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Cost-utility analyses of interventions for informal carers: A systematic and critical review

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Abstract

Background Demographic and epidemiological changes place an increasing reliance on informal carers. Some support programmes exist, but funding is often limited. There is a need for economic evaluation of interventions for carers to assist policymakers in prioritising carer support.

Objective To systematically review and critically appraise cost-utility analyses of interventions for informal carers, in order to assess the methods employed and the quality of the reporting.

Methods A systematic review of databases was conducted using MEDLINE, EMBASE, PsycInfo, and Econlit of items published between 1950 and February 2019. Published studies were selected if they involved a cost-utility analysis of an intervention mainly or jointly targeting informal carers. The reporting quality of economic analyses was evaluated using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement.

Results An initial set of 1,364 potentially relevant studies was identified. The titles and the abstracts were then screened, resulting in the identification of 62 full-text articles that warranted further assessment of their eligibility. Of these, 20 economic evaluations of informal carer interventions met the inclusion criteria. The main geographical area was the UK (N = 11). These studies were conducted in mental and/or behavioural (N = 15), cardiovascular (N = 3), or cancer (N = 2) clinical fields. These cost-utility analyses were based on randomized clinical trials (N = 16) and on observational studies (N = 4), of which only one

presented a Markov model-based economic evaluation. Four of the six psychological interventions were deemed to be cost-effective versus two of the four education/support interventions, and four of the nine training/support interventions. Two articles achieved a CHEERS score of 100% and nine of the economic evaluations achieved a score of 85% in terms of the CHEERS criteria for high-quality economic studies.

Conclusions Our critical review highlights the lack of cost-utility analyses of interventions to support informal carers. However, it also shows the relative prominence of good reporting practices in these analyses that other studies might be able to build on.

Key Points for Decision Makers

Only 20 published cost-utility analyses of carer-focused interventions were identified in the literature.

The main types of interventions were psychological, training/support, and educational/support interventions, with mixed evidence regarding the cost-effectiveness.

Most of the studies adopted a societal perspective, but there were differences in terms of what costs and outcomes were included.

The reporting quality of the studies was generally quite good and there appeared to be a tendency whereby the studies with better reporting deemed the intervention to be not cost-effective.

1 Introduction

The demographic and social changes associated with aging of the population and the increasing incidence of chronic diseases underscore the important role of informal carers [1–3]. Eurocarers defines a carer as “a person who provides – usually – unpaid care to someone with a chronic illness, disability or other long-lasting health or care need, outside a professional or formal framework.”¹ Therefore, carers have a ubiquitous and very substantial presence throughout the world. The International Alliance of Carer Organizations (IACO) estimates the number of informal carers to be approximately 43.5 million in the USA (2015) and 8.1 million in Canada (2012)². The estimates presented in the Eurocarers 2019 publication³ are 5.5 million informal carers in the UK (2011), 3.2 million in Germany, 4 million in Italy, and 8.3 million in France (2008). Furthermore, as a result of significant changes in how people with disabilities around the world are cared for, informal carers play an increasingly important role in the activities of daily living of their loved ones [4,5]. There is evidence suggesting that when carers experience challenges in end-of-life care, hospital admission becomes more likely [6]. Due to the prominence of informal carer, the time spent on care provision in household tasks and on activities of daily living may have a substantial influence on economic evaluations [7–12].

Many varieties of interventions have been developed that are aimed at providing support to carers or to family carers/members. Some studies have tended to focus on a particular type of support intervention, such as psychosocial interventions [13–21], education and training, support [13,22–27], respite care [24,28–30], or patient-focused and multicomponent interventions [31–34]. Although some support interventions for informal carers have been reported to reduce the burden of informal care provision [26], there is a need for further documentation of the value-for-money of these interventions. Furthermore, patient intervention may also affect the lives of family carers. Notably, most economic evaluations of patient interventions typically fail to include the spillover impact on carers and/or family [35–37].

¹ <https://eurocarers.org/>

² <https://internationalcarers.org/carers-facts/global-carer-stats/>

³ <https://eurocarers.org/download/6372/>

The purpose of this study was to identify Cost-Utility Analyses (CUAs) of interventions for carers by means of a systematic review of the literature and to perform a critical appraisal using the CHEERS instrument checklist in order to assess the methods employed and the quality of the reporting of published CUAs.

2 Methods

The systematic review of published economic evaluations was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines [38].

2.1. Research strategy

We searched the literature for pertinent articles published between 1950 and February 2019, using the following list of electronic databases and search engines: health- or medical-related databases (MEDLINE, EMBASE, PsycInfo) and an economics database (Econlit). The search process consisted of combinations of four categories of potential identifying keywords using Boolean operators (e.g. “AND”/ “OR”). We searched for additional records using Google Scholar and the Global Health Cost-Effectiveness Analysis (GH CEA) Registry (the Center for the Evaluation of Value and Risk in Health (CEVR), Tufts Medical Center).

A list of keywords was generated based on items in the existing literature [28,33]. The keywords selected for the search strategy are listed in Table 1 according to the study design, the targeted population, the supportive interventions, and the health outcomes.

Table 1: The keywords used in the search

Study design keywords	Population keywords	Support program keywords	Health outcome keywords
<i>Economic evaluation</i>	<i>Caregiver*</i>	<i>Support</i>	<i>QALY</i>
<i>Cost-effectiveness</i>	<i>Informal care</i>	<i>Program*</i>	<i>Quality-adjusted life</i>
<i>Cost-benefit analysis</i>	<i>Carer</i>	<i>Intervention</i>	<i>years</i>
<i>Cost-utility analysis</i>	<i>Caregiving</i>	<i>Respite care</i>	<i>EQ-5D</i>
<i>Health economics</i>	<i>Family</i>	<i>Education</i>	<i>DALY</i>
	<i>Family member</i>	<i>Training</i>	
	<i>Relatives</i>	<i>Psychology</i>	

* The asterisk is used as a truncation or wildcard operator in the search equation.

The search included all studies for which the titles and abstracts contained one or more keywords from each health outcome, population, support program, and study design category of interest to the review.

2.2. Inclusion criteria

The screening of studies from the initial database searches to the final list of studies included in the review was comprised of two steps:

Step 1: following screening of the titles and abstracts, articles were excluded if they met one or more exclusion criteria. We excluded studies that were not economic evaluations (e.g., reviews, systematic reviews, clinical effectiveness studies, costing studies, critical reviews and study protocols, or conference abstracts). Studies were excluded if they did not clearly comprise a cost-effectiveness analysis (no incremental cost per outcome), cost-consequence, and cost-benefit. We also excluded studies that did not clearly comprise a cost-utility analysis and that did not clearly relate to the economic evaluation of a carer intervention. Studies were excluded if population terms (e.g., family, carer, informal care) were not mentioned in a relevant part of the abstract. Studies in any language other than English were excluded.

Step 2: further assessment of the articles remaining from the screening in Step 1 was performed. Publications that did not use a measure of carer health utility were excluded; if the study met any other exclusion criteria from Step 1 of the review, and lastly if the study was inaccessible and did not explicitly specify in the title or the abstract that carer QALYs were included in the study.

2.3. Study selection

All of the authors reviewed a random sample containing 5% of the studies in order to validate the process of inclusion of articles in the review. Two of the authors then independently reviewed the remaining studies to verify whether they met the inclusion criteria mentioned above. For each article deemed to have met the inclusion criteria based on an independent screening of the titles and the abstracts in Step 1, the full-texts of the articles were accessed in order to identify eligible studies. In case of any discordance, a third author was consulted to settle the matter and to try to reach a consensus.

2.4. Data extraction

Two of the authors extracted the key characteristics of the selected studies, as presented in Table 2: the names of the authors; the year of publication; the country; the underlying condition; the disease area, the population subjected to the intervention, the intervention type including a brief description; and in Table 3: the perspective, the follow-up duration, the study design, the year of the cost valuation, the scope of the costs, the type of carers, the direct and indirect costs, the scope of the outcome, the instrument used for utility assessment, the type of sensitivity analysis performed, and lastly the incremental cost-effectiveness ratio (ICER). In keeping with related studies, we used different conventional thresholds to determine whether or not interventions were cost-effective: using the range £20,000–30,000 per QALY gain [39], €30,000 per QALY gain, and \$50,000 per QALY gain [40]. It should be noted that studies often make an adoption decision by comparing the cost-effectiveness ratio of an intervention to a predefined standard, i.e., the maximum acceptable cost-effectiveness ratio [41].

2.5. Quality of reporting assessment and data summary

We used the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist to evaluate the quality of reporting assessment [42]. This checklist developed by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Task Force contains 24 items for scoring by means of a dichotomous answer (Yes/No). Two of the authors independently critically reviewed the selected articles by applying the CHEERS checklist. A random reading list of articles was assigned for critical appraisal by the two authors. Modelling-related criteria (i.e., items 15 and 16) were omitted for single study-based cost-effectiveness evaluations. Studies fulfilling the CHEERS criteria were scored ‘Yes’ and assigned a score of 1 per correct item (‘No’ was assigned a score of 0). As each item on the checklist can be scored as “Yes” or “No”, the quality score of each study was calculated by adding up all of the points for questions answered with “Yes”. The total score per study was divided by the total number of items (N = 22 items). An exception was made for one article that included a model-based economic evaluation for which the score was divided by (N = 24 items). All of the score calculations are expressed as percentages (%). To resolve any disagreement between the two reviewers, a consensus procedure was used. A third co-author was consulted when disagreements persisted. The overall score for each study was presented as a percentage score of the applicable items.

3 Results

3.1. Search results

A total of 1,484 articles were identified in Medline, Embase, PsycInfo, and Econlit, and 3 additional studies were identified through Google Scholar and the Global Health Cost-Effectiveness Analysis (GH CEA) Registry (the Center for the Evaluation of Value and Risk in Health (CEVR), Tufts Medical Center). The literature search identified 1,364 studies (once duplicates had been removed) published between 1950 and February 2019. These articles were screened based on their titles and the abstracts, resulting in 1,302 being excluded. A total of 62 full-texts were identified that warranted further assessment of their eligibility. We eliminated 6 studies that were not economic evaluations; 22 studies that did not include a measure of carer utility; 6 studies pertaining to informal care spillovers of patient interventions; and 2 articles were duplicates of other publications. We included the 20 studies that met the inclusion criteria for our final review.

Figure 1 summarizes the overall search and selection process by means of the PRISMA flow diagram.

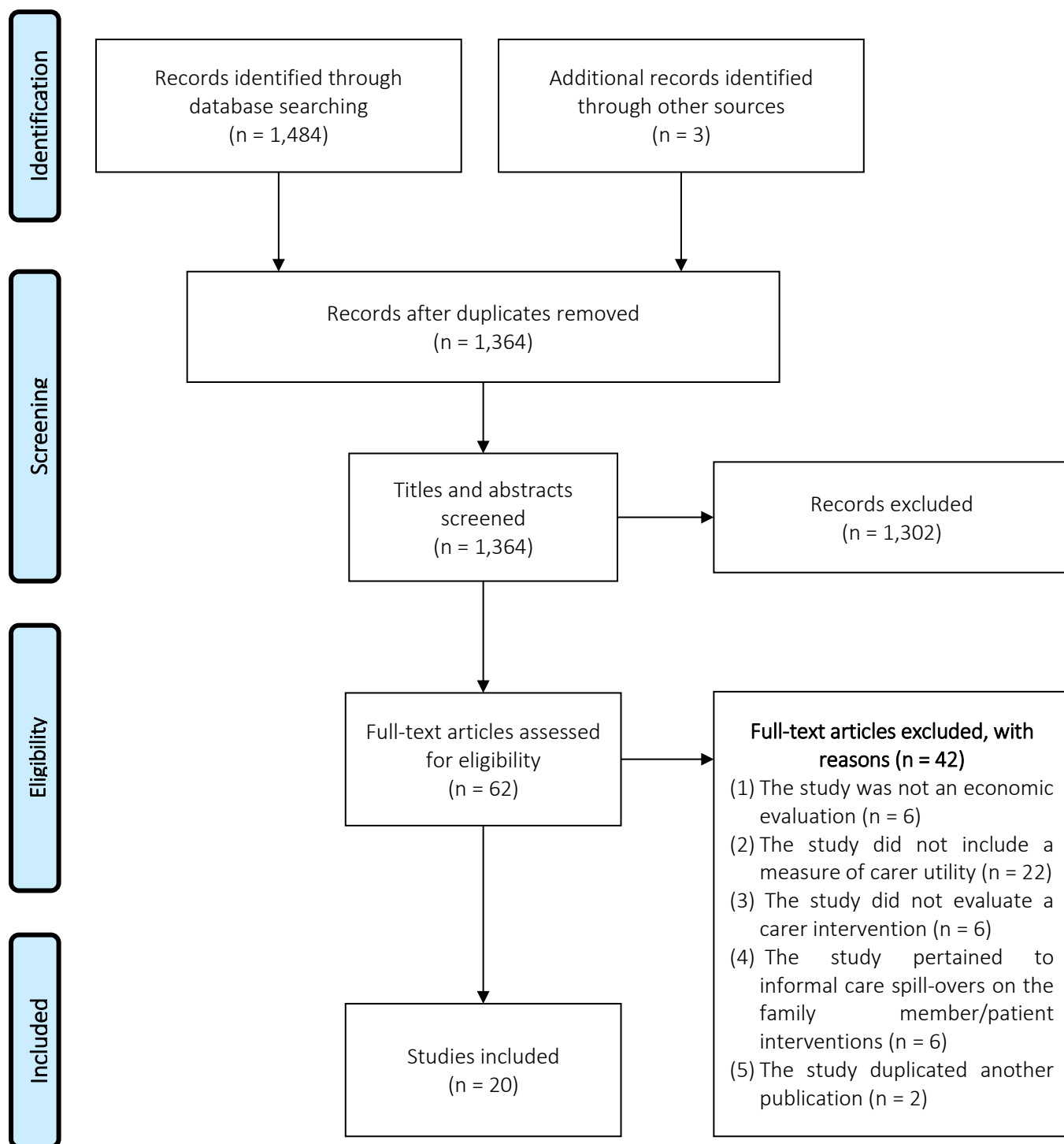


Figure 1: PRISMA flow diagram

3.2. Study characteristics

Table 2 and Table 3 report the characteristics of the included studies. The interventions were: psychological interventions (N = 6) [43–48], respite care/support (N = 1) [49], training/support (N = 9) [50–58], or education/support (N = 4) [59–62]. The majority of the studies (N = 15) were published between 2010 and 2019. A total of eleven studies took place in the UK [43,45,58,46,48,50,51,53–55,57] and three studies were performed in the Netherlands [56,60,62]. The most common disease areas were mental health and/or behavioural health (N = 15), i.e., Dementia (N = 14) [43,45,59–62,46,48,49,52–54,57,58], Parkinson’s disease [56], cardiovascular diseases (N = 3) [50,51,55], and cancer (N = 2) [44,47]. A large proportion of the studies were based on Randomized Clinical Trials (RCT) (N = 16) [43,44,55–58,60,61,45–48,50,51,53,54]. A small proportion of the studies were observational studies (clinical trials) (N = 4) [49,52,59,62]. Only one study using observational data employed a model-based economic evaluation. Martikainen *et al.*, (2004) performed a modelling approach (a basic Markov model in three states) where the model parameters were derived from another publication [63] for the economic evaluation of Alzheimer’s disease in Finland. N = 13 studies adopted a societal perspective [43,45,60–62,48,50,51,53–56,59].

The majority of the CUAs (15 out of 20) used the EQ-5D instrument for the health utility assessment. Seven studies included QALYs for the carers only [43,45–47,49,53,55], whereas thirteen studies took into account both the carers and the patients in the QALYs calculation [44,48,60–62,50–52,54,56–59].

In terms of the informal care cost methodologies, health/social care costs were included as direct costs in all of the studies, and the carer out-of-pocket costs were considered in N = 2 studies [44,47]. Regarding indirect costs, N = 11 studies considered the time spent caring [43,47,61,48,50,51,53,55–57,60] and of these, N = 7 valued the productivity loss [47,53,56,57,60–62] and N = 2 valued the leisure time loss [47,54]. Seven studies did not take into account the indirect carer costs and they essentially considered the health/social care direct costs [45,46,49,51,52,58,59].

Most studies reported the incremental cost-effectiveness ratios (ICERs). The interventions for the informal carers were deemed to be cost-effective in eleven studies [44,45,62,46,47,49,52,53,55,56,59] and not cost-effective in nine studies

[43,48,50,51,54,57,58,60,61]. Four of the six psychological interventions were deemed to be cost-effective [44–47] versus four of the nine training/support interventions [52,53,55,56], and two of the four education/support interventions [59,62]. The respite/support intervention was deemed to be cost-effective [49]. Six of the thirteen CUAs with a societal perspective were cost-effective; Five of the twelve studies that included both the patients and the carers in the scope of the costs were cost-effective [53,55,56,59,62], while two of the three CUAs that conjointly included both the patients and the carers in the scope of costs and the carers only in the scope of the outcomes were cost-effective [53,55]. The single CUA that focused only on carer costs and outcomes was cost-effective [45]. Further details are provided in the additional file.

Table 2: Characteristics of the interventions

References	Geographical area	Underlying condition	Disease areas	Intervention type	Population concerned by the intervention (age) ^(a)	Intervention name - Brief description of the intervention
Charlesworth <i>et al.</i> (2008)[43]	UK	Dementia	Mental/behavioural	Psychological	Both Carers (68) Patients (78)	Befriending scheme for carers Befriender facilitator (BF) -based with charitable/voluntary-sector organisations, were responsible for local befriending schemes, including recruitment, screening, training, and ongoing support for befriending volunteers and for matching carers with befrienders. Their role was to provide emotional support for carers.
Chatterton <i>et al.</i> (2016)[44]	Australia	Cancer	Cancer	Psychological	Both Carers (NS) Patients (NS)	Psychologist-led, individualised cognitive behavioural intervention (PI) Patients and carers received up to five weekly sessions of telephone-based counselling from a psychologist (2 to 5 years of experience in psycho-oncology) following the principles of cognitive behavioural therapy.
Dahlrup <i>et al.</i> (2014)[59]	Sweden	Dementia	Mental/behavioural	Education/support	Both Carers (62) Patients (84)	Psychosocial intervention The psychosocial intervention consisted of educating and informing (provision of a support group) the family caregiver. The intervention started approximately one month after the person was diagnosed with dementia.
Drummond <i>et al.</i> (1991)[49]	Canada	Dementia	Mental/behavioural	Respite care/support	Both Carers (66) Patients (77)	Caregiver Support Program (CSP) The experimental set of supportive interventions was aimed at helping the caregivers to enhance their competency at providing care. Caregiver support nurses (CSNs) were assigned to assist carers, and on a regular basis to schedule home visits with the carer's family physicians whenever the carer's health was deemed to be unstable. The CSP included a 4-hour block of scheduled weekly in-home respite, with additional respite on demand.
Forster <i>et al.</i> (2013)[50]	UK	Stroke	Cardiovascular	Training/support	Both Carers (61) Patients (71)	Training programme for caregivers after stroke The intervention consisted of 14 training components (six mandatory) that were identified as important knowledge/skills that caregivers would need to be able to care for a stroke patient after discharge home. Training continued until the caregiver was deemed to be sufficiently competent.
Forster <i>et al.</i> (2015)[51]	UK	Stroke	Cardiovascular	Training/support	Both Carers (61) Patients (71)	Longer-Term Stroke Care (LoTS) LoTS aim to meet the longer-term needs of patients with stroke and their carers living at home. The intervention comprised a framework of 16 structured assessment questions that pertained directly to longer-term stroke problems previously identified by patients with stroke and their carers and related prompts provided in a care plan.

Table 2: (Continued)

References	Geographical area	Underlying condition	Disease areas	Intervention type	Population concerned by the intervention (age) ^(a)	Intervention name - Brief description of the intervention
Joling <i>et al.</i> (2013)[60]	The Netherlands	Dementia	Mental/behavioural	Education/support	Both Carers (68) Patients (73)	<p>Family Meetings Intervention</p> <p>Caregivers in the intervention group were invited to participate in six in-person counselling sessions. The family meetings consisted of providing psycho-education, teaching of problem-solving techniques, and mobilization of the existing family networks of the patient and primary caregiver in order to improve emotional and instrumental support. The total estimated time for the intervention was 6.5 hours per patient-caregiver dyad, including the time spent on the individual and family sessions (5.5 hours) and the administration and preparation time for the counsellor (1 hour). The intervention participants also had access to all of the usual types of care.</p>
Knapp <i>et al.</i> (2013)[45]	UK	Dementia	Mental/behavioural	Psychological	Carers (NS)	<p>STrategies for Relatives (START)</p> <p>Family carers of people with dementia received eight sessions (in their home) delivered by psychology graduates, with no clinical training but trained to deliver the intervention by adhesion to the manual added to usual treatment. Each carer received a manual and a compact disc to guide them with relaxation exercises.</p>
Livingston <i>et al.</i> (2014)[46]	UK	Dementia	Mental/behavioural	Psychological	Both Carers (56) Patients (78)	<p>STrategies for Relatives (START)</p> <p>Family carers received eight sessions, usually in their home, without the patient being present in the room and at a time convenient to them. The intervention was individually tailored to address the particular problems the carer was experiencing with the person for whom they were providing care.</p>
Martikainen <i>et al.</i> (2004)[52]	Finland	Alzheimer	Mental/behavioural	Training/support	Both Carers (NS) Patients (NS)	<p>Cognitive-behavioural family intervention (CBFI)</p> <p>The cognitive-behavioural family intervention provided to carers and patients consisted of short courses in rehabilitation centres with the comprehensive support of dementia family care coordinators. The courses included physical and recreational training for AD patients, and psychological as well as educational support and counselling for the caregivers.</p>
Orgeta <i>et al.</i> (2015)[53]	UK	Dementia	Mental/behavioural	Training/support	Both Carers (66) Patients (78)	<p>Individual cognitive stimulation Therapy (iCST)</p> <p>The intervention consisted of one-on-one, home-based, structured cognitive stimulation sessions for people with dementia, provided by the family carer. Dyads were asked to complete up to three 30-minute sessions per week over 25 weeks. Seventy-five activity sessions focusing on different themes, such as being creative were provided, as well as resources including a manual, an activity workbook, a carer's diary, and a toolkit containing items such as compact discs.</p>

Table 2: (Continued)

References	Geographical area	Underlying condition	Disease areas	Intervention type	Population concerned by the intervention (age) ^(a)	Intervention name - Brief description of the intervention
Orrell <i>et al.</i> (2017)[54]	UK	Dementia	Mental/behavioural	Training/support	Both Carers (67) Patients (80)	Support at Home - SHIELD CSP: peer support - RYCT: Joint group reminiscence - Combination SHIELD CSP-RYCT The SHIELD CSP intervention was based on peer support for family carers by family carers. The target number of meetings for the carer support intervention was for 12 weekly meetings (1 hour each), followed by meetings for the next 5 months. RYCT targeted both the family carer and the person with dementia invited to attend a local reminiscence group. Twelve weekly sessions (2 hours each) covered various themes. (3) Combined intervention (SHIELD CSP-RYCT).
Patel <i>et al.</i> (2004)[55]	UK	Stroke	Cardiovascular	Training/support	Both Carers (NS) Patients (NS)	Caregiver training The intervention consisted of caregiver training in basic nursing and facilitation of personal care techniques compared with the absence of training.
Richards-Jones <i>et al.</i> (2019)[47]	Australia	Cancer	Cancer	Psychological	Both Carers (NS) Patients (NS)	Proactive telephone outcall intervention The outcall intervention consisted of making telephone contact with the caregivers initiated by the Cancer Council nurses to reduce carer burden. The intervention comprised support service outcalls to carers from a trained oncology nurse, with outcall one at baseline, outcalls two and three at one and at four months, respectively, post-baseline.
Søgaard <i>et al.</i> (2014)[61]	Denmark	Alzheimer	Mental/behavioural	Education/support	Both Carers (NS) Patients (≥50)	Psychosocial intervention Patients and carers were randomised to an intensive, multicomponent, semi-tailored psychosocial intervention programme with counselling, education, and support lasting 8–12 months after diagnosis and follow-up at 3, 6, 12, and 36 months.
Sturkenboom <i>et al.</i> (2015)[56]	The Netherlands	Parkinson	Mental/behavioural	Training/support	Both Carers (71) Patients (67)	Occupational Therapy in Parkinson's Disease (OTiP) Patients and carers in the intervention group received 10 weeks (maximum, 16 h) of individualized therapy, delivered by 18 trained occupational therapists in the patient's home environment and focused on improving performance in daily activities selected and prioritized by the patient. The caregivers' needs in supporting the patients in daily activities were evaluated and addressed if required.

Table 2: (Continued)

References	Geographical area	Underlying condition	Disease areas	Intervention type	Population concerned by the intervention (age) ^(a)	Intervention name - Brief description of the intervention
						Two Forms of Case Management (COMPAS)
Vroomen <i>et al.</i> (2016)[62]	The Netherlands	Dementia	Mental/behavioural	Education/support	Both Carers (64) Patients (80)	Case Management was provided within a given care organization (intensive case management model, ICMM: guiding and supporting people with dementia for long periods of time usually starting after diagnosis, and providing medical and psychosocial services); Case management whereby care was provided by different care organizations within one region (Linkage model, LM: collaboration between multiple care providers providing healthcare services in the region and a mandate to initiate case management services).
						Structured befriending service
Wilson <i>et al.</i> (2009)[48]	UK	Dementia	Mental/behavioural	Psychological	Carers (NS)	Carers enrolled in a BECCA-managed befriending scheme had access to an employed BF, and they were offered contact with a trained volunteer befriender for the duration of the scheme. The stated expectation was that befriending visits by the trained volunteer befrienders would be weekly home visits for at least 6 months, with variations in the location, duration, and frequency of the contact negotiated between each carer volunteer pairing.
						REMCARE: REMiniscence groups for PwD and CAREgivers
Woods <i>et al.</i> (2012)[57]	UK	Dementia	Mental/behavioural	Training/support	Both Carers (69) Patients (78)	The intervention consisted of joint reminiscence groups held weekly for 12 consecutive weeks, followed by monthly maintenance sessions for a further 7 months. The sessions followed a treatment manual and they were led by two trained facilitators in each centre, supported by a number of volunteers.
						REMCARE: REMiniscence groups for PwD and CAREgivers
Woods <i>et al.</i> (2016)[58]	UK	Dementia	Mental/behavioural	Training/support	Both Carers (70) Patients (77)	The intervention joint reminiscence groups emphasised active and passive reminiscence by both carers and people with dementia. The group sessions were held weekly over 12 consecutive weeks, followed by seven monthly maintenance group sessions. The sessions were led by two trained facilitators in each centre, supported by trained volunteers.

Abbreviations. NS: Not specified; UK: United Kingdom; CSP: Caregiver Support Program; Population concerned by the intervention: Carer and/or Patient; Both (Carer and patient). PwD: Person with Dementia. (a) Mean

Table 3: Characteristics of the included studies (CUA)

References	Perspective	Follow-up	Study design	Cost valuation year	Scope of costs ^(a)	Type of carer direct costs	Type of carer indirect costs	Scope of outcome	Instrument used for utility assessment	Type of sensitivity analysis ^(b)	ICER ^(#)	Conclusion
Charlesworth <i>et al.</i> (2008)[43]	Society	15-months	RCT	2005	Both	Health/social care	Time providing care	Carers	EQ-5D	Probabilistic	£105,954/QALY	Not cost-effective
Chatterton <i>et al.</i> (2016)[44]	Health sector	12 months	RCT	2011-2012	Both	Health/social care - Out-of-pocket	NS	Both	AQOL-8D	Deterministic and Probabilistic	£8,703 to 40,428/QALY	Cost-effective
Dahlrup <i>et al.</i> (2014)[59]	Society inferred	60 months (5 years)	NRS	2010	Both	Health/social care	NS	Both	EQ-5D	NS	NS ^(c)	Cost-effective
Drummond <i>et al.</i> (1991)[49]	Payers	6 months	NRS	1988	Both	Health/social care	NS	Carers	CQLI	NS	20,036 CAN\$/QALY	Cost-effective
Forster <i>et al.</i> (2013)[50]	Health and social care - Society	6, 12 months	RCT	2009-2010	Both	Health/social care	Time providing care	Both	EQ-5D	Deterministic and Probabilistic	>£20,000/QALY	Not cost-effective
Forster <i>et al.</i> (2015)[51]	Health and social care - Society	6, 12 months	RCT	2010-2011	Both	Health/social care	Time providing care	Both	EQ-5D	Probabilistic	NS ^(d)	Not cost-effective
Joling <i>et al.</i> (2013)[60]	Society	12 months	RCT	2009	Both	Health/social care	Time providing care - Loss of productivity	Both	SF6D	Probabilistic	€157,534/QALY	Not cost-effective
Knapp <i>et al.</i> (2013)[45]	Payers and Society	8 months	RCT	2009-2010	Carers	Health/social care	NS	Carers	EQ-5D	Probabilistic	£5,452/QALY	Cost-effective
Livingston <i>et al.</i> (2014)[46]	Health and social care	4, 8, 12 and 24 months	RCT	2009-2010	Carers	Health/social care	NS	Carers	EQ-5D	Probabilistic	£11,200/QALY	Cost-effective
Martikainen <i>et al.</i> (2004)[52]	Payers	5 years	NRS	2001	Patients	Health/social care	NS	Both	HUI:2 ^(e)	Probabilistic	NS ^(f)	Cost-effective

Table 3: (continued)

References	Perspective	Follow-up	Study design	Cost valuation year	Scope of costs ^(a)	Type of carer direct costs	Type of carer indirect costs	Scope of outcome	Instrument used for utility assessment	Type of sensitivity analysis ^(b)	ICER	Conclusion
Orgeta <i>et al.</i> (2015)[53]	Health and social care - Society	26 weeks	RCT	2012-2013	Both	Health/social care	Time providing care - Loss of productivity - Out-of-pocket	Carers	EQ-5D	Probabilistic	£3,100/QALY	Cost-effective
Orrell <i>et al.</i> (2017)[54]	Health and social care - Society	5, 12 months	RCT	2011	Both	Health/social care	Leisure time lost ^(e)	Both	EQ-5D	Probabilistic	>£30,000/QALY	Not cost-effective
Patel <i>et al.</i> (2004)[55]	Society	12 months	RCT	2001-2002	Both	Health/social care	Time providing care	Carers	EQ-5D	Deterministic and Probabilistic	NS ^(h)	Cost-effective
Richards-Jones <i>et al.</i> (2019)[47]	Health sector	1, 6 months	RCT	2013	Both	Health/social care - Out-of-pocket	Time providing care - Loss of productivity - Leisure time lost	Carers	AQoL-8D	Probabilistic	-\$18,500/QALY	Cost-effective
Søgaard <i>et al.</i> (2014)[61]	Society	3, 6, 12 and 36 months	RCT	2008	Both	Health/social care	Time providing care - Loss of productivity	Both	EQ-5D	Probabilistic	NS ⁽ⁱ⁾	Not cost-effective
Sturkenboom <i>et al.</i> (2015)[56]	Society	6 months	RCT	N/A	Both	Health/social care	Time providing care - Loss of productivity	Both	EQ-5D	Probabilistic	NS ^(j)	Cost-effective
Vroomen <i>et al.</i> (2016)[62]	Society	4, 8, 12 and 24 months	NRS	2010	Both	Health/social care - Time providing care	Loss of productivity	Both	EQ-5D	Probabilistic	€-425,349/QALY	Cost-effective
Wilson <i>et al.</i> (2009)[48]	Society	15 months	RCT	2005	Both	Health/social care	Time providing care	Both	EQ-5D	Probabilistic	£105,954/QALY	Not cost-effective
Woods <i>et al.</i> (2012)[57]	Public sector	10 months	RCT	2010	Both	Health/social care	Time providing care - Loss of productivity	Both	EQ-5D	Probabilistic	^(k) £2,586/QALY	Not cost-effective
Woods <i>et al.</i> (2016)[58]	Public sector	10 months	RCT	2010	Both	Health/social care	NS	Both	EQ-5D	Probabilistic	>£20,000/QALY	Not cost-effective

Abbreviations. RCT: randomized controlled trial; NRS: non-randomized study (observational study); ICER: Incremental Cost-Effectiveness Ratio, (#): The ICERS are as reported; EQ-5D: EuroQol – Five-Dimensions scale; CQLI: Caregiver Quality of Life Instrument; AQOL-8D: Assessment of Quality of Life – Eight-Dimensions; SF6D: Short-Form – Six-Dimensions; HUI-2: Health Utilities Index Mark 2NS: Not specified; (a) Carer and/or patient; (b) Deterministic and/or Probabilistic; (c): Not calculated. Authors' conclusion based on the cost and outcome analysis. Outcomes were interpreted to produce positive effects on family caregivers; (d): No cost–outcome combination suggested statistically significant between-group increases; (e) QALYs calculations were provided by another study (Neumann *et al.* 1999); (f): The CBFi program is more effective and less costly; (g) The costs of unpaid family carer inputs were calculated following the approach used for volunteers. For the societal perspective, the opportunity cost approach assumed that the unpaid carer would be able to find employment with a wage rate equal to the national minimum wage, and the replacement cost was estimated as the hourly cost of a healthcare assistant, under the assumption that a care worker would need to be hired to provide care if the unpaid family carer was unable to do so. (h); (i); (j): Costs and outcomes were not significant; (k) The Confidence Interval (CI) at 95% was –20,280 to 24,340 and in light of this high level of uncertainty, the authors concluded that the intervention was not cost-effective.

3.3. Overall quality of the reporting

Table 4 provides the note of the articles per item of the CHEERS Statement. Six items (“Comparators”, “Choice of health outcomes”, “Measurement of effectiveness”, “Measurement and valuation of preference-based outcome”, and “Funding sources”) were reported in 100% of the studies. All of the included studies clearly exceeded more than a half (50%) of CHEERS items (N =20) [43,44,53–62,45–52], and two articles achieved CHEERS scores of 100% [46,50]. A total of nine economic evaluations (45%) had 85% or greater for quality reporting [43,46,50,51,53,57,60–62]; one study (5%) achieved 82% of the CHEERS items [58]. A total of six studies (30%) [44,47,48,52,54,56] had CHEERS score ranging from 73 to 79% quality reporting. A total of four studies (4%) [45,49,55,59] had quality of reporting scores between 59 and 68%. Overall, the average quality score was 81.35%, with the lowest rating at 59% [59].

Of the ten studies that had a quality of reporting score higher than the average quality score, seven were in regard to the societal perspective [43,50,51,53,60–62] and only two concluded that the interventions were cost-effective [53,62].

Table 4: Economic evaluation as assessed by the CHEERS Statement (per item)

CHEERS items	Charlesworth <i>et al.</i> (2008) [43]	Chatterton <i>et al.</i> (2016) [44]	Dahlrup <i>et al.</i> (2014) [59]	Drummond <i>et al.</i> (1991) [49]	Forster <i>et al.</i> (2013) [50]	Forster <i>et al.</i> (2015) [51]	Joling <i>et al.</i> (2013) [60]	Knapp <i>et al.</i> (2013) [45]	Livingston <i>et al.</i> (2014) [46]	Martikainen <i>et al.</i> (2004) [52]	Orgeta <i>et al.</i> (2015) [53]	Orrell <i>et al.</i> (2017) [54]	Patel <i>et al.</i> (2004) [55]	Richards-Jones <i>et al.</i> (2019) [47]	Sogaard <i>et al.</i> (2014) [61]	Sturkenboom <i>et al.</i> (2015) [56]	Vroomen <i>et al.</i> (2016) [62]	Wilson <i>et al.</i> (2009) [48]	Woods <i>et al.</i> (2012) [57]	Woods <i>et al.</i> (2016) [58]	Yes	%	No	%	Total
1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	19	95	1	5	20
2	✓	✓			✓		✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	15	75	5	25	20
3	✓		✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	18	90	2	10	20
4	✓		✓	✓	✓	✓	✓		✓		✓	✓				✓	✓		✓	✓	13	65	7	35	20
5	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓		✓		✓	✓	17	85	3	15	20
6	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	19	95	1	5	20
7	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	20	100	0	0	20
8	✓				✓	✓	✓		✓		✓		✓		✓	✓	✓				10	50	10	50	20
9		✓			✓	✓			✓						✓		✓	✓	✓	✓	9	45	11	55	20
10	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	20	100	0	0	20
11	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	20	100	0	0	20
12	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	20	100	0	0	20
13	✓	✓		✓	✓	✓	✓		✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	16	80	4	20	20
14	✓	✓	✓	✓	✓	✓	✓		✓		✓	✓	✓	✓		✓	✓		✓	✓	16	80	4	20	20
15 ^a										✓											1	100	0	0	1
16 ^b										✓											1	100	0	0	1
17	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	19	95	1	5	20
18	✓			✓	✓				✓		✓		✓			✓		✓	✓	✓	10	50	10	50	20
19	✓				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	16	80	4	20	20
20	✓	✓			✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓			15	75	5	25	20
21		✓	✓		✓	✓	✓		✓	✓	✓	✓			✓	✓	✓		✓	✓	14	70	6	30	20
22	✓	✓		✓	✓	✓	✓		✓	✓	✓			✓	✓	✓	✓	✓		✓	13	65	7	35	20
23	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	20	100	0	0	20
24	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	19	95	1	5	20
CHEERS Score	91	77	59	64	100	86	91	64	100	79	95	73	68	77	86	77	95	77	86	82	Overall average CHEERS score: 81%				

^{a, b} Only for model-based economic evaluation; “✓” = “Yes”

4 Discussion

This is the first systematic review of economic evidence (CUAs) that focuses solely on interventions to support informal carers. We searched for articles in four electronic databases using a set of key search terms. The systematic review conducted by two of the authors followed the gold standard recommendations (PRISMA) for conducting systematic reviews [43], and a critical appraisal through a validated checklist [44]. Only 20 published CUAs of carer-focused interventions were identified in the literature. The main types of interventions were psychological, training/support, and education/support interventions, with mixed evidence regarding the cost-effectiveness. Most studies adopted a societal perspective, but there were differences in terms of what costs and outcomes were included. The reporting quality of the studies was generally quite good.

Conducting CUA with carer interventions is subject to a number of methodological challenges, for instance, do the methodologists need to include both the carer and the patient costs? Should the measurement and the valuation of health benefits be carried out for both the carers and the patients? Our results show that both the carer and the patient costs were largely taken into account (seventeen out of the twenty studies), as well as both the carer and the patient outcomes (thirteen out of the twenty studies). These findings are of particular relevance for the methodological guidelines used in Health Technological Assessment (HTA) [64].

The societal perspective was included in most of the studies (13 out of 20), and 12 out of 13 of these studies used the EQ-5D metric for the utility assessment (QALYs), which is in accordance with the national recommendations. These findings facilitate comparison between carer interventions [43,45,61,62,48,50,51,53–56,59].

Overall, there appeared to be a tendency whereby studies with better reporting deemed the intervention to be not cost-effective. More precisely, seven out of ten CUAs exceeding the average quality score of CHEERS (81%) were designated as being not cost-effective [50,51,57,58,60,61], and they included both carer and patient costs and both carer and patient outcomes. It would have been interesting to know if a change in the scope of the costs and/or the outcomes would have changed the conclusion of the economic evaluation. This suggests that sensitivity analyses based on different methodological assumptions may be desirable [64]. It is also important to note that some CUAs of carer interventions omitted

informal care costs, while [47] and [57] found that inclusion of the time providing care (and the value of the consequent loss of productivity) costs affected the cost-effectiveness results of the intervention. For studies that omitted informal care time, for example [45], the incremental cost-effectiveness ratio (in this particular case £5,452/QALYs) might not truly reflect how costly (or cost saving) the intervention is to society [11,13].

Fourteen of the sixteen economic evaluations of interventions for patient and carer dyads with a randomized controlled trial (RCT) design were performed throughout the European geographical area, with 11 of the 16 in the UK [43,45,58,46,48,50,51,53–55,57]. The geographical focus of this review (UK, and to a lesser extent Netherlands) could be due to the focus on cost-utility analyses rather than other types of economic evaluation. It could also reflect the fact that certain countries (including the UK) have substantial government funding (National Institute for Health Research (NIHR) - Health Technology Assessment (HTA) Programme in the UK, for example) and use for economic evaluation of healthcare interventions.

Our study focused on a critical review of economic evaluations in order to identify cost-utility analyses of interventions for carers. Close comparisons of the relative cost-effectiveness of carer interventions are complicated by differences between studies in terms of the design, the interventions that were compared, the inclusion of direct/indirect cost of the carers, and other study characteristics listed above. Thus, although all of the selected economic evaluations measured the same health outcome (QALYs), the transferability and generalizability of the results (across diseases: dementia, stroke, cancer, and Parkinson's disease) is limited. This is due specifically to the choice of the method; differences in intervention contexts and intervention costs; and the types of economic evaluations, such as decision models (simulation)-based and empirical (including trial-based) economic evaluations [65], and cost-effectiveness thresholds [39].

As we chose to focus on carer interventions assessed by a cost-utility analysis approach, several publications that used other approaches to economic evaluation were not considered [66,67]. However, because QALYs were systematically used as the measure of health benefits in this review, there is a better level of comparability of the results between interventions for informal carers. Nevertheless, differences in methodologies across studies remain significant, such as the degree to which the informal carer's time is costed and the methods employed to do this, for example.

Based on our review, we suggest the following recommendations for future cost-utility analyses of carer-focused interventions to improve comparability and transferability. Firstly, CUAs should employ both a healthcare and a societal perspective for the analysis. This is recommended by the 2nd US panel on cost-effectiveness [68]. Secondly, CUAs under the societal perspective should, at the very least, consider carer time costs, to avoid adversely cost-shifting care to family carers. Thirdly, CUAs should consider outcomes for both family carers and patients to ensure that societal health gains are maximised. Fourthly, CUAs should adhere as much as possible to the CHEERS guidelines in order to promote transparency in reporting.

5 Conclusion

Our review highlights the lack of cost-utility analyses regarding interventions to support informal carers, but, more positively, the relative prominence of good reporting practices. The main types of interventions were psychological, training/support, and educational/supporting interventions, with mixed evidence regarding the cost-effectiveness. There appeared to be a tendency whereby the studies with better reporting deemed the intervention to be not cost-effective, compared to the studies with fewer items on the CHEERS checklist. Hence, some divergences in findings noticed across the studies cannot be attributed solely to differences in the type of interventions undertaken, but also to the methodological trade-off. Most studies adopted a societal perspective, but there were differences in terms of what costs and outcomes were included. Lastly, by stating fundamental methodological and structural specifications, it is likely that there will also be improvements in the consistency and the quality of health economic evaluations of informal care.

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Compliance with Ethical Standards

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Author contributions

Concept and overall approach: W.G., H.A. and L.P. Search strategy: W.G., H.A. and L.P. Review of search results and selection of studies: W.G., H.A. and L.P. Critical appraisal W.G. and L.P., and Interpretation of results W.G., H.A. and L.P. Drafting of the manuscript: W.G. Critical review of the manuscript: W.G. and L.P.

Supplemental Materials

There is a Supplementary Materials section accompanying this article.

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