International Journal of Clinical Pharmacy (2023) 45:1326–1348
https://doi.org/10.1007/s11096-023-01590-0

REVIEW ARTICLE

Economic evaluation of pharmacy services: a systematic review of the literature (2016–2020)

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Received: 17 October 2022 / Accepted: 1 April 2023 / Published online: 26 May 2023

Abstract

Background Economic evaluation is crucial for healthcare decision-makers to select effective interventions. An updated systematic review of the economic evaluation of pharmacy services is required in the current healthcare environment.

Aim To conduct a systematic review of literature on economic evaluation of pharmacy services.

Method Literature (2016–2020) was searched on PubMed, Web of Sciences, Scopus, ScienceDirect, and SpringerLink. An additional search was conducted in five health economic-related journals. The studies performed an economic analysis describing pharmacy services and settings. The reviewing checklist for economic evaluation was used for quality assessment. The incremental cost-effectiveness ratio and willingness-to-pay threshold were the main measures for cost-effective analysis (CEA) and cost-utility analysis (CUA), while cost-saving, cost–benefit-ratio (CBR), and net benefit were used for cost-minimization analysis (CMA) and cost–benefit analysis (CBA).

Results Forty-three articles were reviewed. The major practice settings were in the USA (n = 6), the UK (n = 6), Canada (n = 6), and the Netherlands (n = 6). Twelve studies had good quality according to the reviewing checklist. CUA was used most frequently (n = 15), followed by CBA (n = 12). Some inconsistent findings (n = 14) existed among the included studies. Most agreed (n = 29) that pharmacy services economically impact the healthcare system: hospital-based (n = 13), community pharmacy (n = 13), and primary care (n = 3). Pharmacy services were found to be cost-effectiveness or cost-saving among both developed (n = 32) and in developing countries (n = 11).

Conclusion The increased use of economic evaluation of pharmacy services confirms the worth of pharmacy services in improving patients' health outcomes in all settings. Therefore, economic evaluation should be incorporated into developing innovative pharmacy services.

Keywords Community pharmacy · Economic evaluation · Hospital · Pharmacy service · Primary care · Systematic review

Impact statements

- Pharmacy services contribute clinical benefits, save costs, and are cost-effective. They should be acknowledged as a part of healthcare services while developing new programmes and interventions.
- An increased trend in the economic evaluation of pharmacy service underlines its importance for policy decision-making. Thus, it should be incorporated into developing future innovative pharmacy services globally.
- Economic evaluation of pharmacy services in primary care settings remains limited. Therefore, further studies are needed to confirm the benefit in such areas.

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Introduction

An economic evaluation of healthcare compares alternative options in terms of costs and consequences [1]. This assessment has become increasingly used by policymakers as it helps to decide on interventions or technology to be included in health benefit schemes. Alternative options refer to new ways to increase population health outcomes [2]. Four economic evaluation methods currently being used include cost-minimisation analysis (CMA), cost-effectiveness analysis (CEA), cost–benefit analysis (CBA), and cost-utility analysis (CUA). Each method is used for a different purpose. The CMA is appropriate when the equivalence of healthcare alternatives has already been proven. The CBA uses a welfarist approach which is concerned with an individual's judgement on how a particular consequence affects individual wellbeing [3]. The outcome of CBA has to be transformed into monetary units. CEA is frequently considered when comparing effectiveness using the clinical outcomes of interventions. CUA is commonly used for policy decision-making and considers the health-related quality of life (quality-adjusted life-year; QALY) as a measure of effectiveness [4].

A systematic review of the literature on the economic evaluation of pharmacy services between 2010 and 2015 revealed that pharmacy services tend to be cost-effective in improving medication-related outcomes and quality of life [5]. After 2015, two similar systematic reviews were published that only focused on community pharmacy. One reported the benefit of the community pharmacist in improving clinical outcomes of patients with chronic diseases [6]. However, these findings contradict the European-based review indicating insufficient evidence to prove the cost-effectiveness for community settings [7].

This study explores global literature on economic evaluation for pharmacy services and their economic impacts. This is to provide a wider perspective by covering pharmacy service in all settings and to update findings from a previous systematic review [5].

Aim

To conduct a systematic review of literature on economic evaluation of pharmacy services.

Method

A standard approach for conducting systematic reviews, PRISMA, was employed [8].

A literature search was performed through PubMed, Web of Sciences, Scopus, ScienceDirect, and Springerlink. Five health economic-related journals were searched: Health Policy, Expert Review of Pharmacoeconomics and Outcomes Research, Journal of Health Economics, Pharmacoeconomics, and The European Journal of Health Economics. Moreover, PlosOne, PlosMedicine, and Nature databases were searched. For the health economic-related journals, the only keyword used was 'pharmacy service'. A manual search of the references for the included articles was also performed. The search was limited to literature written in the English language. The search was limited from January 1, 2016, to December 31, 2020. The following search terms were used: "health economics" and "evaluation" "assessment" or "appraisal," "methods," "hospital" or "community" or "residential care," "pharmacy" or "pharmacy services" and "cost-minimization analysis" or "cost-utility analysis" or "cost-effectiveness analysis" or "cost–benefit analysis" (Supplementary material 1). The systematic review web application (rayyan.qcri.org) was used to screen and select the recruited articles [9]. This review obtained the PROSPERO registration number CRD42021266620 before conducting the study.

Selection of studies

Identified studies were selected based on the following inclusion and exclusion criteria. *Inclusion criteria*: (1) economic analysis undertaken using a modelling approach or along with experimental studies such as randomised controlled trials, non-randomised controlled trials, cross-sectional studies, and retrospective studies; (2) Studies must describe the details of pharmacy services, and the setting of services must be specified. *Exclusion criteria*: Review articles, case reports, news reports, editorials, commentaries, and opinions were excluded. The PICO elements that framed the selection criteria are listed in Table 1.

Article selection and data extraction

Two authors independently reviewed the titles and abstracts according to the inclusion criteria. Conflicts were resolved by a senior author. The full texts of the selected articles were reviewed by two researchers. Eligible articles were then evaluated and extracted using the following items: authorship, year of publication, location/region of study, economic evaluation method, study design, study perspective, time horizon, discounting, clinical outcomes and economic outcomes. A third opinion was sought if disagreements arose between the two researchers.

Table 1 The PICOS elements for study selection

Participants (P)	–
Intervention (I)	Pharmacy service: any pharmacy service delivered via any pharmacy setting: hospital, community pharmacy, or primary care
Comparator (C)	Usual care, no intervention, or other pharmacy services
Outcome (O)	Clinical and economic outcomes
Study design (S)	Economic evaluation: cost-minimisation analysis (CMA), cost-effectiveness analysis (CEA), cost–benefit analysis (CBA), and cost-utility analysis (CUA)

Study quality assessment

The quality assessment of individual studies was performed using a tool-'Reviewing economic evaluations: a checklist'-which contains fifteen review questions with thorough descriptions for assessment [10]. All studies were first evaluated by KS, then a random sample of 9 manuscripts (~20%) was re-evaluated by PS to confirm and validate the assessment's results [11]. We used 80% of the total items [12] ('yes' given to at least 12 items) to primarily indicate 'good quality' for individual studies.

Analysis of included studies

The results from the base-case analysis were primarily drawn and considered to indicate the value for money. The incremental cost-effectiveness ratio (ICER) was used for CEA and CUA. Pharmacy interventions that demonstrated 'lower cost-better effects' for economic outcomes were considered cost-effective. Conversely, the intervention was not cost-effective if it demonstrated a poorer health outcome. The willingness-to-pay (WTP) threshold indicated cost-effective intervention for CEA and CUA results that fell within the costlier and more effective range; thus, the WTP threshold value must be specified. The intervention was considered cost-effective when the ICER was below the threshold. The study was indicated as CEA; however, QALY was an outcome. Hence this study should be regarded as a CUA analysis. The measures used for CMA and CBA were cost-saving, cost-benefit ratio (CBR), and net benefit. The results were interpreted as cost-saving or cost-beneficial, whichever was appropriate. When the above information was not specified, the interpretation was deemed unclear. The included studies were grouped using a set of pharmacy services and settings for delivery to summarise their economic impacts. The findings are described by a narrative synthesis approach.

Results

Characteristics of included studies

The search identified 2261 potential articles. Two hundred and seventy-eight articles were excluded as they were duplicate articles. All titles and abstracts were screened, and another 1,837 articles were excluded for the following reasons: the study was not an economic evaluation (n = 970), not pharmacy-related (n = 674), not a research article (n = 120), was a background article (n = 71), and the publication date was not within 2016–2020 (n = 2). Finally, 146 articles were screened. Ultimately, 43 full-text articles were included in the study (Fig. 1).

The number of publications by year was plotted to reveal the growth of economic evaluation studies. Eight to ten studies were published annually between 2016 and 2020 (Fig. 2). Based on the review of 43 publications, the economic evaluation of pharmacy services was predominantly based in the US (n = 6) [14–19], the UK (n = 6) [20–25], Canada (n = 6) [26–31], and the Netherlands (n = 6) [32–37]. Pharmacy services in the studies were delivered via three settings: hospital (n = 20, Table 2) [14, 16, 17, 24, 25, 32, 34, 35, 38–49], community pharmacy (n = 20, Table 3) [18–23, 26–31, 33, 36, 37, 50–54], and primary care (n = 3, Table 4) [15, 55, 56]. Various perspectives were focused on, and the healthcare provider's or hospital's perspective was mostly taken (n = 22) [14, 16–19, 21, 24, 27, 29, 30, 35, 39, 42–45, 49, 51, 53, 55, 56]. In contrast, four studies did not specify this [32, 38, 47, 48]. The time horizon varied from the shortest (24 h after discharge) [32] to the longest being lifetime [15, 22, 23, 29, 31, 44, 54] or 100 years [20]. Thirteen studies applied discounting to the analysis: both costs and outcomes (n = 9) [15, 17, 22, 23, 26, 29, 31, 54, 56], and only cost (n = 4) [19, 20, 27, 41] with the discounting value ranging from 1–5%. The national consumer price index was used in five studies [27, 33, 49, 53, 55], whereas one study used price discounts and inflation rates [39].

Quality of included studies

Twelve studies adhered strictly to the reviewing checklist [10], they followed to at least 12 assessment questions [15, 17, 20, 22, 23, 27, 29, 31, 33, 41, 54, 56]. The time horizon was vaguely stated in seven studies [18, 21, 28, 34, 38, 48, 49], but one did not specify this. Only four studies accounted for equity consideration by conducting a subgroup analysis [22, 29, 33, 54]. Four studies did not apply discounting in their analyses despite the time horizon being over one year [25, 40, 44, 55]. Seven studies lacked performing the sensitivity analysis [18, 19, 36, 38, 39, 42, 46] (Supplementary material 2).

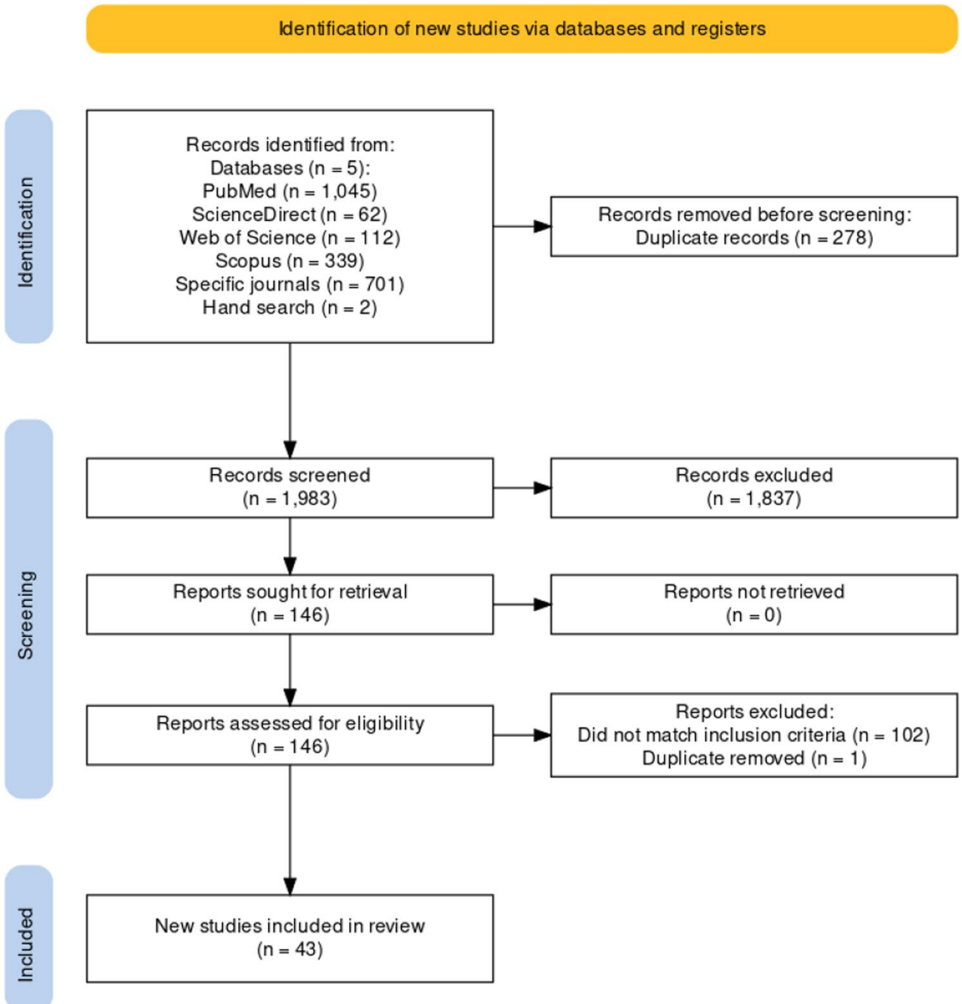

Fig. 1 A PRISMA flow diagram describing the study selection process [13]. Reasons to exclude 1837 records were: the study was not an economic evaluation (n = 970); not pharmacy-related (n = 674); not a research article (n = 120); was a background article (n = 71); was published before 2016 or after 2020 (n = 2)

Methods used for the economic evaluation of pharmacy services

Cost utility analysis (CUA)

CUA was used in fifteen studies to evaluate the cost-utility of a range of pharmacy services: pharmaceutical care [15, 25, 41, 46, 47], health screening or diagnostic testing [20, 31, 54], medicines use review [53], medication therapy management [17, 29], new medicine service [22, 23], prescribing [26], and minor ailments [50]. All these studies presented QALY as the main outcome. Model-based analysis was conducted to predict cost-effectiveness for a longer time horizon [15, 17, 20, 22, 26, 31, 41, 54], while a trial-based was often used when the time horizon was less than a year [25, 46, 47, 50, 53].

Cost effectiveness analysis (CEA)

CEA was used in nine studies to evaluate the cost-effectiveness of pharmaceutical care [18, 55, 56], health screening or diagnostic screening [27], medication use review [37, 43], medication therapy management [14], prescribing [44], and smoking cessation [21]. Six studies performed economic evaluation alongside randomised trials [14, 18, 37, 43], quasi-experiments [55], or retrospective observations [21]. Six studies observed the economic outcomes for at least one year [14, 37, 56] or up to a lifetime [44]. Modelling was used

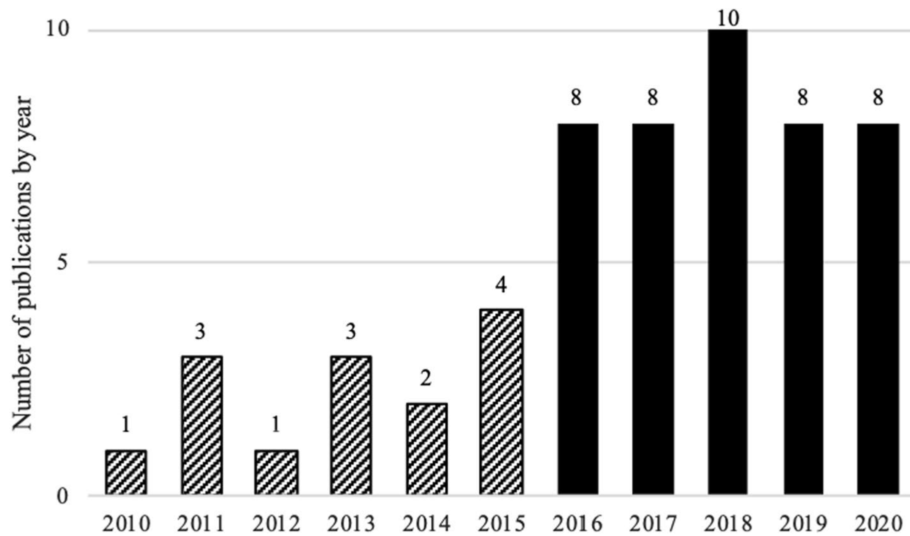

Fig. 2 Number of publications by year 2010–2015 data drawn from the previous work by Gammie et al. [5]

in only three studies [27, 44, 56]. The outcome was mainly the number of patients who achieved the clinical goal, such as patient's blood pressure controlled in the year [55], a person achieved good refill adherence [18], and others.

Cost utility analysis (CUA) and cost effectiveness analysis (CEA)

Five studies performed using both CEA and CUA. These studies included cost-effectiveness and cost-utility of pharmaceutical care [33], medication management therapy [19, 36], and prescribing in community pharmacies. Only one study evaluated hospital-based pharmaceutical care [34]. Four studies collected costs and outcomes alongside the randomised trial [33, 34] and quasi-experiment [19, 36], while one study was model-based [30]. Three studies reported an incremental analysis, stating incremental cost per unit of achieving clinical outcomes and per QALY gained [19, 33, 34].

Cost benefit analysis (CBA)

Twelve studies used CBA. These studies evaluated the cost–benefit of pharmaceutical care [38, 40, 42, 48], health screening or diagnostic testing [51], medicine use review [45, 52], medication reconciliation [16, 24, 32], antibiotic stewardship [39], and home medicine use review [49]. CBA was frequently used for evaluating hospital-based pharmacy services [16, 24, 32, 38–40, 42, 45, 48, 49], but only in two studies were conducted in community pharmacy setting [51, 52]. Five studies observed outcomes retrospectively. The other studies collected data alongside the randomised trial [49, 52], quasi-experiment [32, 39], cross-sectional study [51], and prospective cohort [40], whereas one study was done through the model-based [16]. All studies reported clinical and economic outcomes with appropriate CBA measures: net benefit or CBR. Nevertheless, none of these studies focused on patients or societal perspectives.

Cost minimisation analysis (CMA)

CMA was used in two studies: one hospital-based parenteral injection preparation [35] and one strep-throat test in a community pharmacy [28]. Both studies used a model approach for analysis from the payer's [28] and provider's perspectives [35]. Neither of them provided evidence of effectiveness equivalence between the comparators and alternatives.

Economic impacts of pharmacy services

Pharmacy services contributed to economic benefit for the healthcare system. The studies based in developed countries (n = 32) mainly evaluated hospital-based and community pharmacy services. The rest from developing countries (n = 11) predominantly examined hospital-based and primary primary-care pharmacy services.

Hospital-based pharmacy services

Hospital-based pharmaceutical care was the major service provided [25, 38, 40, 41, 47, 48], followed by medication

Table 2 Characteristic of studies that performed an economic evaluation of hospital-based pharmacy service (n = 20)

Author country	Method perspective	Intervention (I) Health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Dehmer et al. 2018 [14] US	CEA healthcare	I: Medication therapy management (MTM) by a pharmacist—blood pressure telemonitoring H: Hypertension	12 months	n/a	n/a	MTM by pharmacist cost US$ 7,337 per person achieving hypertension control and US$ 139 or US$ 265 per mmHg reduction in systolic or diastolic blood pressure, respectively WTP threshold: n/a	Unclear
Najafzadeh et al. 2016 [16] US	CBA hospital	I: Pharmacist-led medication reconciliation H: Cardiovascular disease	30 days	n/a	Pharmacist-led medication reconciliation at hospital discharge could reduce medication errors by 52%. The number of preventable adverse drug event-related rehospitalizations and emergency department visits reduced to 199 and 215, respectively	At hospital discharge, pharmacist-led medication reconciliation had a significant net benefit of US$ 206 (95% CI US$ 73–US$ 373) per patient	Cost-saving
Okere et al. 2018 [17] US	CUA healthcare	I: (1) Dual anti-platelet therapy (DAPT) + point-of-care phenotypic and genetic testing (POCP); (2) DAPT + MTM with POCP (MTM-POCP); (3) MTM-clopidogrel; (4) MTM-ticagrelor H: Acute coronary syndrome and elderly	21 years	3.5% both costs and outcomes	n/a	Relative to MTM—clopidogrel, MTM-POCP and MTM-ticagrelor had an ICER of US$ 14,140.80 and US$ 41,345.99, respectively, per QALY WTP threshold: US$ 50,000 per QALY	Cost-effective
Onatade and Quaye 2018 [24] UK	CBA healthcare	I: Pharmacy-led medication reconciliation (by the pharmacist and pharmacy technician) H: Internal medicine	n/a	n/a	There were 118 preventable adverse drug events averted due to medication reconciliation over the 12 half-hospital days (6 full days); 98% (116/118) were rated for clinical significance	Conducting 6 days of all medication reconciliations had a net benefit of £ 29,604–£ 68,718: £ 34–£ 80 per medication reconciliation. The cost–benefit ratio was 5.53:1–11.51:1	Cost-saving

Table 2 (continued)

Author country	Method perspective	Intervention (I) Health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Twigg et al. 2019 [25] UK	CUA NHS	I: Pharmacy care plan service-medication review using relevant guidance and clinical tools to provide personalised care plans H: Outpatient	12 months	n/a	Pharmacist intervention improved medication adherence (mean difference: 0.26, 95% CI: 0.14–0.4), systolic blood pressure (mean difference BP: -2.90 mmHg, 95% CI: -4.7–-1), diastolic blood pressure (mean difference: -1.81 mmHg, 95% CI: -2.8–-0.8), patient activation score (mean difference 5.39; 95% CI 3.9–6.9), and EQ-5D-5L score (mean difference: 0.029, 95% CI 0.015–0.044)	ICER for pharmacy care plan service was £8,495 WTP threshold: £20,000 per QALY	Cost-effective
Bosma et al. 2018 [32] Netherlands	CBA n/a	I: Medication reconciliation by the pharmacist H: Intensive care	24 h	n/a	The proportion of patients with at least 1 medication transfer error (MTE) at ICU admission reduced from 45.1 to 14.6% (OR_{adj}: 0.18, 95% CI: 0.11–0.30) and after discharge from 73.9% to 41.2% in the post-intervention phase (OR_{adj}: 0.24, 95% CI: 0.15–0.37). The proportion of patients with preventable adverse drug reactions at ICU admission reduced from 34.8 to 8.0% (OR_{adj}: 0.13, 95% CI 0.07–0.24)	Medication reconciliation had a cost–benefit ratio of 2.48, and the net cost–benefit was € 103 per patient	Cost-saving

Table 2 (continued)

Author country	Method perspective	Intervention (I) Health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Karapinar-Çarkit et al. 2017 [34] Netherlands	CEA/CUA societal	I: Continuity of Appropriate pharmacotherapy, patient Counselling, and information transfer in Healthcare (COACH) H: Internal medicine	n/a	n/a	No significant difference was observed in the proportion of patients with unplanned rehospitalizations (21.4% COACH vs 20.5% usual care). The mean difference of QALY between the pharmacist's intervention and usual care was -0.0085 (95% CI -0.0170–0.0001)	For unplanned and drug-related rehospitalizations, ICER were -€ 627,251 and -€ 128,804, respectively. This indicates that COACH had lower costs but higher undesired outcomes. For CUA, ICER was € 137,059 per QALY gained in the control group compared to the intervention group WTP threshold: €50,000 per QALY	Not cost-effective
Larmené-Beld et al. 2019 [35] Netherland	CMA provider	I: Ready to administer prefilled sterilised syringe (PFSS) produced by the pharmacy H: n/a	1 year	n/a	n/a	Conventional preparation method by nurses cost € 14.0 million annually, while PFSSs cost € 4.1 million. PFSSs saved €9.9 million compared to the conventional method	Cost-saving
Bao et al. 2018 [38] China	CBA n/a	I: Pharmacists intervened in inappropriate prescriptions (IPs) in real-time and summarised and analysed the information monthly H: Outpatients	n/a	n/a	Pharmacist interventions decreased the number of IPs yearly from 1,845 (2011) to 238 (2016)	The benefit of the pharmacist's intervention, expressed as the total cost of all inappropriate issues, decreased from US$ 43,500.30 to US$ 8,978.16. The benefit was higher than the cost, and the benefit-to-cost ratio was > 1	Cost-saving
Borde et al. 2016 [39] Germany	CBA provider	I: Antibiotic stewardship H: Hip, knee, and shoulder	1 month	n/a	The overall use of anti-infectives in the post-intervention period was reduced from 334.9 to 221.4 recommended daily doses/per 1000 patient days. The drug use density of daptomycin dropped by 75%	The monthly cost saved due to changes in antimicrobial prescribing was € 4,563 ($p < 0.001$) owing to decreased daptomycin consumption	Cost-saving

Table 2 (continued)

Author country	Method perspective	Intervention (I) Health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Maurilio de Souza Cazarim et al. 2020 [40] Brazil	CBA provider and healthcare	I: Pharmacotherapeutic follow-up and identification of drug-related challenges for inpatients H: Neurological diseases	36 months	n/a	Of all pharmacist interventions, the percentage of acceptance by the health team was 70%. Of the 506 interventions, medication introduction was the most frequently provided (29%)	Pharmacist intervention contributed no monetary benefit from the hospital's perspective: the cost–benefit ratio was zero, and the net benefit was negative. However, the cost–benefit ratio was 3.0, with a net benefit of US$ 51,049 from the public health system's viewpoint	Negative cost–benefit
Chang et al. 2017 [41] Taiwan	CUA payer	I: Pharmacist-assisted warfarin monitoring (PAWM) H: Warfarin therapy	20 years	3% for cost	n/a	ICER for PAWM was NT$ 410,749 per QALY gained WTP threshold: Taiwanese GDP per capita in 2012 (NT$ 631,142, NT: New Taiwanese dollars)	Cost-effective
Chen et al. 2020 [42] Taiwan	CBA healthcare	I: Revisions in medication orders and active recommendations (orders: order modification, monitoring of drug therapy, key-in error, and violation of regulations) H: Haematology	12 months	n/a	After clinical pharmacist involvement, the intercepted preventable adverse drug events increased from 58 to 230. The average length of hospitalization reduced from 19.27 to 16.69 days	The intervention had cost savings (NT$ 37,080 and NT$ 252,280) and avoidance (NT$ 582,100 and NT$ 2,304,600), and the cost–benefit ratio (0.77 and 3.19) increased after clinical pharmacist deployment	Cost-saving
Gallagher et al. 2016 [43] Ireland	CEA provider	I: Structured Pharmacist Review of Medication Clinical Decision Support Software (SPRM/CDSS) Intervention H: Elderly	3 months	n/a	The effectiveness measures favoured the intervention strategy. The odds ratio for experiencing an adverse drug reaction was 0.655 (95% CI: 0.431–0.994; $p=0.047$) when comparing pharmacist intervention with usual care	The intervention was linked with an € 807 reduction in mean health costs and a -0.064 reduction in the mean number of adverse drug reaction occurrences per patient compared to conventional care WTP threshold: only hypothetical threshold is indicated	Unclear

Table 2 (continued)

Author country	Method perspective	Intervention (I) Health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Hale et al. 2018 [44] Australia	CEA healthcare	I: Doctor-pharmacist Collaborative prescribing H: Venous thromboembolism	Lifetime	n/a	n/a	A pharmacist prescribing was non-significantly less costly than a doctor prescribing by AU$ 31 (95% CI: -AU$ 97, AU$ 160) per patient compared with conventional care, and produced 0.02 (95% CI: -0.01, 0.05) QALYs per patient. ICER is not shown. (AU = Australian dollars) WTP threshold: AU$ 40,000 per QALY	Unclear
Han et al. 2016 [45] South Korea	CBA provider	I: pharmacists reviewed chemotherapy prescriptions H: Chemotherapy preparation	1 year	n/a	Among the 631 pharmacist intervention cases, the acceptance rate was 72.1%. Of 455 cases that accepted pharmacist interventions, 362 (79%) were related to preventing adverse drug events	The cost–benefit analysis of pharmacists' prescription review had a net cost–benefit of US$ 116,493 and a cost–benefit ratio of 3.64:1	Cost-saving
Mateti et al. 2018 [46] India	CUA patient	I: Pharmaceutical care—motivation and patient education about medication, diseases, and lifestyle modification for patients with CKD/ESRD H: Haemodialysis	1 year	n/a	n/a	ICER of pharmaceutical care compared with usual care was 86,230 Indian Rupee (INR) per QALY WTP threshold: n/a	Unclear

Table 2 (continued)

Author country	Method perspective	Intervention (I) Health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Tanaka et al. 2019 [47] Japan	CUA n/a	I: Pharmacist's counselling for breast cancer outpatients H. Breast cancer	6 months and 1 year	n/a	The EQ-5D score across the time points were 0.831, 0.757, and 0.791 for the control group and 0.882, 0.883, and 0.921 for the pharmacist counselling group	Over six months, the ICER of the pharmacist counselling group was performed at 3 time points. Before the second chemotherapy was 860,711 Yen per QALY. Before the third course was 279,351 Yen per QALY, and the mean of both courses was 511,141 Yen per QALY WTP threshold: n/a	Unclear
Ah et al. 2016 [48] South Korea	CBA n/a	I: Providing pre/post-transplant medication education, counselling, and monitoring medication use in the outpatient clinic, reviewing inpatient pharmacotherapy, participating in medical rounds, coordinating the drug protocol development H: Liver transplant	n/a	n/a	There were 489 interventions (26%) related to cost avoidance	The pharmacist-led intervention had a net cost–benefit of €94,900 and a cost–benefit ratio of 3.8	Cost-saving
Al-Qudah et al. 2020 [49] Jordan	CBA provider	I: Treatment-related challenges and home medication management review (HMMR) H: Chronic disease	n/a	n/a	Treatment-related challenges identified via pharmacist intervention were 158: diabetes (18.4%), hyperlipidaemia (18.6%), hypertension (9.5%), asthma (9.5%), and pre-diabetes (6.3%)	The monthly cost of pharmacist intervention was JD 764, and the total monthly benefit was JD 4,570. The cost–benefit ratio was 5.98. (JD = Jordanian dollars)	Cost-saving

95% CI: 95% Confidence interval, CBA: cost–benefit analysis, CEA: cost-effectiveness analysis, CMA: cost-minimization analysis, CUA: cost-utility analysis, ICER: Incremental cost-effectiveness ratio, QALY: Quality-adjusted life year, n/a: not applicable reconciliation [16, 24, 32]. Most of these services provided good value for money. Among 20 hospital-based studies, 13 demonstrated that hospital-based pharmacy services were cost-effective. Pharmaceutical care provided to outpatients in the UK [25] and patients using warfarin in Taiwan [41] was cost-effective, reporting the incremental cost per QALY being under the national WTP threshold.

Pharmaceutical care in Taiwan [42], South Korea [48], and China [38] also reported a net benefit for patients with haematologic diseases, those undergoing liver transplants, and those in outpatient clinics. Medicine use reviews for chemotherapy prescriptions in South Korea were also beneficial [45]. Medication management provided for the elderly with acute coronary syndrome [17] was cost-effective. Medication reconciliation delivered for cardiovascular disease [16], intensive care [32], and internal medicine [24] was a cost-saving alternative compared to the usual care. Antibiotic stewardship [39], home medicine use review [49], and injection preparation [35] were also cost-saving. Nonetheless, several studies reported contradicting results (Table 2).

Community pharmacy service

Health screening or diagnostic testing was the service frequently explored in economic evaluation [20, 27, 28, 31, 51, 54], followed by medicine use review [37, 52, 53], and medication therapy management [19, 29, 36]. Community pharmacist delivered screening for diabetes in Japan [54] and testing for hepatitis C virus in the UK [20], both were found to be cost-effective.

A rapid diagnostic test performed by community pharmacists to identify malaria and strep throat also contributed a net benefit in Nigeria [51] and Canada [28]. Medicine use review for Italian asthmatic [53] and Spanish polypharmacy [52] was cost-effective. Medication management therapy in the US for HIV [19] and in Canada for cardiovascular disease [29] was cost-effective. The UK-based studies examined the new medication service for chronic disease and minor ailments and were also cost-effective [22, 23]. Canadian pharmacy prescribing [26], Australian minor ailment service [50], and UK smoking cessation [21] were also cost-effective. However, few other studies revealed inconsistent findings (Table 3).

Primary care pharmacy service

One study was performed using CUA [15], and two employed CEA [55, 56] for pharmacy services in primary care. Several studies reported that pharmaceutical care was cost-effective for chronic diseases. This was observed in Jordan [56], the US [15], and Brazil [55] (Table 4).

Discussion

Statement of key findings

This systematic review demonstrated that the number of published studies on the economic evaluation of pharmacy services noticeably increased between 2010 and 2020 compared to previous years [5]. Some studies reported diverse findings (14 out of 43); however, most studies in this review (29 out of 43) agreed that pharmacy services would result in improving health outcomes and they are 'value for money'. The results in this review are consistent with those of previous reviews of pharmacy interventions. [57–59]

Uaviseswong et al. reported that pharmacist interventions provided economic benefits and saved the cost of preventable adverse drug events [57]. This was due to a reduction in medication errors. In China, antimicrobial management, chronic disease management, and multidimensional clinical pharmaceutical services were associated with cost-saving and improved patient outcomes [58]. US-based clinical pharmacy services, including pharmacotherapy, disease management, ambulatory care, and those provided in community pharmacies are more effective at a lower cost [59].

Evidence is also well established that optimal hospital pharmacy is cost-saving and community pharmacy services are cost-effective. Hospital pharmacy services are often related to providing pharmaceutical care [25, 38, 41, 42, 48] and medication reconciliation [16, 24, 32]. This is also evident from a Jordanian home medication use review, showing that hospital pharmacy services could result in cost-saving [49]. This also indicates the possibility of hospital pharmacist's involvement in primary care.

Community pharmacies are involved in improving medication use, such as medicine use review [52, 53], medication therapy management [19, 29], and new medication service [22, 23]. They also screen for issues, such as health-related risks of chronic [54] and infectious diseases [20, 28, 51]. These findings reiterate that pharmacy service is increasingly acknowledged as an important part of health service system.

In many countries, such as the UK [60], Canada [61], Europe and others [62], some pharmacy services are part of the national health benefit package, which means they are remunerated by the public payer [63]. The number of studies from the developed countries was about three times higher than that from the developing ones. However, they

Table 3 Characteristic of studies that economically evaluated community pharmacy service (n = 20)

Author country	Method perspective	Intervention (I) health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Shireman and Svarstad 2016 [18] US	CEA provider	I: Pharmacists and pharmacy technicians using novel tools for improving adherence and feedback to hypertensive patients and physicians H: Hypertension	n/a	n/a	The six-month blood pressure control was achieved in 53.8% and 36.7% in the intervention and control groups, respectively ($\chi2 = 14.19$, df = 1, $p < 0.001$). Patients who achieved good refill adherence were significantly higher in the intervention than the control group (59.7% vs 36.1%; $\chi2 = 24.78$, df = 1, $p < 0.001$)	The cost of helping one more person achieve the blood pressure goal (< 140/90 mmHg) was US$ 665.2 ± 265.2; that of helping one more person achieve good refill adherence was US$ 463.3 ± 110.7 WTP threshold: n/a	Unclear
Shrestha et al. 2020 [19] US	CEA/CUA provider	I: Medication therapy management by a pharmacist H: HIV	1 year	3% for cost	In total, 200 patients were virally suppressed post-intervention, with the incremental number of virally suppressed patients being 45. The intervention averted 2.75 HIV transmissions and saved 12.22 QALY	For CEA, medication therapy management by pharmacists had an incremental cost per patient virally suppressed of US$ 5039. For CUA, the ICER of the intervention was -US$ 86,157 (less costly, greater QALY) WTP threshold: US$ 100,000 per QALY	Dominant
Buchanan et al. 2019 [20] England	CUA patient	I: Dry blood spot testing for hepatitis C virus in community pharmacies H: Hepatitis C	Attained age 100	3.5% for costs	Of 186 tests conducted over 24 months, 13 were positive for hepatitis C virus RNA, and 10 were current or former people with a history of injecting drug use (PWID). All were genotype 1a (32%) or genotype 3a (68%)	ICER for the intervention was £ 3,689 per QALY gained WTP threshold: £ 20,000 per QALY	Cost-effective

Table 3 (continued)

Author country	Method perspective	Intervention (I) health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Csikar et al. 2016 [21] England	CEA provider and NHS	I: Smoking cessation H: Smoking	12 weeks	n/a	The percentage of quits by carbon monoxide verified for NHS stop smoking services, pharmaceutical services, and dental care were 31.66%, 36.36%, and 33.33%	From the NHS perspective, pharmacy-based smoking cessation was a dominant option with ICER of -£ 2.31 per quit compared to the NHS stop smoking services WTP threshold: n/a Note: cost-effectiveness was compared to a conventional NHS service	Cost-effective
Elliott et al. 2017 [22] UK	CUA NHS	I: New medicine service by the pharmacist H: Antiplatelet/ anti-coagulant drugs, asthma/ COPD, Hypertension, type II diabetes	Lifetime	3.5% for costs and outcomes	n/a	The new medicine service generated a mean of 0.04 more QALYs per patient than normal practice, at a mean reduced cost of -£139 WTP threshold: £ 20,000 per QALY	Dominant
Elliott et al. 2020 [23] UK	CUA NHS	I: New medicine service led by a pharmacist H: Minor ailment condition	Lifetime	3.5% for costs and outcomes	57.1% and 65.6% of patients adhered to conventional practice and new medicine service arms, respectively (OR_{adj}: 1.50; 95% CI 0.93–2.44, p = 0.095)	At the 26th-week follow-up, the new medicine service generated a mean of 0.04 more QALYs per patient, with a mean reduction in the lifetime cost of −£113.9 compared to the conventional practice WTP threshold: £ 20,000 per QALY	Dominant

Table 3 (continued)

Author country	Method perspective	Intervention (I) health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Al Hamarneh et al. 2019 [26] Canada	CUA payer	I: Community pharmacist prescribing H: Cardiovascular disease	30 years	1.5% for costs and outcomes	Over 30 years, pharmaceutical care prevented over 8.9 million CV events compared to conventional care if applied to only 15% of eligible adults	Community pharmacist prescribing gained 0.19 QALY, experienced 0.10 fewer cardiovascular events, and accrued Can$ 2,149 less in direct medical costs compared to not receiving the intervention. This indicates that the intervention was dominant WTP threshold: n/a	Cost-effective
Coronado et al. 2016 [27] Canada	CEA healthcare	I: Pharmacy-based teleophthalmology program H: Diabetic retinopathy	5 years	5% for costs	Pharmacy-based teleophthalmology increased screening compliance from 51.1% to 56.2%. The intervention accurately detected and diagnosed 136 and 688 more cases than in-person examination only	The ICER of Pharmacy-based teleophthalmology was $ 314.10 per additional case detected and $ 73.24 per additional case correctly diagnosed. the programs were nondominant; hence, the program was always costlier but was more effective than in-person examinations alone WTP threshold: n/a	Unclear
Lathia et al. 2018 [28] Canada	CMA payer	I: Pharmacy offering strep throat (rapid antigen detection test; RADT) H: Strep throat	n/a	n/a	n/a	The mean cost of treating severe sore throat per patient at a community pharmacy was the lowest compared to other settings (Can$ 19.18–Can$ 21.83 in five participating provinces)	Cost-saving

Table 3 (continued)

Author country	Method perspective	Intervention (I) health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Tam-Tham et al. 2019 [29] Canada	CUA healthcare	I: Medication therapy management review, laboratory assessment, individualised CV risk assessment, education, and prescription H: Strep throat	Lifetime	1.5% for costs and outcomes	At 3 months, there was a statistically significant difference in the change in HbA1c between intervention and usual care groups (-0.92%, 95% CI: -1.12%–-0.72%, P < 0.001)	Intervention saved Can$ 4,770 per patient over a lifetime and gained 0.18 QALY (less costly, greater QALY). The intervention dominated usual care across all time horizons WTP threshold: n/a	Dominant
Sanyal et al. 2019 [30] Canada	CEA/CUA healthcare	I: Pharmacists examined patients with uncomplicated UTI symptoms and initiated antibiotic treatment (community pharmacist-initiated) H: Uncomplicated urinary tract infection	1 month	n/a	n/a	Pharmacist-initiated management was less costly (Can$78.70) and had lower effects (0.75232 QALMs) than family and emergency physician-initiated management WTP threshold: n/a	Unclear
Tarride et al. 2017 [31] Canada	CUA payer	I: Atrial fibrillation screening by the pharmacist H: Atrial fibrillation	Lifetime	1.5% for costs and outcomes	n/a	The pharmacist intervention resulted in higher expected costs (Can$ 26), more life-years (0.0032), and more QALYs (0.0035) over a lifelong time horizon, yielding an incremental cost per QALY gained of Can$ 7,480 WTP threshold: n/a	Unclear

Table 3 (continued)

Author country	Method perspective	Intervention (I) health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Bosmans et al. 2019 [33] Netherland	CEA/CUA societal	I: pharmacist-led Cardiovascular medication non-Adherence Tailored Intervention (CATI) H: Hypertension	3, 6, and 9 months	n/a	There were no significant differences in any of the effect outcomes (self-reported adherence: Medication Adherence Report Scale; MARS, and Specific Beliefs about Medicines Questionnaire; BMQ) between the group	No significant differences in costs or effects existed between the intervention program and usual care WTP threshold: € 20,000 per QALY	Not cost-effective
Van Der Heijden et al. 2019 [37] Netherlands	CEA societal	I: Clinical medication review by a pharmacist H: Vulnerable older patients	1 year	n/a	After 12 months of follow-up, the intervention group had a significant decrease in drug-related problems (mean difference: -0.2, 95% CI: -0.4–0.0) compared to the control group	The cost of the intervention group was €1,654 higher than that of the control group but not significant. The incremental cost of reducing one drug-related problem by a clinical medication review amounted to €8,270 WTP threshold: n/a	Unclear
Van Boven et al. 2016 [36] Netherlands	CEA/CUA payer and societal	I: Medication Monitoring and Optimization targeted COPD intervention (MeMO) H: COPD	1 year	n/a	Medication adherence and exacerbation between pre- and post-intervention were not different	The cost differences between both groups were not significant. Not all health outcomes, such as the Clinical COPD Questionnaire (CCQ) score and QALYs, were influenced by pharmacy intervention	Unclear
Dineen-Griffin et al. 2020 [50] Australia	CUA societal	I: Minor ailment service by the pharmacist H: Minor ailments	14 days	n/a	n/a	ICER of pharmacist intervention was AU$ 2,277 per QALY WTP threshold: AU$ 28,033 per QALY	Cost-effective

Table 3 (continued)

Author country	Method perspective	Intervention (I) health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Ezennia, Nduka, and Ekwunife 2017 [51] Nigeria	CBA provider	I: Rapid diagnostic test by the pharmacist H: Malaria	n/a	n/a	82.2% of respondents (suspected malaria cases) preferred rapid diagnostic tests before malarial treatment	The average willingness to pay for the rapid diagnostic test was US$ 1.23. The cost–benefit ratio of the test-based malaria treatment was 6.7 (95% CI: 6.4–7.0)	Positive cost–benefit
Malet-Larrea et al. 2017[52] Spain	CBA NHS	I: Medication review with follow-up by the pharmacist H: Aged polypharmacy	6 months	n/a	The number of uncontrolled health problems decreased in the intervention group was > 50% ($p > 0.001$), similar to the control group. Emergency department visits or hospitalizations decreased in the intervention group significantly	Medication review with follow-up yielded an estimated saving of 273 € per patient-year. The cost–benefit ratio was €3.3–€6.2 for every €1 invested in the pharmacist intervention	Cost-saving
Manfrin et al. 2017 [53] Italy	CUA healthcare and societal	I: 9 months Italian medication use review H: Asthma	9 months	n/a	The intervention group provided an odds ratio for improved asthma control of 1.76 (95% CI: 1.33–2.33), and the number needed to treat was 10 (95% CI: 6–28). Adherence improved by 35.4% at 3 months post-intervention and 40.0% at 6 months ($p < 0.01$)	The difference in yearly patient costs from a healthcare perspective was -€122.63 in the intervention group and -€113.29 in the control group. The difference in QALY was 0.02 and 0.10, respectively. ICER value is not shown, but the cost-effectiveness plane is presented WTP threshold: €30,000 per QALY	Cost-effective

Table 3 (continued)

Author country	Method perspective	Intervention (I) health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Shono et al. 2018 [54] Japan	CUA societal	I: Fingertip HbA1c testing by a pharmacist H: Diabetes	Lifetime	3% both costs and outcomes	n/a	HbA1c testing at community pharmacies saved a total cost of $ 527 (JPY 52,722) per individual aged 40–74 years, with 0.0203 QALY gained (less costly and greater QALY) compared to conventional care. (JPY = Japanese Yen) WTP threshold: US$ 50,000 (JPY 5,000,000)	Dominant

95% CI: 95% Confidence interval, CBA: cost–benefit analysis, CEA: cost-effectiveness analysis, CMA: cost-minimization analysis, CUA: cost-utility analysis, ICER: Incremental cost-effectiveness ratio, QALY: Quality-adjusted life year, n/a: not applicable

have similar findings showing cost-effectiveness or cost-saving of pharmacy services across the board.

Regarding the use of the economic evaluation method, Costa et al. reported that CEA is the most common type of economic analysis used, followed by CUA [63]. However, CUA is the most commonly used approach in the community pharmacy setting. This approach typically uses QALY as an outcome, making the cost-effectiveness results comparable to other interventions for any disease.

Cost-benefit analysis is often used to evaluate hospital-based pharmacy services using monetary outcomes such as cost avoided from adverse events [48] and cost of inappropriate prescription [38].

Several tools/checklists are available for assessing the quality of economic evaluation for example the Drummond checklist, BMJ checklist (15.8%), and CHEERS statement [12]. We used the one proposed by the Centre for Epidemiology and Evidence, Australia because of its thorough definition of assessment [10]. Nonetheless, the items in those tools/checklists are very similar. Only about one-third (12 out of 43) of the included studies were of good quality.

The previous reviews have also shown that challenges emerged in evaluating pharmacy services due to methodological complexities [63, 64]. All studies in this review fulfilled three criteria: (1) a well-defined objective; (2) the target group clearly stated; (3) the relevant costs and outcomes were identified. Transferability was found to be difficult to judge since the pharmacy intervention is specific to each country, and the resource inputs vary from one setting to another.

Strengths and weaknesses

This review synthesised global literature regarding the use of economic evaluation methods and covers pharmacy service in broader settings, distinguished from the previous ones which focused on one particular aspect: the cost-effectiveness of pharmacy service in the community setting [7] and clinical pharmacy service [58], while two other reviews focused on economic evaluation methodologies [63, 64].

This review has the strength that it gathered a large number of economic evaluation studies. The review does not include unpublished studies. Various databases and specific journals were searched; however, a few other databases were not included (e.g. NHS EED, CRD, EBSCO). This may lead to a few missing articles.

Interpretation and future research

There is an increasing trend to use economic evaluation for pharmacy services globally, this underlines its importance for policy-making decision. This also implies that it should be incorporated into developing future innovative pharmacy

Table 4 Characteristic of studies economically evaluated primary care pharmacy service (n = 3)

Author country	Method perspective	Intervention (I) Health issues (H)	Time-horizon	Discounting	Clinical outcome	Economic outcome	Interpretation
Kulchaitanaroaj et al. 2017 [15] US	CUA payer	I: Pharmacists collaborated with physicians on intervention and provided counselling concerning medications and lifestyle therapy to patients H: Hypertension	5, 10 years and lifetime	3% for costs and outcomes	n/a	The ICER of the physician–pharmacist collaborative intervention was US$ 26,807.83 per QALY gained. In shorter horizons of 5 and 10 years, the ratios were US$ 78,547.07 and US$ 39,084.65, respectively WTP threshold: US$ 50,000 per QALY	Cost-effective
Maurı´lio de Souza Cazarim and Pereira 2018 [40] Brazil	CEA healthcare	I: The pharmacist conducted monthly consultations for patients with hypertension (follow-up, blood pressure measurement, review medications, education) H: Hypertension	2 years	n/a	The pre-pharmaceutical care (PC) year and post-period years were more effective than conventional treatment	The ICER equated to US$ 478.41 and US$ 42.95 per patient's blood pressure controlled within the year, during pharmaceutical care, and in the post-period, respectively. Even with the highest ICER, the values were below the cost-effectiveness threshold, implying that PC was a cost-effective strategy WTP threshold: US$ 30,721.28 (3 times GDP per capita) per patient's blood pressure control in the year	Cost-effective
Mousa and Hammad 2021[56] Jordan	CEA provider	I: Pharmaceutical care services and therapy optimization from a trained clinical pharmacist in preventing cardiovascular diseases in diabetes H: Asthma/chronic obstructive pulmonary disease, hypertension, type 2 diabetes, anticoagulant/antiplatelet agent	1 and 10 years	4.75% for costs and outcomes	n/a	The pharmacist-led care resulted in an incremental cost of JD 1,238.78 (US$ 1,747.24) and incremental life years of 0.29 gained compared to the conventional care group WTP threshold: US$ 4,241.79 (JD 3,008.36; very cost-effective) to US$ 12,723 (JD 9,023.23; cost-effective) per health benefit	Cost-effective

95% CI: 95% Confidence interval, CBA: cost–benefit analysis, CEA: cost-effectiveness analysis, CMA: cost-minimization analysis, CUA: cost-utility analysis, ICER: Incremental cost-effectiveness ratio, QALY: Quality-adjusted life year, n/a: not applicable service models. However, performing economic evaluation is challenging due to its methodological complexities and lack of workforce in this area. Additionally, performing economic evaluation is specific to the context of each country. Similar interventions are used; nonetheless, the evaluation results may differ between countries.

Conclusion

The increased use of economic evaluation of pharmacy services confirms that pharmacy services can contribute economic impacts and improve patients' health outcomes in all settings: hospitals, community pharmacies, and primary care. Cost utility and cost-benefit analyses were found to be the common approaches used to assess pharmacy services. Economic evaluation underlines its importance for policy-making decisions and thus should be incorporated into developing innovative pharmacy services.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11096-023-01590-0.

Acknowledgements We thank Editage (www.editage.com) for English language editing.

Funding This research project was financially supported by the Mahasarakham University.

Conflicts of interest The authors have no conflicts of interest to declare.

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