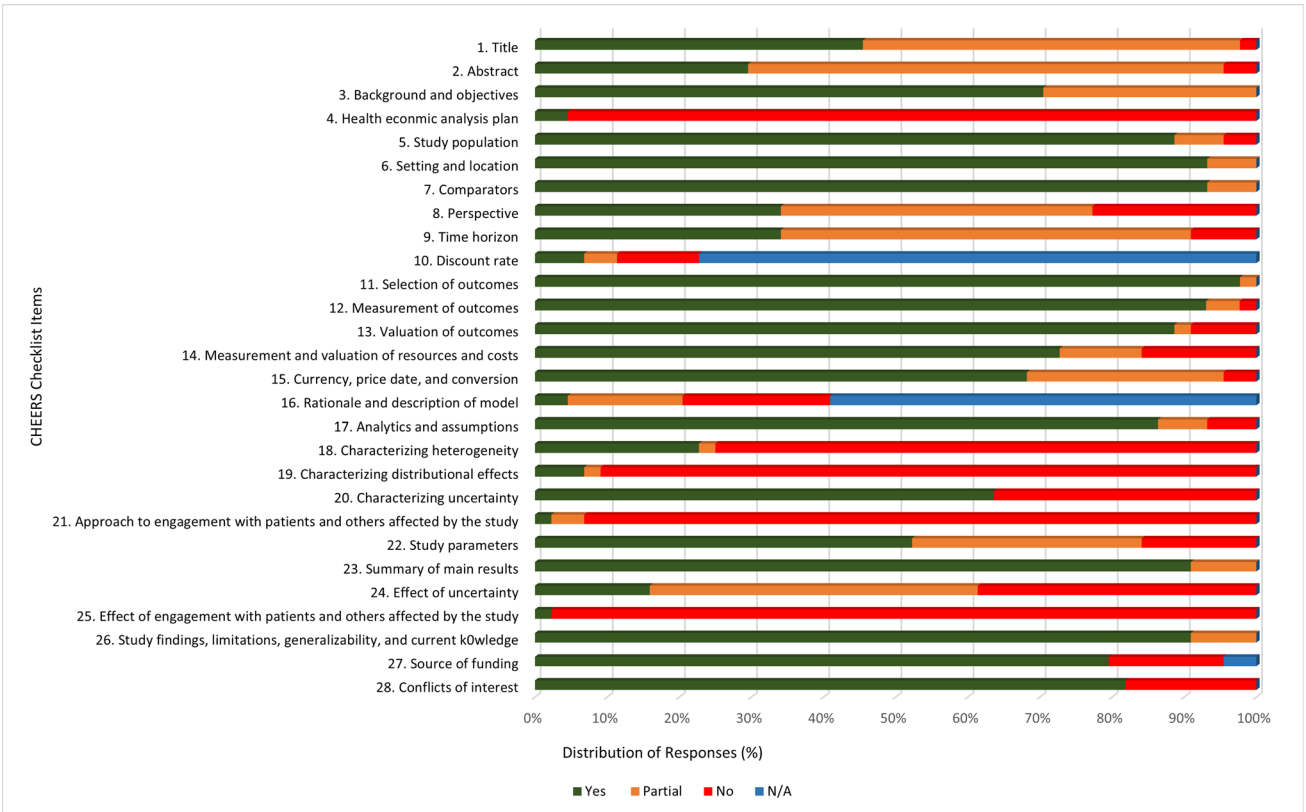

Fig. 2 Percentage of responses (yes, no, partial or N/A) for each CHEERS item

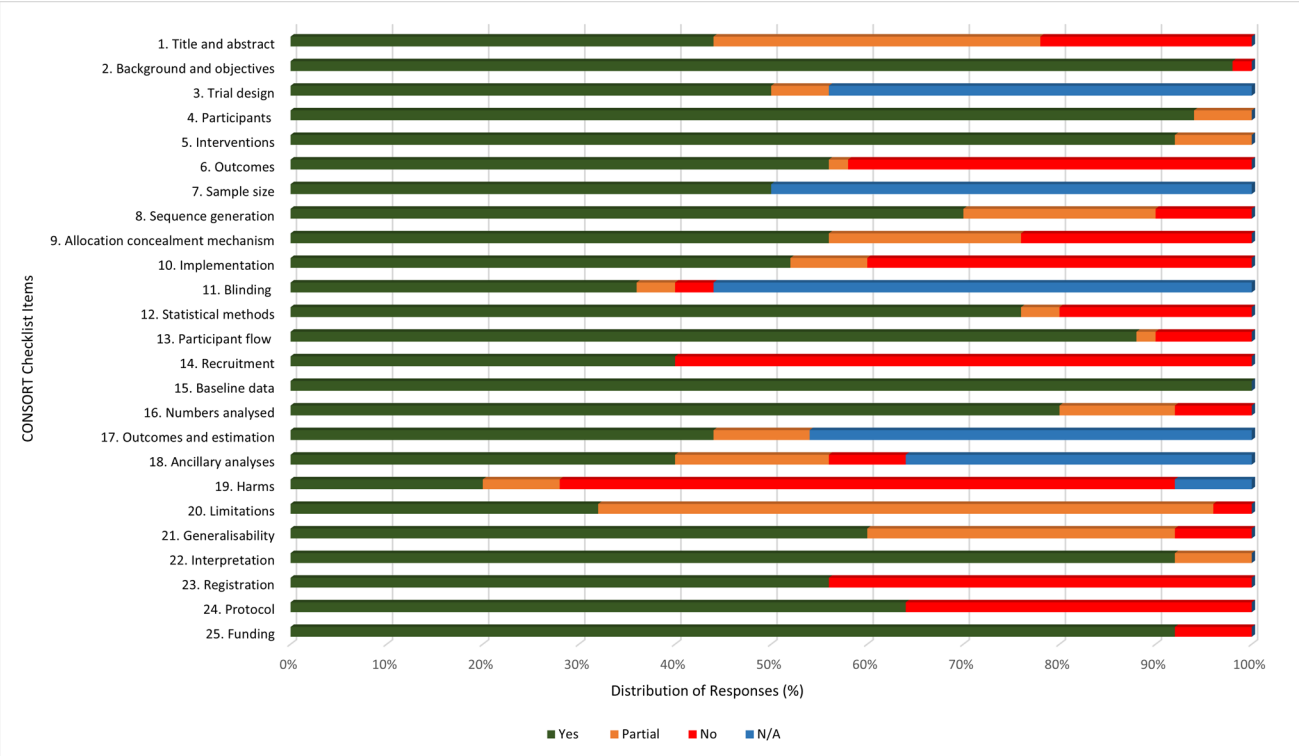

Fig. 3 Percentage of responses (yes, no, partial or N/A) for each CONSORT item

The highest performing QHES dimensions were dimension 15, which concerns justification for conclusion/recommendations on the basis of the study results, achieving a mean score of 100 and dimension 3, which involves the use of estimates from the best available source in the analysis with a mean score of 92. The high score for dimension 3 is primarily due to 64% of the studies relying on estimates from RCTs for their analysis. Dimension 12 (study methods and analysis) also achieved a mean score of 92, indicating strong overall performance. Similarly, the costing element (dimension 9), also performed well overall, with a mean score of 80.

Collectively, 23 studies [20, 22, 23, 27, 28, 31, 32, 37–40, 42, 43, 48–50, 53, 54, 58–61, 63], scoring between 50 and 75, were of moderate quality, while 7 studies, [21, 24–26, 29, 41, 57] scoring between 25 and 50, were of poor quality. No study scored below 25. Overall, studies with cost-effectiveness and cost–utility analysis designs achieved higher mean QHES scores compared with other economic evaluations. This could be attributed to the fact that cost-effectiveness and cost–utility studies had more structured and rigorous methodology that better aligned with the criteria assessed by the QHES checklist. Just over a quarter of the included studies clearly and specifically presented their objectives in a measurable way (dimension 1), stated and justified the perspective of their analysis (dimension 2) and handled uncertainty through both statistical analysis and sensitivity analysis (dimension 5). Over half of the studies did not specify whether a discount rate was applied or justified its use. Only few studies explicitly discussed direction and magnitude of potential biases, resulting in a low mean score of 42. In total, 45% of the studies conducted an incremental analysis using a relevant comparator as required by dimension 6.

3.4.2 Model Validation in Decision Analytic Studies

Ten studies included in this review employed model-based economic evaluations [20, 30, 31, 33, 34, 36, 40, 55, 56, 61]. The validation status of these decision-analytic models was assessed using the ADViSHE checklist [19]. Detailed results are presented in Online Supplementary Material 3, Table 4. Figure 6 shows the percentage of responses (yes, no, partial or N/A) for each ADViSHE item. All ten studies performed poorly across every item in the checklist. Five of these studies were conducted before the introduction of the ADViSHE checklist, which may partially account for their lower validation scores. However, even the more recent studies demonstrated suboptimal performance in this area.

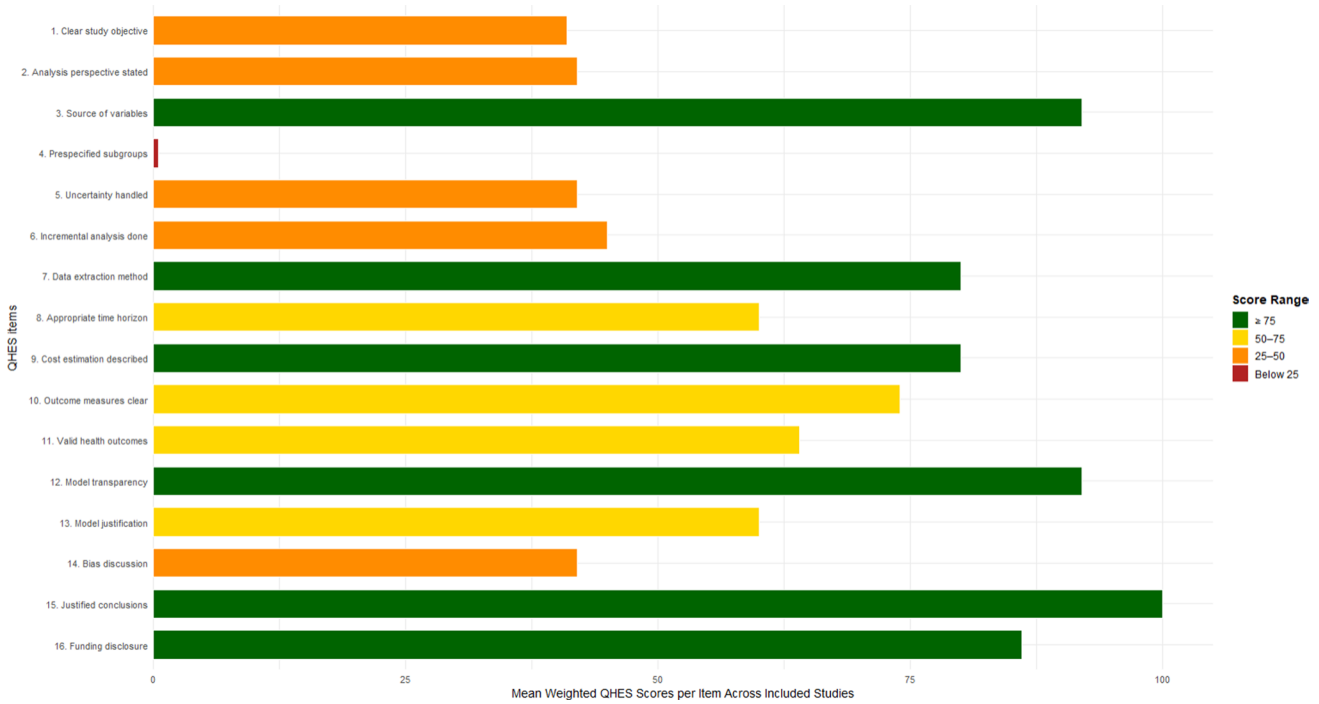

Fig. 4 Mean weighted QHES scores per item across included economic evaluations

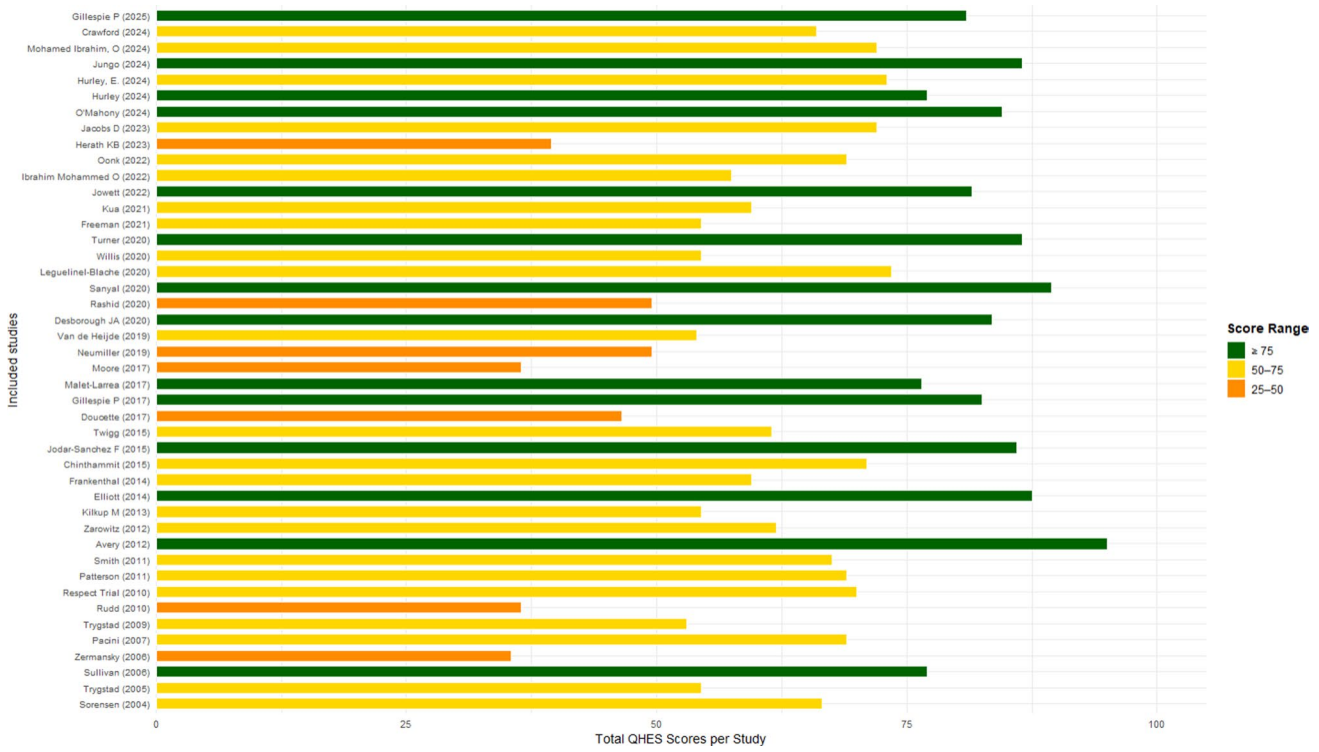

Fig. 5 Total QHES scores per included economic evaluations

4 Discussion

Medication errors remain a major source of preventable patient harm globally, contributing to a significant public health burden [67]. Medication safety interventions play a vital role in healthcare, helping to substantially reduce both the clinical risks and healthcare costs. This is an area that is not just limited to hospitals or GP practices but extends across every aspect of the healthcare system. This review examined economic evaluations of medication safety interventions in primary and long-term care, aiming to identify key unmet needs and support optimal resource allocation. We identified 44 studies evaluating medication safety interventions in primary care.

This review has several strengths and limitations. This review is the most up-to-date literature review including all relevant economic evaluations of medication safety interventions. The search strategy drew upon an existing Cochrane review, offering a high-quality and systematic foundation for the evidence base. Moreover, methodological and reporting quality of the included studies were rigorously assessed using four validated checklists, providing a thorough critical appraisal. This enhances the robustness and credibility of the findings of this review. These strengths enhance the reliability and relevance of our findings, offering valuable insights for policymakers and healthcare practice. One key limitation was that this review was restricted to English-language publications. The variability in quality assessment scores across different checklists may have impacted the robustness of our conclusions.

Most studies assessed the effectiveness of medication reviews, revealing a high prevalence of polypharmacy. Polypharmacy, defined as the use of multiple medications to treat conditions, is a growing concern in older adults, as excessive medication use may increase harm rather than providing therapeutic benefits. A 2024 UK study found that 22.8% of adults aged 65 years and over were prescribed more than five drugs within a 6-month period [68]. This underscores that the need for targeted interventions to address polypharmacy remains a significant burden, highlighting the need to prioritise. Medication reviews that require multifaceted decision-making and the involvement of patients and/or caregivers should be prioritised in practice [69].

The WHO recommends several international programmes to tackle polypharmacy, including: Optimising Therapy to Prevent Avoidable Hospital Admissions in the Multimorbid Elderly (OPERAM), PRIMA-eDS (Polypharmacy in Chronic Diseases: Reduction of Inappropriate Medication and Adverse Drug Events in Older Populations by Electronic Decision Support) and Stimulating Innovation Management of Polypharmacy and Adherence in the Elderly

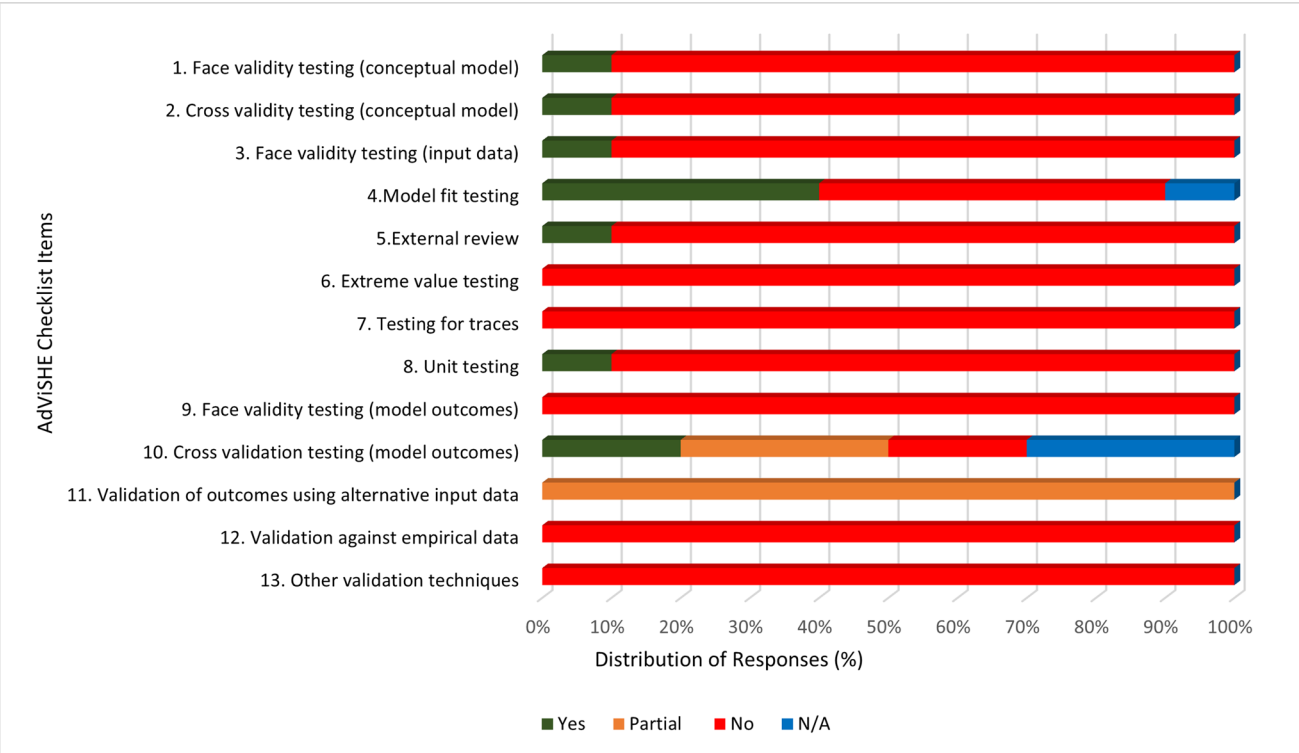

Fig. 6 Percentage of responses (yes, no, partial or N/A) for each ADViSHE item

(SIMPATHY) [69]. This review identified a gap in economic evidence of technology-driven interventions that support medication reviews. Given the increasing complexity of prescribing, there is an urgent need for innovative digital solutions that support medication reviews, patient engagement and medical adherence. Such interventions could empower patients and/or caregivers to proactively participate in treatment decisions, ultimately improving health outcomes.

An important gap identified in this review is the lack of economic evaluations of interventions addressing transfer-of-care, with only four studies focusing on this area. Transfer-of-care are high-risk transitions where medication errors frequently occur owing to information loss between healthcare professionals, providers and settings [70]. These errors may lead to preventable adverse events, hospitalisations and substantial economic burden.

Patient transitions often involve multiple healthcare professionals, and ensuring accurate information exchange is essential for preventing medication errors. Several studies included in this review underscore the value of digital and interoperable systems in enhancing medication safety during these transitions. For instance, Avery et al. (2012) and Elliott et al. (2014) evaluated the PINCER intervention, a pharmacist-led, IT-based strategy that uses electronic health record data to identify and reduce prescribing errors in general practice [33, 34]. Both studies demonstrated that a technology-enabled intervention improved prescribing safety and was cost-effective from a health system perspective. Similarly, Camacho et al. (2024) highlighted the significant benefits of interoperable prescription information systems in reducing errors during patient handovers, advocating for a unified digital record accessible across healthcare providers [67]. These studies provide some evidence that investing in interoperable digital infrastructure can enhance care continuity, reduce preventable harm and support more effective medication safety strategies across the healthcare continuum.

The National Health Service (NHS) in England has introduced a nationwide initiative to introduce interoperability into all NHS healthcare and social care settings [71]. This is part of the English NHS Long Term Plan and digital transformation agenda and the UK government's Health and Social Care Committee's commitment to the digitisation of the NHS. However, our review highlights a persistent gap in interventions supporting transfer-of-care, reinforcing the need for greater policy focus and investment in interoperable digital solutions.

Many studies in this review emphasised the key role of pharmacists in identifying and preventing medication errors. Several of the studies showed that pharmacists working alongside other health professionals resulted in positive clinical and economic outcomes. Collaborative medication management supported by continuous patient engagement and interoperable systems could significantly reduce medication errors and their associated costs. Ensuring that pharmacists play an active role in medication safety interventions should remain a policy priority.

Most of the studies in this review used safety-relevant process indicators, such as medication errors, to assess effectiveness. However, errors are a process indicator that act as a surrogate for patient outcome. Some errors may cause little or no harm if they reach the patient. If harm does occur, the error may be only one of several factors leading to a poor outcome. Estimating patient harm caused by medication errors has challenges. First, following a known error prospectively through the medication use process to assess potential harm is unethical. Second, there is often little data linking errors to subsequent harm at cohort or individual patient level.

Routine data collection where both errors and harm are collected for an individual patient can be informative but is often not available. In addition, many types of medication errors cannot currently be detected in routine data records, such as most medication administration errors.

Where there is no direct evidence to link errors to harm, one approach is to link a known adverse event back to a medication error [72–74]. This requires subjective judgments about causality and preventability. A second approach is to rank errors by subjective judgment of potential harm severity, [75–79], for example, dividing errors into 'minor', 'moderate' or 'severe' [80]. A third approach is to use modelling approaches to link medication errors to harm. For example, this team built five state-transition models to estimate the harm and cost from NSAIDs in five high-risk populations [81]. This is also the method used to estimate the harm and costs in the related study included in this review [34]. Some of the models in the study by Elliott et al. were severely limited by the lack of data available around the link of error to harm, introducing significant uncertainty into the overall results.

A significant gap was identified in patients and the public involvement and engagement (PPIE) in the design and conduct of studies. This raises questions about how patient-centred these evaluations truly are, especially in the context of medication safety. Similarly, the studies also had limited attention to how interventions might differentially affect population subgroups based on age, ethnicity or socioeconomic status ('equality, diversity and inclusion' [EDI]). Literature suggests that addressing inequalities is not only a moral obligation but also an economic necessity, as inequalities in healthcare hinder economic prosperity across nations [82].

Ethnic minority consumers may experience inequity in the safety of care and be at higher risk of patient safety events [83]. Research suggests that ethnic minorities have significant increased distrust of healthcare overall [84]. This

review found very limited evidence on the economic evaluation of interventions that help to make healthcare safer for minority ethnic groups. The review also had very low representation of studies from low- and middle-income countries (LMICs). Only studies by Herath et al. (2023) and Ibrahim et al. (2022) were from LMICs, [57, 59] which limits the generalisability of findings to resource-constrained settings where medication safety challenges may be even more pronounced.

Medical errors in general may be associated with a decreased trust of patients and citizens in healthcare systems and providers, leading to reduced service uptake or political support [85], lost productivity from healthcare professionals blamed for committing an error and litigation and compensation costs [86]. Perceptions of patient safety may affect healthcare demand through reduced trust. Distrust in healthcare is associated with delays in care seeking, low attendance and poor adherence, such as lower vaccination uptake [87]. There is likely to be an economic impact of reduced trust in healthcare services. This distrust may lead to care avoidance among 'silent members' [88], who are known to pose a higher future cost risk—an effect that may vary by sociodemographic factors. We found no evidence in the studies in this review that examined distrust in the healthcare system following medication errors, as well as the associated downstream consequences such as medication discontinuation, nonadherence and reduced engagement with care. This could be owing to the methodological challenges associated with quantifying both distrust and its effects on healthcare utilisation.

A key limitation is the heterogeneity between the included studies, which varied in healthcare settings, study design, interventions and outcome measures. The studies were conducted in different countries and different healthcare systems, making it challenging to synthesise data and compare findings between the studies. A noticeable gap is the lack of studies assessing carer perspective and productivity loss. Given that medication errors, particularly polypharmacy, disproportionally affect older and frail individuals who often rely on caregivers, further research is needed to explore the economic impact on caregivers as well as the healthcare system.

The use of a wide range of evaluation frameworks prevented meaningful comparison between studies, highlighting the need for improved standardisation in reporting economic evaluations of medication safety interventions. However, our review has identified specific areas where future research can develop and improve the current evidence base. Greater emphasis should be placed on evaluating systems and technology-supported interventions, particularly those that purport to improve medication safety across healthcare settings. Increased meaningful involvement of PPIE in research design and conduct, inclusion of ethnic minority and low- and middle-income countries and examination of distrust in the healthcare system following medication errors are also needed.

Most of the included studies focused solely on interventions to reduce prescribing or monitoring errors and, therefore, more research is needed in every aspect of medicine use, including dispensing and administration. Future research should also focus on estimating the indirect cost associated with medication errors, including productivity losses among patients and caregivers. Given the significant economic burden of medication-related harm, a comprehensive assessment of both direct and indirect costs is needed to better guide policy decisions around prioritising medication safety interventions. Furthermore, very few studies looked beyond the initial prescribing, monitoring or adverse drug events to estimate effects of harm over the longer term, to provide a better approximation of actual economic impact. This needs to be addressed because healthcare funders are increasingly keen to see the effects of improved medication safety on 'real outcomes' such as hospitalisations. The review also identified the need for enhanced transparency around design and validation of decision-analytic models.

5 Conclusions

Our review highlights the substantial economic burden associated with medication errors in primary and long-term care and identified several cost-effective interventions to prevent them. However, most of the interventions focused on monitoring and prescribing and overlooked other aspects of the medication use process. The review identified a gap in transfer of care, systems-based and technology-driven interventions.

The quality of some studies is not very good, with generally poorly validated models. This work suggests a greater need for targeting of studies to patients or settings most vulnerable to harm from medication errors, evaluation of the impact of digital innovation and system-wide initiatives on medication safety, and increased involvement of patients and carers in decisions about medication safety interventions and how to evaluate them.

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Declarations

Author contributions Research ideas for the grant application were informed by our PSRC PPIE group. RAE, DA, AA and AC developed the review research idea. LP, SA and RC ran the systematic searches, managed references and developed the flow chart, under the supervision of RAE. LP, SA and RC contributed to data extraction, and AM

provided external cross-checking of data extraction. LP, SA and RC extracted and cleaned data, led analyses, involvement and wrote the first draft. RAE, DA, AA, AC and AM contributed to discussions over inclusion/exclusion, quality, content, methodological evaluation and writing. All authors contributed towards interpretation, conclusions, implications and writing.

Patient and public involvement Our patient colleague AC was involved throughout the research process and is a co-author. AC contributed to the development of the research questions for this review, reviewed results and contributed to interpretations, conclusions and implications. AC co-wrote the Plain Language Summary. There is patient and public involvement in our dissemination plan, which includes communicating key findings to relevant patient groups, carers and health services.

Conflict of interest All authors are partly funded by the NIHR Greater Manchester Patient Safety Research Collaboration (GM PSRC), University of Manchester, Manchester, UK. The authors declare that they have no other conflicts of interest.

Role of the funder/sponsor The funder had no role in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; and decision to submit the manuscript for publication.

Data availability The authors confirm that all data generated or analysed during this study are included in this published article.

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Authors and Affiliations

Sneha T. Amritlal[1,2] · Rosalyn Chandler[1,2] · Alireza Mahboub-Ahari[1,2] · Luke Paterson[1,3] · Anthony J. Avery[2,4] · Darren M. Ashcroft[2,5] · Antony Chuter[2] · Rachel A. Elliott[1,2]

✉ Rachel A. Elliott
Rachel.A.Elliott@manchester.ac.uk

[1] Manchester Centre for Health Economics, University of Manchester, Jean McFarlane Building-4.311, Manchester, UK

[2] NIHR Greater Manchester Patient Safety Research Collaboration (GM PSRC), University of Manchester, Manchester, UK

[3] Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford, Oxford, UK

[4] Centre for Academic Primary Care, University of Nottingham, Nottingham, UK

[5] Centre for Pharmacoepidemiology and Drug Safety, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK