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REVIEW ARTICLE

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Economic evidence for nonpharmacological asthma management interventions: A systematic review

C-J. Crossman-Barnes | A. Peel | R. Fong-Soe-Khioe | T. Sach | A. Wilson | G. Barton

Norwich Medical School, University of East Anglia, Norwich, UK

Correspondence
C-J. Crossman-Barnes, Faculty of Medicine and Health Sciences, Norwich Medical School, University of East Anglia, Norwich, UK.
Email: c.crossman-barnes@uea.ac.uk

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Abstract

Asthma management, education and environmental interventions have been reported as cost-effective in a previous review (*Pharm Pract* (*Granada*), 2014;12:493), but methods used to estimate costs and outcomes were not discussed in detail. This review updates the previous review by providing economic evidence on the cost-effectiveness of studies identified after 2012, and a detailed assessment of the methods used in all identified studies. Twelve databases were searched from 1990 to January 2016, and studies included economic evaluations, asthma subjects and nonpharmacological interventions written in English. Sixty-four studies were included. Of these, 15 were found in addition to the earlier review; 53% were rated fair in quality and 47% high. Education and self-management interventions were the most cost-effective, in line with the earlier review. Self-reporting was the most common method used to gather resource-use data, accompanied by bottom-up approaches to estimate costs. Main outcome measures were asthma-related hospitalizations (69%), quality of life (41%) and utility (38%), with AQLQ and the EQ-5D being the most common questionnaires measured prospectively at fixed time points. More rigorous costing methods are needed with a more common quality of life tool to aid greater replicability and comparability amongst asthma studies.

KEYWORDS
asthma, cost-effective, methodology, review

1 | INTRODUCTION

Asthma is a chronic lung disease, which affects over 300 million people worldwide.[1] Monitoring asthma through personalized asthma action plans (PAAPS), taking medication as prescribed, having self-awareness of potential triggers and attending regular asthma reviews are some of the ways to manage asthma.[2]

Much work has explored asthma pharmacological interventions, and fewer works have considered nonpharmacological.[3] It has been recognized that there needs to be clearer reporting of methods, outcome measures and all appropriate costs to improve generalizability and validity.[3,4] Previous reviews have been heavily focused on clinical interventions and their level of cost-effectiveness.[4-7] In order to ensure appropriate healthcare decisions are made, it is essential to understand what methodologies underpin these results.

Due to an earlier comprehensive review discussing enhanced asthma management interventions,[3] the objective of this review was to update and extend this work to include a more critical review about the methodologies used to estimate costs and outcomes. The update compares the cost-effectiveness of interventions from post-

2012 until January 2016, and the extension identifies, describes and assesses the array of methods used in estimating and evaluating both costs and outcomes for economic analyses from 1990 to January 2016. The protocol for this review was registered with PROSPERO International Prospective Register of Systematic Reviews with registration number: CRD42016032963.

2 | METHODS

2.1 | Eligibility criteria

2.1.1 | Study design

Original research articles were considered for inclusion. These were defined as an economic evaluation: cost-effectiveness analysis (CEA), cost utility analysis (CUA), cost benefit analysis (CBA) or a cost consequences analysis (CCA). Other types of economic studies were excluded, alongside letters, editorials, magazines, conference abstracts and reviews.

2.1.2 | Population

Participants with different severities of asthma of any age and from any country were included.

2.1.3 | Intervention and comparators

Nonpharmacological asthma interventions were included, such as educational, environmental or self-management interventions. Comparators of pharmacological, nonpharmacological or usual care alternatives were permitted.

2.1.4 | Outcomes

The primary outcomes were to identify the incremental cost-effectiveness ratios (ICERs) and net benefit results to compare the cost-effectiveness results in all studies found from the updated search. The secondary outcomes were to identify the effectiveness and monetary outcomes (eg, willingness to pay) to explore how they were evaluated across all included studies.

2.2 | Search strategy

A comprehensive database search was conducted (search terms; Appendix S1), including databases searched from Yong and Shafie[3] and additional databases to ensure all relevant databases were searched. The included databases searched are as follows: ScienceDirect, Wiley Online Library, EbscoHost, Embase (via OvidSP), Medline (via OvidSP) and Scopus, and additional databases: CINAHL (via EbscoHost), Cochrane (CENTRAL), NHS Economic Evaluation Database (NHS EED), ClinicalTrials.gov, ProQuest and Open Grey. The latter 3 databases were included to identify any unpublished literature. Truncation and phrase searching were used for an inclusive search and to retrieve papers that included the specific quoted phrases. All databases were restricted to the English language only with searches from 1990 until January 2016.

2.3 | Study selection

All studies retrieved from the database search were transferred into EndNote software manager, with duplicates removed. All titles and abstracts were independently screened for eligibility by 1 reviewer (CJCB) and then second reviewers (AP, RFSK). Full texts of included articles were assessed for eligibility, and if any uncertainties arose, then discussions between 2 reviewers occurred (CJCB, AP or CJCB, RFSK) with a third reviewer required if there were any discrepancies (RFSK, AP).

2.4 | Data extraction

Data were extracted from included studies into a predesigned table (Appendix S2) by 1 independent reviewer (CJCB) with second reviewers (AP, RFSK) confirming accuracy and discussing any discrepancies.

2.5 | Quality assessment

Two quality assessment checklists were used in this review: Quality of Health Economic Studies (QHES) (Appendix S3) adapted by Yong and Shafie,[3] but originally designed by Chiou et al,[8] and the Philips et al's[9] criteria for model-based studies. Quality assessment occurred independently by 1 reviewer (CJCB), with second reviewers (AP, RFSK) checking for accuracy and resolving any discrepancies through discussion.

3 | RESULTS

The extensive search retrieved 2118 studies. After duplicates were removed (287), a further 1715 studies were excluded from the title and abstract screening. After reviewing the full texts of the remaining studies, 64 studies were included for analysis (Figure 1). Of the 64, 15 studies were found in addition to Yong and Shafie.[3]

3.1 | Characteristics of the 15 additional papers

Table 1 describes the characteristics of the included studies found in addition to Yong and Shafie.[3]

3.1.1 | Study design

There were 5 CEA,[10-14] 1 CUA,[15] 4 CBA[16-19] and 5 CCA[20-24] studies included. Of these, 7 were randomized control trials,[11,14,15,18,21,22,24] 3 before and after studies,[12,20,23] 2 model-based studies,[13,17] 2 cohort studies[16,19] and 1 quasiexperimental study.[10]

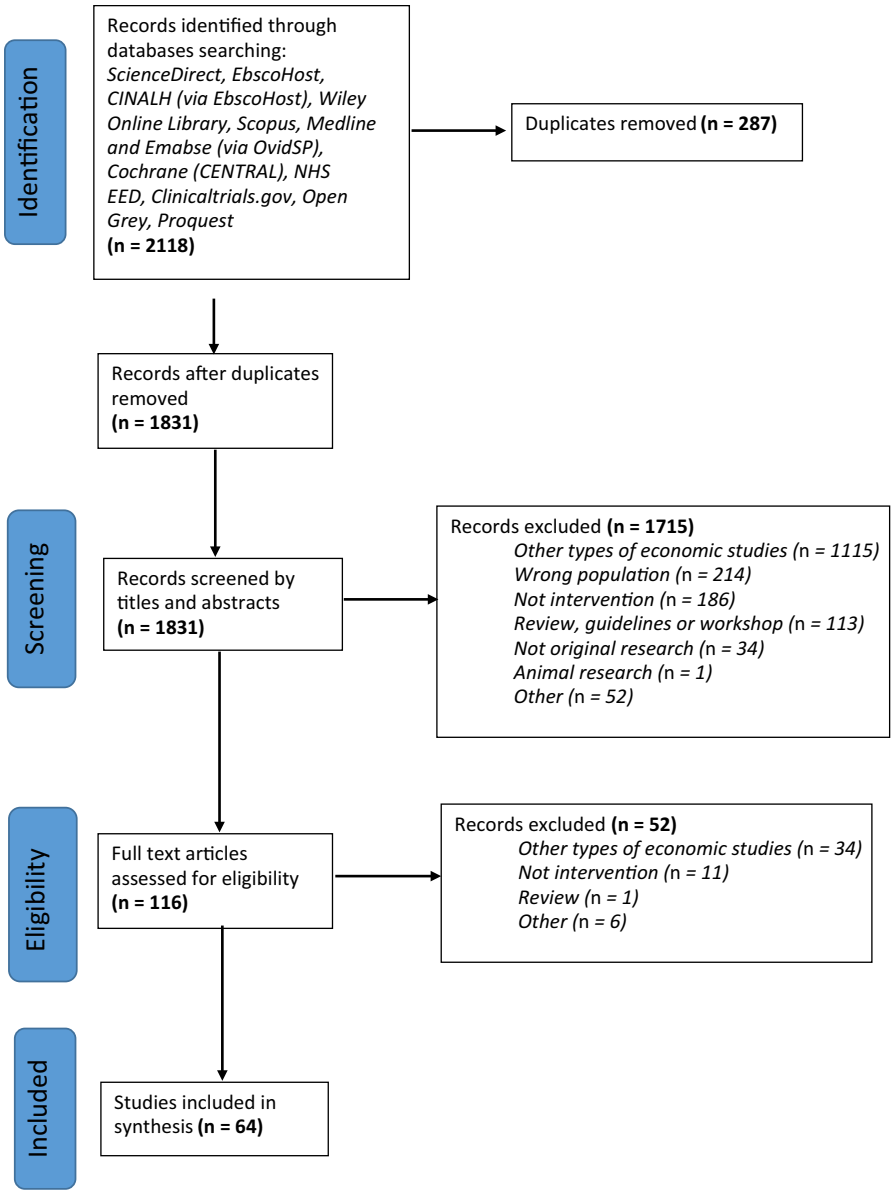

FIGURE 1 PRISMA flow diagram

3.1.2 | Population

Population groups chosen were mostly children-focused[10-12,16-20,22,23] with 1 adult-only study,[21] and combination of the 2.[13-15,24] Only 7 studies[12,14,16,18,20,21,23] stated the ethnic background of the populations chosen, with 5 of those representing a mixed ethnic population.[16,18,20,21,23]

3.1.3 | Interventions

Interventions compared were mainly educational based provided by school, health professionals or environmental assessors;[10-12,15,16,18,20,21,23] asthma management based using applications and/or at-risk registers;[13,14,19,22,24] and environmental based.[17]

3.1.4 | Perspective and time horizon

Study cost perspectives included societal,[10,15,16,19] governmental,[17] health care[13-15,24] and individual payer[18] with the remaining studies not stating their perspective.[11,12,20-23] Time horizons varied with 1 study having 3 months,[10] 2 studies having 6 months,[14,21] 7 studies having 1 year,[11-13,15,20,23,24] 3 studies ranging between 2 and 4 years[16,18,22] and 1 study having 10 years.[17]

3.2 | Cost-effectiveness of 15 additional papers

Two studies were dominant (the intervention was less costly and more effective) compared to the comparator,[11,12] and both had time horizons of 1 year. Two of 5 of the CEA studies were cost-effective (the ICER was lower than the stated willingness to pay threshold)[10,13] and had varied time horizons (3 months and 1 year, respectively), perspectives (societal and health care, respectively) and thresholds. The stated threshold for Atherly et al[10] was AUS $50 000/DALY, whereas Mogasale and Vos[13] did not state the willingness to pay threshold. One of the CEA studies was not cost-effective.[14] The only CUA study[15] presented with a cost-effective ICER and had a time horizon of 1 year based on a

TABLE 1 Characteristics of the 15 additional studies

First author, year, country of population	Study design (type of economic evaluation)	Patient population group	Description of intervention & comparator(s)	Intervention participants (No., mean age, gender [%], ethnicity [%])	Comparator participants (No., mean age, gender [%], ethnicity [%])	Study cost perspective, time horizon, discount rate	Currency & price year	Statistical analysis, sensitivity analysis	ICER or Net benefit/Net present value
Atherly et al, 2009, United States[10]	Prospective quasiexperimental (CEA)	524 asthma adolescents from middle and high schools	Int: power breathing education programme Com: no education programme	No. 225 Mean age: 13.90 Male: 54.4% Female: 46.6% Ethnicity: not stated	No. 233 Mean age: 13.40 Male: 49.3% Female: 50.7% Ethnicity: not stated	Societal 3 months Not Applicable	US ($) 2003-2004	Mean comparisons; ordinary least-squares regression analysis; *t* test. Not stated	$3.90 per symptom-free day gained
Bhaumik et al, 2013, United States[16]	Prospective cohort (CBA)	661 people hospitalized or had asthma-related emergency department (ED) visits from 4 low-income urban zip codes in Boston	Int: received services provided by the community asthma initiative (CAI). Com: did not receive services provided by CAI	No. 102 Mean age: 7.90 Male: 53.9% Female: 46.1% White: 6.9% African American: 41.2% Hispanic/Latino: 46.1% Asian/Pacific Islander/ Native American: 5.9%	No. 559 Mean age: 7.1 Male: 59.8% Female: 40.2% White: 4.1% African American: 59.2% Hispanic/ Latino: 34.6% Asian/Pacific Islander/ Native American: 2%	Societal 3 years 10%	US ($) 2006	χ^2 test; Paired & unpaired *t* tests; Multivariate regression analysis. Not stated	Net present value: Adjusted cost savings for year 1 = $111 588, year 2 = $16 365, year 3 = $83 863
Castro et al, 2003, United States[21]	Prospective RCT (CCA)	96 asthma hospital patients	Int: daily "asthma care" flow sheet, asthma education, self-management plan and consultations. Com: normal care	No. 50 Mean age: 35.00 Male: 20% Female: 80% African American: 86% Non-African American: 24%	No. 46 Mean age: 38 Male: 15% Female: 85% African American: 78%, none African American: 22%	Not stated 6 months Not applicable	US ($) 1999	*T* tests and χ^2 tests Wilcoxon's test; logistic regression; log-rank test Not stated	Not applicable Mean cost: Int = $5726; Con = $12 188 Mean change in AQLQ: Int = 1.4, Con = 1.2
Fabian et al, 2014, United States[17]	Prospective Model (CBA)	1 million children living in low-income multifamily housing	7 interventions: fix/operate kitchen and bathroom exhaust fans; replace gas stoves with electric ovens; eliminate the use of stove for heating by fixing the heating system; smoke-free housing policy; use of HEPA filters; integrated pest management; weatherization.	Not stated	Not stated	Government 10 years Not stated	US ($) 2009	Probabilistic model.	Not stated
Flores et al, 2009, United States[11]	Prospective RCT (CEA)	220 African American and Latino asthmatic children enrolled from 4 hospitals	Int: parent mentors provided education, meals and social interaction monthly sessions Com: traditional asthma care	No. 112 Mean age: 7.10 Male: 59.8% Female: 40.2% Ethnicity: not stated	No. 108 Mean age: 7.3 Male: 52.8% Female: 47.2% Ethnicity: not stated	Not stated 12 months Not applicable	US ($) Not stated	Wilcoxon's tests; Fisher's exact test; logarithmic regression. Not stated.	Dominant
Higgins et al, 1998, United States[20]	Prospective before & after (CCA)	61 paediatric asthma patients without a primary care provider identified during an acute asthma exacerbation	Int: patients assigned a primary care provider and parents of patients had five 1-h asthma education sessions.	No. 61 Mean age: 8.40 Male: 67.2% Female: 32.8% Caucasian: 50.9% African American: 38.6% Asian: 4.0% Hispanic: 2.0% (4 patients did not state their race)	Not applicable	Not stated 12 months Not applicable	US ($) 1997	Paired *t* test. Not stated.	Not applicable Intervention savings on resource use = $4845.29 Mean monthly hospital admissions: before = 0.149, after = 0.007

(Continues)

TABLE 1 (Continued)

First author, year, country of population	Study design (type of economic evaluation)	Patient population group	Description of intervention & comparator(s)	Intervention participants (No., mean age, gender [%], ethnicity [%])	Comparator participants (No., mean age, gender [%], ethnicity [%])	Study cost perspective, time horizon, discount rate	Currency & price year	Statistical analysis, sensitivity analysis	ICER or Net benefit/Net present value
Karnick et al, 2007, United States[18]	Prospective RCT (CBA)	212 children recruited from ED, inpatient units, and from referrals to paediatric pulmonologist for consultation	Three interventions. 1) 20- to 30-min asthma education group sessions with referrals to GP if needed. 2) Reinforced education group: same as group 1 plus further education through phone calls (minimum monthly calls) 3) Case management and reinforced education group	1) No. 74 Mean age: 5.54 Male: 55% Female: 45% Non-Hispanic Black: 70% Hispanic: 30% 2) No. 68 Mean age: 5.13 Male: 66% Female: 34% Non-Hispanic Black: 65% Hispanic: 35% 3) No. 70 Mean age: 5.71 Male: 59% Female: 41% Non-Hispanic Black: 64% Hispanic: 34% Other: 1%	Not Applicable	Payer 1 year retrospectively & 9 months prospectively Not stated	US ($) 1998	χ^2 or Fisher's test; ANOVA; paired *t* test. Not stated.	Not stated
Lara et al, 2013, Caribbean[12]	Prospective before & after (CEA)	145 children with moderate to severe asthma from local healthcare clinics	Int: *La red*—combined clinic and home-based intervention adapted from Yes We Can program and Inner-City Asthma Study	No. 145 Mean age: 5.00 Male: 61.4% Female: 38.6% Hispanic/Puerto Rican: 100%	Not applicable	Not stated 12 months Not applicable	US ($) 2009	Monte Carlo simulation.	Dominant
McCowan et al, 1997, United Kingdom[22]	Prospective RCT (CCA)	2557 children with diagnosed asthma	Int: individuals identified by GP practice had clinical review and has guidelines for diagnosis & management of asthma in records. Com: standard medical care	No. 1288 Mean age: 7.67 Male: 55.4% Female: 44.6% Ethnicity: not stated	No. 1269 Mean age: 7.8 Male: 59.6% Female: 40.4% Ethnicity: not stated	Not stated 4 years Not stated	GBP (£) 1991	Not stated. Not stated.	Not applicable Year 1: Int = £68 500 Con = £57 780. Year 2: Int = £62 300 Con = £53 910. Year 3: Int = £45 700 Con = £45 280. Year 4: Int = £43 550 Con = £44 960 No. of children with hospital admissions: Year 1: Int = 33 Con = 18. Year 2: Int = 24, Con = 25. Year 3: Int = 11, Con = 12. Year 4: Int = 9 Con = 14

(Continues)

TABLE 1 (Continued)

First author, year, country of population	Study design (type of economic evaluation)	Patient population group	Description of intervention & comparator(s)	Intervention participants (No., mean age, gender [%], ethnicity [%])	Comparator participants (No., mean age, gender [%], ethnicity [%])	Study cost perspective, time horizon, discount rate	Currency & price year	Statistical analysis, sensitivity analysis	ICER or Net benefit/Net present value
Mogasale et al, 2013, Australia[13]	Prospective Model (CEA)	Asthma patients	Int: asthma clinical approach. Com: current practice of asthma management	Not stated	Not stated	Health care 1 year 3%	AUS ($) 2003	Three Monte Carlo simulation scenarios: (1) assumed intervention only; (2) assumed interventions reduced ED visits and days off work; (3) assumed intervention reduced ED visits, unscheduled GP visits, hospitalization and days off work	Without time and travel costs: Scenario 2 = $24 000 and Scenario 3 = $17 000. With time and travel costs: Scenario 2 = $30 000 and Scenario 3 = $20 000
Ryan et al, 2012, United Kingdom[14]	Prospective RCT (CEA)	288 adolescents and adults with poorly controlled asthma from 32 practices. Prior to randomization, 30-min educational training was given.	Int: mobile phone-based monitoring using an asthma application. Com: standard paper-based monitoring	No. 145 Mean age: 46.60 Male: 34% Female: 66% White: 97% Non-White: 3%	No. 143 Mean age: 51.50 Male: 41% Female: 59% White: 99% Non-White: 1%	National Health Service 6 months Not applicable	GBP (£) Not stated	*T* test; Mann-Whitney test; ANOVA. Per-protocol sensitivity analysis including patients who completed all questionnaires at all time points.	Not stated
Smith et al, 2012, United Kingdom[24]	Prospective RCT (CCA)	911 at-risk asthma patients with severe exacerbations recruited from 29 primary care practices	Int: electronic alerts on computerized records at GP practices to flag at-risk asthma patients with training provided to staff. Com: usual care	No. 14 practices, 457 patients Mean age: 46.40 Male: 37.2% Female: 62.8% Ethnicity: not stated	No. 15 practices, 454 patients Mean age: 44.60 Male: 40.2% Female: 59.8% Ethnicity: not stated	National Health Service 1 year Not applicable	GBP (£) 2007-2008	Odds ratios; Mann-Whitney test; ICCs; random-effects negative-binomial models producing rate ratios. Not stated	Not applicable Mean change in annual level of resource use: Int = £60.23 and Con = £149.14 Moderate-severe asthma exacerbation: Int = 53.6% and Con = 46.5%
Tai et al, 2011, United States[19]	Prospective cohort (CBA)	School children with asthma	Int: school-based health clinics nationwide including disease management and self-care monitoring skills Com: Traditional medical services	Not stated	Not stated	Societal Not stated 3%	US ($) 2006	Not stated. Not stated.	Not stated
Turcotte et al, 2014, United States[23]	Prospective before & after (CCA)	170 children recruited in Massachusetts with a diagnosis of asthma.	Int: environmental assessor walked through homes to assess the presence of triggers with visits ranging from 4 to 9 times during the year.	No. 170 Mean age: 6.08 Male: 59% Female: 41% Black: 5%, White: 12%. Asian: 15%, Hispanic: 53%, Other: 15%	Not applicable	Not stated 1 year Not applicable	US ($) Not stated	Wilcoxon's rank-sum test. Not stated	Not applicable Net savings from intervention: 4 week = $38 522; 6 months = $394 332 and 12 months = $821 304 Decrease in occurrence: hospitalization = 8, emergency department = 29, doctor visit = 76

(Continues)

TABLE 1 (Continued)

First author, year, country of population	Study design (type of economic evaluation)	Patient population group	Description of intervention & comparator(s)	Intervention participants (No., mean age, gender [%], ethnicity [%])	Comparator participants (No., mean age, gender [%], ethnicity [%])	Study cost perspective, time horizon, discount rate	Currency & price year	Statistical analysis, sensitivity analysis	ICER or Net benefit/Net present value
Willems et al, 2007, Netherlands[15]	Prospective RCT (CUA)	Asthma outpatients with severity stages I to III from the GINA guidelines.	Int: nurse-led telemonitoring—portable asthma monitor at home for spirometry Com: regular outpatient care: stable asthma—3-6 monthly check-ups; exacerbations—additional GP or outpatient care.	No. adults (26) Children (29) Mean age: adults (45.65), children (10.57) Male: adults (42.3%), children (72.4%) Female: adults (57.7%), children (27.6%) Ethnicity: not stated	No. adults, (27) children (27) Mean age: adults (45.90), children (10.85) Male: adults (33.3%), children (55.6%) Female: adults (66.7%), children (44.4%) Ethnicity: not stated	Health care & societal 1 year Not applicable	Euro (€) 2002	Bootstrap simulation; ANCOVA. One-way sensitivity analysis testing 2 cost components.	Healthcare perspective = €15 366/QALY gained. Societal perspective = €31 035/QALY gained.

ANCOVA, analysis of covariance; ANOVA, analysis of variance; AQLQ, Asthma Quality of Life Questionnaire; AUS, Australian; CBA, cost benefit analysis; CCA, cost consequences analysis; CEA, cost-effectiveness analysis; Com., comparator; CUA, cost utility analysis; ED, emergency department; GBP, Great British Pound; GINA, Global Initiative for Asthma; GP, general practitioner; HEPA, high-efficiency particulate air; ICCs, intracluster correlation coefficient; ICER, incremental cost-effectiveness ratio; Int., intervention; No., number; QALY, quality-adjusted life year; RCT, randomized control trial; US, United States.

societal and healthcare perspective separately. Only 1 CBA study[16] of 4 CBA studies produced positive net present values for the adjusted cost savings for years 1, 2 and 3, meaning that the benefits outweighed the costs and the intervention should be implemented. The remaining CCA studies[20-24] did not present with an ICER value and therefore were not compared for cost-effectiveness; however where available, the cost and outcome results are detailed in Table 1.

3.3 | Quality assessment for the 15 additional papers

The QHES checklist score varied across the 15 additional studies found (Table 2). Eight studies scored within the range of fair quality (50%-74%).[10,12,17,19-23] The remaining 7 studies[11,13-16,18,24] scored within the range of high quality (>74%). Two studies were model based, and Fabian et al[17] provided a sound quality for the majority of the assessment categories in the Phillips criteria; however, a reference to cycle length, internal consistency or methodological, structural and heterogeneity uncertainty was not mentioned. Mogasale and Vos[13] also provided a good quality assessment overall, but were lacking in areas considering cycle length and uncertainties.

3.4 | Methods used to estimate and value costs across all 64 papers

Multiple methods were used to gather resource-use data across the included studies; however, not all studies reported the associated unit cost for the resource use (Appendix S4). The most commonly reported items of resource use were asthma-related hospitalizations (72%) and emergency department visits (70%), with physician visits (58%), other healthcare professional visits (28%), lost productivity (38%) and medication use (44%) also collected.

Data were mostly gathered from medical or computerized records (19%) for hospital-related costs,[14,21,24-35] wage rates by employers or case managers for productivity loss (22%)[11,13,15,16,19,26,29,30,33,36-40] and by patient or parent self-reported data (80%) for productivity loss and quality of life.[11,15,21,26,29,30,32,33,41-45] Claims, billing or reimbursement data (25%) were often used for those countries who operate on healthcare insurance systems to also capture hospital-related costs.[15,17,35-37,44,46-50] Costing manuals for health care were mostly used to gather the unit costs of resources amongst the papers, such as the Dutch Drug Compendium, 2000, and the Dutch Manual for Costing in Economic Evaluations[51] and the Pharmacy price listing.[20]

The methods used to estimate the intervention components' resource use were not always clearly stated, with all of the necessary individual components needed to form the successful running of the intervention and the costing behind this, not often reported. Staff costs, programme materials and training were the most commonly reported intervention component costs; however, only some studies stated the unit costs of the components[11,15,29,30,38,39,43,44,49,50,52-56] (Appendix S4). Only a select few papers took into account any associated travel costs involved in the intervention,[29,30,37,38,50,55] and some

studies reimbursed participants for taking part in their research.[10,11,23,35,55] Likewise, with estimating the wider health resource use, some papers were more detailed with the microcosting of the intervention component (of which was summed) than others (Appendix S6 and Appendix S7). The bottom-up approach (individual's healthcare service use aggregated) (78%) was generally a more popular method used to estimate and value the resource-use costs including most of the intervention component costs, as opposed to the top-down approach (total healthcare service costs divided by activity days).[18-20,25,31,32,36,41,57-61] Methods used to estimate productivity loss also varied between the human capital approach (each hour lost at work per patient),[30,40,43] the friction cost method (each hour lost at work until the employer replaces the patient who is unable to work)[15,33] or using the caregivers income multiplied by the mid-point of the family's income.[11]

3.5 | Methods used to estimate and value outcomes (1990 to January 2012)

The outcomes measured varied widely, across all included studies, with multiple data collection methods often used within each study (Appendix S5). The hospital visits and emergency department visits were the most frequently stated resource use, and they were also the most common type of outcomes measured. Over two-thirds identified the emergency department visits or hospitalizations (46 papers or 45 papers, respectively), followed by approximately one-third investigating quality of life and physician (GP) visits (26 papers and 29 papers, respectively). Other papers reported a wide range of other outcomes, including intensive care admissions,[23,28,32,58] frequency of exacerbations and symptoms,[11,14,22,62,63] asthma knowledge,[10,39,48,60] peak expiratory flow (PEF),[30,38,42,48,54,58,63-67] forced expiratory volume,[15,26,30,31,37,42,43,54,58,64-66] forced vital capacity (FVC)[15,30,31,37,42,54,58,64-66] and medications.[18,30,39,47,50,58,68,69] A PEF meter was used to estimate the PEF, a spirometry was used to estimate the forced expiratory volume in one second and FVC, and histamine was used to estimate airway responsiveness.

A wide selection of health questionnaires were used to collect data in the studies (Figure 2), mostly by patient self-report, but often in conjunction with face-to-face visits[12,14,37,39,40,51,58,64-66,70] or telephone interview sessions.[11,13,18,25,36,44,50,53,57,60,62,69-71] Other options of completing questionnaire data were by proxy, that is, parent-reported questionnaires,[12,42,55,70] caregivers' questionnaires[40] or case managers' self-reported questionnaires.[16,56]

The disease-specific questionnaires—Asthma Quality of Life Questionnaire (AQLQ)[15,21,34,43,48,58] and the St. George's Respiratory Questionnaire (SGRQ)[31,37,64-66]—and the generic questionnaires—EuroQol-5 Dimensions (EQ-5D)[15,29,33,42] and 15 Dimensions (15D)[64-67]—were the most commonly used. The studies that used the EQ-5D and Short Form-6 Dimension (SF-6D)[15] converted the scores into utility values and used these to estimate quality-adjusted life years (QALYs). Other studies that did not estimate QALYs used total and/or overall mean scores from the health questionnaires in their analysis.

4 | DISCUSSION

This systematic review updated and extended a previous study that evaluated the cost-effectiveness of nonpharmacological asthma interventions with databases searched from 1990 until 2012.[3] The extension included extending this database search until January 2016, and the update included an assessment of the methods used to estimate both costs and outcomes in all studies found from 1990 until 2016.

4.1 | Main findings

In line with the findings from Yong and Shafie,[3] the additional education and self-management study-based interventions found in this review were deemed most cost-effective or dominant. The quality of studies has since improved with the additional studies presenting with fair (50%-74%) to high (>74%) quality. Multiple methods were often used to gather resource-use data with self-report being the most common, the bottom-up approach being the most common estimation method of resource use gathered, and health-related questionnaires being a common outcome measure with AQLQ and EQ-5D being the most common HRQOL questionnaires.

4.2 | Comparison with other studies

Earlier systematic reviews of asthma interventions also highlighted the importance of the quality assessment in studies.[5,6,72,73] One study, in particular, believed their peak flow monitoring intervention was cost-effective, but could not conclude this due to the study qualities being so low.[72] This review shows that the quality of studies has much improved since then, with nearly 50% of the studies found post-2012 presenting with high quality.

Although improvement has been noticed in the quality of the studies, some still have an inadequate follow-up, which can reduce validity and generalizability.[74] It was previously acknowledged that a short time horizon was inadequate for chronic conditions,[6] with a time horizon of 3 months or less considered to be unacceptable.[4] The additional studies found in this review presented with 1 study having a time horizon of 3 months,[10] and others longer at between 6 months and 10 years.

As different cost perspectives are used amongst the included studies in this review, it becomes difficult to compare the total costs associated with each intervention. An earlier review noted that the author's definitions of direct medical costs, direct nonmedical costs and indirect costs sometimes varied, where costs assigned to direct nonmedical costs should have been assigned to indirect costs.[72] Previous literature discusses that a societal perspective is important to synthesize the evidence and gain a proper understanding on peak flow monitoring interventions.[72,75,76] However, perspectives chosen can differ from country to country and the definitions of a societal perspective can also vary.

It was surprising that only about a quarter of papers included lost productivity as an outcome measure. Due to asthma being a

TABLE 2 Quality assessment scores using QHES checklist for the 15 additional studies

QHES criteria no.[a]	Atherly et al (2009)[10]	Bhaumik et al (2013)[16]	Castro et al (2003)[21]	Fabian et al (2014)[17]	Flores et al (2009)[11]	Higgins et al (1998)[20]	Karnick et al (2007)[18]	Lara et al (2013)[12]	McCowan et al (1997)[22]	Mogasale et al (2013)[13]	Ryan et al (2012)[14]	Smith et al (2012)[24]	Tai et al (2011)[19]	Turcotte et al (2014)[23]	Willems et al (2007)[15]
1	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
2	2	4	0	4	0	0	4	0	0	2	2	2	2	0	2
3	8	6	8	4	8	6	8	6	8	8	8	8	6	6	8
4	0	0	0	1	0	0	1	0	0	0	0	0	0	0	1
5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	0	9	9	4.5	0	4.5	9
6	6	6	0	0	6	0	0	0	0	6	0	6	0	0	6
7	5	5	5	0	5	5	5	5	0	5	5	5	5	5	5
8	7	7	0	5	7	7	7	7	0	0	7	7	0	7	7
9	6	6	2	6	8	8	8	6	8	8	6	6	8	8	8
10	6	6	4	0	6	4	4	6	4	0	4	6	0	4	4
11	0	7	7	0	7	7	7	7	7	7	0	7	0	7	7
12	4	8	8	4.5	4	8	8	5	2	8	8	8	2	4	8
13	3.5	7	3.5	7	3.5	3.5	3.5	3.5	3.5	7	7	7	7	7	3.5
14	0	6	6	0	0	6	6	3	0	0	3	0	6	0	6
15	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
16	0	3	3	3	3	0	3	3	3	3	3	3	0	3	0
Total	67	90.5	66	54	77	74	84	71	50.5	78	77	84.5	51	70.5	89.5

[a]Full table of criteria and scoring system can be found in Appendix S3.

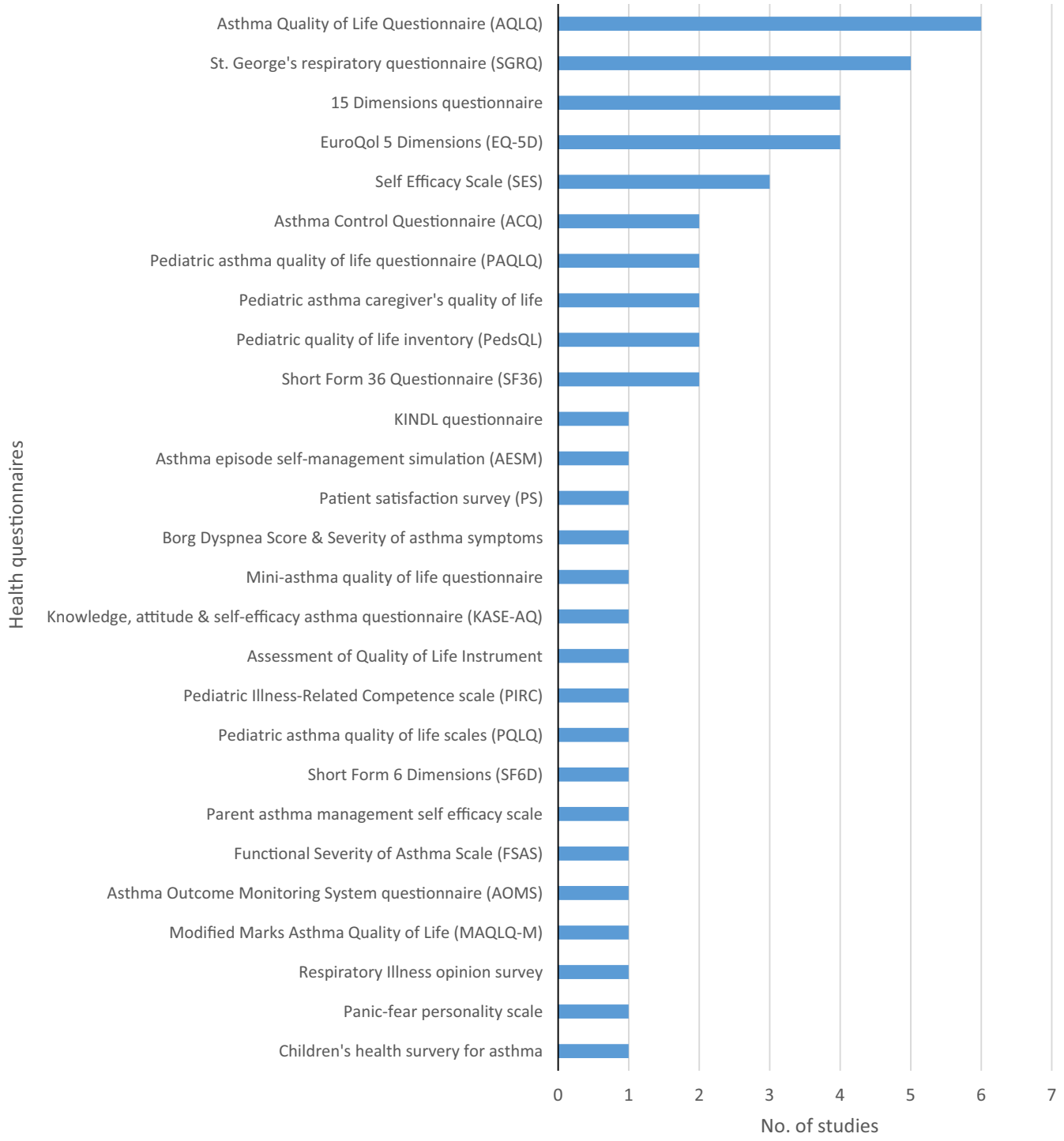

FIGURE 2 Different health questionnaires used in studies

chronic condition, it is thought that more papers would have discussed lost productivity, and the possible implications that this may have on presenteeism and/or absenteeism. With patients who have asthma exacerbations often not well enough to continue at work or with their usual activities, it is important to include nonmedical resource use and productivity costs in studies.[77]

In all of the included studies in this review, the intervention details were often reported, but the details surrounding the costs of conducting the interventions with the associated unit costs were limited. Three studies provided comprehensive details about how they estimated the intervention, including the breakdown of the intervention components, their associated unit costs and the methods chosen to estimate such costs.[15,29,55] The common approach between all 3 was a microcosting approach. Difficulties can sometimes occur with this approach when prices for certain resources are not always available from various data sources, leaving room for customization.[78]

From the 26 studies that also incorporated quality of life as an outcome measure, there were over 20 different questionnaires that were used to measure this. Many of the questionnaires used to analyse quality of life were more specific to asthma, but there did not appear to be a preferred measure that was used across the studies. The EQ-5D-3L questionnaire (5 dimensions with 3 levels: no problems, moderate problems and extreme problems) was used across a number of studies, but often used alone and not in conjunction with another quality of life questionnaire. As discussed by Yong and Shafie,[3] EQ-5D-3L might not be the best tool to use for quality of life in asthma, as it is not seen as sensitive enough to detect differences in HRQOL particularly in people with mild asthma. However, there have been recent developments of a new EQ-5D-5L questionnaire, which includes the same 5 dimensions but with 5 levels: no problems, slight problems, moderate problems, severe problems or extreme problems.[79] The newly developed EQ-5D-5L tool may be more suitable as it was designed to be more sensitive and reduce the high ceiling effects. This has been confirmed in several studies that have shown increased reliabilities, sensitivities and validities.[79,80]

4.3 | Recommendations for future

In the light of the above, there are many areas for which focus is required when conducting an asthma study. The main recommendations are to use time horizons greater than 3 months to ensure adequate follow-up, to include all relevant costs and benefits that have been accounted for as asthma is a chronic condition (particularly the high cost drivers[77]), and to conduct a microcosting approach where possible. For economic evaluations where QALYs are estimated, the EQ-5D-5L can be used as a generic measure. However, even though this has been proven in earlier studies to show positive results in terms of increased sensitivities and validities compared to the EQ-5D-3L, due to it being a relatively new questionnaire, it may be advisable to use this in conjunction with a more established disease-specific questionnaire. Due to the difficulties that arise in economic evaluations and to ensure the comparability across different countries and decision-makers,[81] it may be useful to adhere to an international reference case, which is a useful guide from the planning stages of research through to reporting findings and completion. Future research should also ensure that the appropriate guidelines and checklists are adhered to, such as the TiDieR checklist,[82] the CHEERS statement,[83] CONSORT statement[84] and the COMET initiative[85] for ease of replicability of both the intervention and control groups by clinicians or researchers looking to implement or expand research ideas, respectively. This will in turn aid the comparability of studies.

4.4 | Strengths and limitations

The strength of this review is that it provides a comprehensive synthesis of studies from an extensive database search with studies analysed from 12 databases. The included studies help to understand how asthma interventions and methodologies chosen have evolved over the years, with discussions leading to recommendations for future practice. Bias has been reduced during this review by including 2 independent reviewers during the systematic review process. However, a limitation of this review is that only English language studies were included, with restrictions of this placed during the database search. Therefore, we are unable to acknowledge how many non-English studies have been excluded from this review, but it is apparent that due to this selection bias, additional studies may have been relevant for inclusion in this review.

5 | CONCLUSIONS

The additional 15 studies identified were of fair to high quality. Most of the additional studies found had dominant or cost-effective interventions that were educational or management based, which mirrored the previous review. The methods used to estimate costs and outcomes varied, with the bottom-up approach being the most common approach; however, the reporting of unit costs was lacking amongst some studies, with only a few studies providing detailed microcosting methodologies for the intervention components. For future studies, a thorough description of methods used in all components of the study is needed, including reporting of unit costs and a common quality of life measure to provide more comparability.

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AUTHOR CONTRIBUTIONS

CJCB, TS, AW and GB were involved in the design of the study from conception. CJCB, AP and RFSK participated in the systematic process of screening the titles, abstracts and full texts of articles based on the eligibility criteria. CJCB, AP and RFSK also contributed to the data extraction and quality assessment stages. CJCB drafted the manuscript, with all authors providing critical revisions and final approvals.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

ORCID

C-J. Crossman-Barnes http://orcid.org/0000-0002-2536-7621

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