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SYSTEMATIC REVIEW

Cost-Effectiveness of Non-pharmacological Interventions for Mild Cognitive Impairment and Dementia: A Systematic Review of Economic Evaluations and a Review of Reviews

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Abstract

Background Dementia prevalence is increasing, with no cure at present. Drug therapies have potential side effects and risk of mortality. People with dementia are frequently offered non-pharmacological interventions to improve quality of life and relieve symptoms. Identifying which interventions are cost-effective is important due to finite resources in healthcare services.

Aims The aims were to review published economic evaluations of community and nursing home non-pharmacological interventions for people with mild cognitive impairment or dementia and assess the usefulness of these evaluations for decision making in health services, for use by policy and local and national decision makers.

Methods We conducted a systematic review (PROSPERO CRD42021252999) of economic evaluations of non-pharmacological interventions for dementia or mild cognitive impairment with a narrative approach to data synthesis. Exclusions: interventions for dementia prevention/early detection/end of life care. Databases searched: Academic Search Premier, MEDLINE, Web of Science, EMBASE, Google Scholar, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycInfo, Psychology and Behavioural Sciences Collection, PsycArticles, Cochrane Database of Systematic Reviews, Business Source Premier and Regional Business News; timeframe 1 January 2011–11 May 2023. Reporting quality was assessed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS).

Results The review included 37 economic evaluations and four reviews worldwide across several distinct forms of care: physical activity, cognition, training, multicomponent, assistive technology and other (specialist dementia care, group living, home care vs care home). The intervention with the strongest evidence of cost-effectiveness was maintenance cognitive stimulation therapy. Case management, occupational therapy and dementia care management also showed good evidence of cost-effectiveness.

Conclusion More economic evidence on the cost-effectiveness of specific dementia care interventions is needed, with consistency of methods and outcome measures. This could improve local and national decision makers' confidence to promote future cost-effective dementia interventions.

1 Introduction

The worldwide economic burden of dementia care is high at US$815 billion [1]. The total annual cost of dementia in the UK is estimated at £24.2 billion [2]. With the increase in numbers of people being diagnosed with dementia and the high costs of dementia care, economic evaluations are needed to ensure that non-pharmacological interventions which are offered are cost-effective; however, economic evidence of these interventions remains limited [3].

By 2050, the number of people with dementia (PwD) is projected to rise to 152 million due to population growth and an increasingly ageing population [4]. There is currently no cure for dementia; existing drug therapies are either symptomatic therapies to relieve symptoms of dementia or are primarily indicated for Alzheimer's disease [5]. Drug therapies have the potential for serious side effects including mortality [6]. Non-pharmacological therapies may be considered as complements to pharmacological treatments.

The National Institute for Health and Care Excellence (NICE) guideline for dementia care [7] recommends four non-pharmacological interventions: group cognitive stimulation therapy (CST), group reminiscence therapy and

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Key Points for Decision Makers

This review found that maintenance cognitive stimulation therapy showed the strongest evidence of being cost-effective, but with a small number of economic evaluations; case management, occupational therapy and dementia care management also showed good evidence of cost-effectiveness.

More economic evidence about the cost-effectiveness of dementia care interventions is needed, and researchers need to be consistent with study methods and outcome measures to allow comparison across interventions. Increased economic information and consistency would increase confidence of policy and local and national decision makers when they are planning and implementing dementia care interventions in the future.

cognitive rehabilitation or occupational therapy. The main aim of these types of dementia interventions is to reduce symptoms including cognitive decline, promote independence and wellbeing and improve quality of life.

Existing systematic reviews of economic evidence commonly focus on a particular intervention [8, 9] or dementia symptom [10, 11]. Previous reviews have also included interventions to improve the quality of life of carers as well as PwD [3, 12]. The term 'carer' here refers to anyone supporting a family member, partner or friend and not receiving payment for providing this care [13].

The aim of this review was to provide a comprehensive summary of existing economic evaluations of non-pharmacological interventions delivered in the community and nursing homes, evaluating a wide range of dementia symptoms and interventions that measured the impact on the PwD and not solely their carer. The intended audience of the review is policy makers and key decision makers, including healthcare providers and managers at a local and national level.

2 Methods

The protocol for this systematic review was established before work commenced and was registered on PROSPERO (CRD42021252999). Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) guidelines were followed throughout [14].

2.1 Eligibility Criteria

Inclusion criteria (detailed in Table 1) stated that papers should be trial-based economic evaluations, observational studies or modelling simulations; the population under observation was PwD or those with mild cognitive impairment (MCI). People with MCI were included as a high percentage go on to later develop dementia [15]. To be eligible, interventions needed to aim to delay progression of the disease or improve quality of life. Papers could have evaluated dementia interventions throughout the dementia pathway, ranging in severity from recent diagnosis to advanced dementia, but prevention/early detection of dementia or end-of-life care interventions were excluded. Both narrative and systematic reviews of economic studies were also eligible for inclusion.

2.2 Search Strategy

The databases searched were Academic Search Premier, Google Scholar, Web of Science, Cochrane Database of Systematic Reviews, MEDLINE, Cumulative Index of Nursing and Allied Health Literature (CINAHL), PsycInfo, Psychology and Behavioural Sciences Collection, PsycArticles, Business Source Premier and Regional Business News. Papers published between 1 January 2011 and 11 May 2023 were included to search only recent articles. Articles published in any languages were eligible.

Table 1 Eligibility criteria

Inclusion criteria	Exclusion criteria
Population with dementia (including Alzheimer's disease) or mild cognitive impairment	Studies of intervention purely for the carers of people with dementia
Trial-based economic evaluations, observational or simulation studies	Interventions focusing solely on homeopathic or herbal remedies
Non-pharmacological community and nursing home-based interventions designed to either delay progression of the disease or to improve/maintain health-related quality of life	End-of-life care interventions
All study designs including reviews and systematic reviews	Interventions aimed at prevention/early detection of dementia
Papers in any language, both abstracts and full texts will be translated	Studies without costings/outcomes data
	Letters, commentaries, study protocol papers and conference abstracts

The search terms used within the databases were the disease-specific terms 'dementia', 'Alzheimer's' and 'mild cognitive impairment' combined with the economic terms 'cost*' or 'econ*', with additional search terms to identify interventions: 'intervention' or 'therapy'. The reference lists of primary studies and review articles that met the inclusion criteria were manually searched for other relevant articles for inclusion.

2.3 Study Selection

Titles and abstracts were screened according to inclusion/exclusion criteria by author GE, and results were verified by EG/HJ. Any disputes were resolved by PM. Full texts of selected articles were retrieved and reviewed by GE and EG/HJ, and any disputes were resolved by PM.

2.4 Data Extraction

Extracted data included intervention description, participant numbers, follow-up period, study design, economic evaluation type, main economic outcome measure, primary outcome (PwD only) and perspective (see Table 2). Data extraction was performed by GE, with EG/HJ independently undertaking data extraction for 40% of the included articles. Any disagreement was resolved by PM.

Separate data extraction was undertaken for the review of reviews by GE (see Table 3). Extracted data included interventions reviewed, number of studies included in the review and databases used.

2.5 Data Synthesis

A narrative approach to data synthesis was undertaken to summarise and allow comparison of the methods and results of the included evaluations whilst demonstrating heterogeneity. A narrative reporting approach was used as meta-analysis could not be carried out due to the context-specific nature of the economic evaluations and the numerous outcomes used in studies.

Interventions were classified according to the following categories representing distinct forms of care: physical activity, cognitive interventions, training interventions, multicomponent interventions, assistive technology and other interventions (specialist dementia care, group living, home care vs care home).

2.6 Quality Appraisal

Quality appraisal was undertaken using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement [16] (see Table 7). CHEERS is designed to assess reporting quality rather than the quality of the evaluation. The statements relate to the following aspects: title, abstract, introduction, methods, results, discussion and disclosure. Statements that related only to modelling evaluations were excluded for non-modelling evaluations and resulting scores adjusted accordingly. Each was assigned a score, based on the number of statements met on the CHEERS checklist (0 = unmet, 0.5 = partially met, and 1 = met); the total was then translated into a percentage of items met. Quality appraisal was carried out by GE, EG/HJ undertook an independent appraisal of 30% of the articles, and any disagreement was resolved by PM.

In the review of reviews, A Measurement Tool to Assess Systematic Reviews (AMSTAR 2) [17] (see Table 4) was used to critically appraise the quality of the reviews. GE undertook the initial assessment, and EG independently undertook assessment for 60% of the included articles. The tool includes an assessment of potential bias, assessing each area or domain of the review, with certain domains being defined as critical. An overall rating of confidence in quality was calculated based on the total number of weaknesses in critical domains. These weaknesses were defined by unmet/partial met statements on the AMSTAR 2 checklist according to the following criteria:

- *High confidence* None or one non-critical weakness
- *Moderate confidence* More than one non-critical weakness but no critical flaws
- *Low confidence* One critical flaw with or without non-critical weaknesses
- *Critically low confidence* More than one critical flaw with or without non-critical weaknesses

2.7 Usefulness of Economic Evaluations to Decision Making

A score of usefulness of the economic evaluations to decision making was calculated for each included evaluation. The scoring system was based on an existing method of assessing usefulness of economic evaluations based on data extraction and assessment of reporting quality [18]. Usefulness was then categorised according to these scores: limited ≤ 4, moderate 4.5–5, strong 5.5–6 (details in Table 5).

3 Results

The systematic literature review identified 769 publications, duplicates were manually removed, and 489 articles were screened. Forty-one papers were included in the final review. The articles selected for inclusion comprised 37 single economic evaluations and four reviews. The search strategy has

Table 2 Data characteristics of economic evaluation

Author[a], country[b]	INT	INT description	No.[a]	Time horizon[a]	Study design[b]	EE[a]	Main economic outcome measure	Primary outcome[a]	Perspective[a]
Brown et al. [26], UK	Cog	Maintenance cognitive stimulation therapy with a group that had previously received cognitive stimulation therapy	INT 123, TAU 113	6	RCT	CUA	QALYs	EQ-5D (self and proxy), DEMQOL (self and proxy)	Societal
D'Amico et al. [20], UK	Cog	Maintenance cognitive stimulation therapy in addition to usual care	INT 64 dyads, TAU 67 dyads	6	RCT	CUA	QALYs	ADAS-Cog, QoL-AD	H&SC
Laakkonen et al. [44], Finland	Cog	Separate group rehabilitation sessions run for PwD and for spouses	INT 67, TAU 69	24	RCT	CEA	Patient HRQoL	15D	Not stated
Mervin et al. [49], Australia	Cog	Individual, non-facilitated sessions with a soft toy. Received either a toy with artificial intelligence (PARO) or a soft toy	PARO 138, soft toy 140, TAU 137	2.5	RCT	CEA	Patient agitation level	CMAI-SF	HCP
Orgeta et al. [22], UK	Cog	Home-based, individual cognitive stimulation therapy, led by own carer. Up to three 30-min activity sessions/week over 25 weeks. Initial training and ongoing support provided	INT 180, TAU 176	6.5	RCT	CUA	QALYs	ADAS-Cog, QoL-AD	H&SC/societal
Sado et al. [50], Japan	Cog	A learning therapy INT carried out in nursing homes. A combination of cognitive training and stimulation	INT 30, TAU 27	12	Non-randomised matched control	CBA	CT for CNLTC	CT for CNLTC	HCP

Table 2 (continued)

Author[a], country[b]	INT	INT description	No.[a]	Time horizon[a]	Study design[b]	EE[a]	Main economic outcome measure	Primary outcome[a]	Perspective[a]
Sogaard et al. [47], Denmark	Cog	Intensive, multicomponent, semi-tailored, psychosocial INT programme with counselling, education and support	INT 163 dyads, TAU 167 dyads	36	RCT	CUA	QALYs	EQ-5D-5L	Societal
Spector et al. [23], UK	Cog	A CBT manual developed for anxiety in dementia and trialled in sessions with participant/carer dyads	INT 25, TAU 25	6	RCT	CEA	Patient anxiety	RAID score	H&SC
Woods et al. [19], UK	Cog	Group reminiscence therapy for participants and with carers	INT 196, TAU 140	10	RCT	CUA	QALYs	QoL-AD	Public sector
Ballard et al. [24], UK	Train	Staff training programme on person-centred care for care staff, promoting tailored activities, antipsychotic medication review	INT 404, TAU 443	9	RCT	CEA	Patient quality of life	DEMQOL-(Proxy)	Not stated
El Alili et al. [36], Netherlands	Train	Multicomponent care programme for nursing home residents with advanced dementia	INT 116, TAU 115	12	RCT	CUA	QALYs	QUALID, GAIN	Societal

Table 2 (continued)

Author[a], country[b]	INT	INT description	No.[a]	Time horizon[a]	Study design[b]	EE[a]	Main economic outcome measure	Primary outcome[a]	Perspective[a]
Livingston et al. [27], UK	Train	Evidence-based, manualised, INT, delivered to staff in 6 interactive sessions. Comprising training getting to know and understand residents	INT 189, TAU 215	8	RCT	CUA	QALYs	CMAI	Not stated
Meads et al. [6], UK	Train	Dementia Care Mapping: a care-home staff training INT aimed to embed person-centred care, improve care quality and health outcomes for residents	INT 418, TAU 308	16	RCT	CUA	QALYs	EQ-5D-5L	HCP
Menn et al. [31], Germany	Train	GPs in 3 groups (A, B, C) trained in dementia care. At different timepoints groups B and C actively recommended support groups and promoted caregiver counselling	B 88, C 108, A (TAU) 107	48	RCT	CEA	Time to institutionalisation	Remaining time the patient lived at home	Societal
Romeo et al. [28], UK	Train	Person-centred care INT delivered by staff in nursing homes. Staff were trained in person-centred care, management of agitation, and psychosocial approaches	INT 404, TAU 443	9	RCT	CUA	QALYs	QoL measured by DEMQOL	H&SC

Table 2 (continued)

Author[a], country[b]	INT	INT description	No.[a]	Time horizon[a]	Study design[b]	EE[a]	Main economic outcome measure	Primary outcome[a]	Perspective[a]
Van de Ven et al. [38], Netherlands	Train	Dementia-care mapping, multicomponent INT. Staff from participating nursing homes attended training, then assessed residents' needs and implemented care INTs	INT 154, TAU 164	18	RCT	CBA	Healthcare consumption, falls and psychotropic drug use and staff absenteeism	Healthcare consumption, falls	HCS
Williams et al. [39], USA	Train	Staff training INT to improve communication with residents by encouraging staff to stop using 'childish' language/way of speaking and interacting (elderspeak)	INT 42 dyads, TAU unstated	36	Observational	CEA	% Time staff used elderspeak, % time residents resistive to care	% Time staff used elderspeak, % time residents resistive to care	Not stated
Henderson et al. [54], Italy, Poland, UK	Multi-dimension	Meeting centre support programme; person-centred, psychosocial approach combining day centre services with support for carers	INT 83, TAU 69	6	Non-randomised matched control	CUA	QALYs	QoL-AD	H&SC/societal

Table 2 (continued)

Author[a], country[b]	INT	INT description	No.[a]	Time horizon[a]	Study design[b]	EE[a]	Main economic outcome measure	Primary outcome[a]	Perspective[a]
Jennings et al. [40], USA	Multi-dimension	Dementia care programme co-managed by nurse practitioners and physicians, comprising structured assessments, individualised care plans, referral to community support/advice services, and 24 h access to a clinician	INT 1083, TAU 2186	36	RCT	CEA	Patient healthcare utilisation	Admission to long-term care, healthcare utilisation	Not stated
Jutkowitz et al. [43], USA	Multi-dimension	Modelling simulation on INTs designed to reduce admissions to nursing homes. Using 2 carer support/education INTs and 2 dementia care management INTs	INT 5000, TAU 5000 (simulation)	24	Modelling	CBA	QALYs	Admission to long-term care	Societal
MacNeil Vroomen et al. [35], Netherlands	Multi-dimension	Comparison of 2 types of case management. Intensive Case Management Model: carried out within one care organization, and Linkage Model where care was provided by different care organisations within 1 region	Intensive 234, Linkage 214, TAU 73	24	Non-randomised observational controlled, cohort study	CUA	QALYs	NPI score	Societal

Table 2 (continued)

Author[a], country[b]	INT	INT description	No.[a]	Time horizon[a]	Study design[b]	EE[a]	Main economic outcome measure	Primary outcome[a]	Perspective[a]
Michalowsky et al. [33], Germany	Multi-dimension	Dementia care management INT using multi-disciplinary care to assess and support the dementia patient and carer	INT 315, TAU 129	24	RCT	CUA	QALYs	SF-12	Societal
Mostardt et al. [32], Germany	Multi-dimension	Case management INT aiming to improve support networks and quality of care and enable PwD to stay at home for longer	INT 38, TAU 76	12	Non-randomised matched control	CEA	Additional time in the home environment	Time in the home environment	HCP
Pizzi et al. COPE [41], USA	Multi-dimension	Assessment by occupational therapist and advanced nurse practitioner. Falls prevention strategies, medication review and carer education. Plan to increase physical activity and engagement	INT 130, TAU 120 (dyads)	12	RCT	CBA	Healthcare resource utilisation costs	Healthcare resource utilisation	Healthcare provider
Pizzi et al. [42], USA	Multi-dimension	Occupational therapist assessment—activities tailored to assessment profiles and instructed caregivers in their daily use along with providing disease education and stress reduction techniques	INT 93, TAU 83	6	RCT	CBA	Healthcare utilisation costs	Caregiver reported healthcare utilisation	Healthcare and societal

Table 2 (continued)

Author[a], country[b]	INT	INT description	No.[a]	Time horizon[a]	Study design[b]	EE[a]	Main economic outcome measure	Primary outcome[a]	Perspective[a]
Pizzo et al. [30], UK	Multi-dimension	A community-based occupational therapy INT. Assesses and agrees goals. 1 h a week for 10 weeks	INT 249, TAU 219	6	RCT	CUA	QALYs	Bristol Activities of Daily Living Scale	UK NHS and personal social services
Rädke et al. [34], Germany	Multi-dimension	Dementia care management INT, delivered in participants' homes by dementia-trained nurses. Focus on interprofessional treatment and care, medication management and support/education of carers	INT 315, TAU 129	24	Cluster randomised	CEA	Patient functional independence	SF-12	HCS
Rosenvall et al. [45], Finland	Multi-dimension	Three INTs for people with Alzheimer's: care-management, family support and physical activity. Analysed using existing data, then a modelling simulation was carried out	924 (simulation)	48	Modelling	CBA	Use of health and care services, clinical outcome measures	Delay in transition to long-term care	Not stated
Saxena et al. [52], Singapore	Multicomponent	PCDC compared with a hospital-based MC. PCDC was run by GPs and nurses assisted by the MC team	MC 101, PCDC 99, TAU 63	12	Non-randomised quasi-experimental design	CUA	QALYs	EQ-5D-5L	Societal
D'Amico et al. [21], UK	PE	Individually tailored dyadic regime, walking daily for 12 weeks	INT 30, TAU 22	3	RCT	CUA	QALYs	NPI score	H&SC/societal

Table 2 (continued)

Author[a], country[b]	INT	INT description	No.[a]	Time horizon[a]	Study design[b]	EE[a]	Main economic outcome measure	Primary outcome[a]	Perspective[a]
Davis et al. [51], Canada	PE	Twice-weekly group classes for older women, comparing resistance or aerobic training with balance and tone classes	Resistance 28, aerobic 30, balance and tone 28	6	RCT	CEA	Patient executive cognitive function	Stroop test	HCP
Lamb et al. [25], UK	PE	Weekly group exercise programme of aerobic and resistance training led by a physio	INT 294, TAU 141	12	RCT	CUA	QALYs	EQ-5D-3L	HCP/societal
Pitkäla et al. [46], Finland	PE	Group-based exercise sessions twice a week compared to home-based exercise	Home 70, group 70, TAU 70	12	RCT	CEA	FIM score changes and SPPB score changes	FIM, SPPB	H&SC
Sopina et al. [48], Denmark	PE	Supervised, hour-long group sessions of aerobic exercise, three times a week	INT 107, TAU 93	4	RCT	CUA	QALYs	EQ-5D-5L, EQ-VAS	Danish healthcare perspective
Van Santen et al. [37], Netherlands	PE	Exergaming – an interactive cycling system that mimics outdoor cycling whilst on a stationary bike	INT 53, TAU 29 (dyads)	6	RCT	CUA	QALYs	EQ-5D-3L	Societal
Ghani et al. [53], UK	Assist tech	Tablet app with medication reminders, photos, cognitive games etc.	INT 173, TAU 172	6	RCT	CUA	QALYs	EQ-5D-3L	Healthcare provider

Table 2 (continued)

Author[a], country[b]	INT	INT description	No.[a]	Time horizon[a]	Study design[b]	EE[a]	Main economic outcome measure	Primary outcome[a]	Perspective[a]
Howard et al. [29], UK	Assist tech	Assistive technology and telecare assessment followed by installation of all appropriate devices	INT 248, TAU 247	24	RCT	CUA	QALYs	Time to institutionalisation	H&SC/societal

ADAS-Cog Alzheimer's Disease Assessment Scale – Cognitive subscale, *Assist tech* assistive technology, *CBA* cost-benefit analysis, *CBT* cognitive behavioural therapy, *CEA* cost-effectiveness analysis, *CMAI-SF* Cohen-Mansfield Agitation Inventory – short form, *Cog* cognitive, *CT for CNLTC* Criterion Time for Certification of Needed Long-Term Care, *CUA* cost-utility analysis, *DEMQOL* Dementia Quality of Life, *EE* method of economic evaluation, *EQ-5D* health-related quality-of-life measure, *EQ-VAS* EQ-Visual Analogue Scale, *FIM* Functional Independence Measure, *GAIN* Alzheimer's care instrument, *GP* general practitioner, *H&SC* health and social care, *HCP* healthcare provider, *HRQoL* health-related quality of life, *INT* intervention, *MC* memory clinic, *NHS* National Health Service, *NPI* neuropsychiatric Inventory, *PCDC* primary care dementia clinic, *PE* physical exercise, *PwD* person(s) with dementia, *QALY* quality-adjusted life year, *QoL* quality of life, *QoL-AD* Quality of Life in Alzheimer Disease, *QUALID* Quality of Life in Late-stage Dementia, *RCT* randomised controlled trial, *SF-12* Short Form Health Survey, *SPPB* Short Physical Performance Battery, *TAU* treatment as usual, *Train* training interventions

[a]Data for the economic evaluation

[b]Data for original study

been reported using a PRISMA [14] flow diagram (Fig. 1). The literature search revealed a lack of economic evaluations on the cost-effectiveness of creative therapies such as art, music, drama, creative writing and dance and also sensory therapies such as aromatherapy and massage.

3.1 Study Characteristics

The specific conditions being studied included PwD (n = 29), Alzheimer's disease (n = 2), MCI (n = 2) and mixed populations of MCI/Alzheimer's disease/dementia (n = 4). Types of interventions reviewed were exercise (n = 6), cognitive (n = 9), multicomponent (n = 12), training (n = 8) and assistive technology (n = 2). Studies recruited participants living in a variety of settings: 27 studies were for community dwelling participants, nine were for those in nursing homes, and two were for people living either in a nursing home or the community. Studies used varying criteria to define dementia/MCI in their inclusion criteria, ranging from having symptoms of dementia (n = 1) to a formal diagnosis of dementia (n = 11). A number of studies defined specific Clinical Dementia Rating scores (n = 3) and/or used Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) assessment criteria in their inclusion criteria (n = 8).

The majority of studies evaluated were randomised controlled trials (n = 30), followed by non-randomised studies (n = 5) and two modelling studies. Sample size varied greatly, ranging from 50 to 3269 (10,000 in a modelling evaluation). The international reach of the studies was as follows: the UK (n = 14) [6, 19–30], Germany (n = 4) [31–34], the Netherlands (n = 4) [35–38], the United States (n = 5) [39–43] Finland (n = 3) [44–46], Denmark (n = 2) [47, 48], Australia (n = 1) [49], Japan (n = 1) [50], Canada (n = 1) [51], Singapore (n = 1 [52], Sweden (n = 1) [53] and a multi-national study involving Italy, Poland and the UK [54].

A range of interventions were identified, which focused on improving the behavioural and psychological symptoms of dementia (BPSD), as well as interventions to prevent decline in cognitive function and mobility. In total, 27 different primary outcome measures were used across the included 37 studies. Outcomes included generic, dementia-specific and utility-based quality-of-life scales.

Over half of the evaluations employed a cost-utility analysis (n = 20), followed by cost-effectiveness analysis (n = 10) and cost-benefit analysis (n = 4); quality-adjusted life years (QALYs) were the most frequently used measure of benefit (n = 20). Costs and outcomes are reported in Table 6. It was noted that where studies compared an intervention to treatment as usual (TAU), the meaning and content of TAU varied between studies, potentially affecting the relative effectiveness and cost-effectiveness of interventions.

Fourteen economic evaluations took a societal perspective. A societal perspective takes into account all costs and

Table 3 Review characteristics

Study	Review method	Interventions reviewed	Intervention descriptions	No. studies included	Databases used
Alves et al. [8]	Systematic	Cognitive	Cognitive stimulation, cognitive training or cognitive rehabilitation	5	PubMed, PsychInfo, the Cochrane Library, EMBASE, metaRegister of Clinical Trials, OVID, EBM Reviews
Clarkson et al. [12]	Systematic	Multicomponent	Home support interventions	8	British NHSEED
Livingston et al. [10]	Systematic	Cognitive/multicomponent	Blended inpatient and outpatient programme to reduce hospitalisation. Also an Australian comparison of dementia care mapping and person-centred care programmes	2	MEDLINE, Web of Knowledge; EMBASE; British Nursing Index; the Health Technology, NHSEED, the HTA programme database and the DARE Assessment programme database; PsycInfo; NHS Evidence; System for Information on Grey Literature; the Stationery Office Official Documents website; the Stationery National Technical Information Service; Cumulative Index of Nursing and Allied Health Literature (CINAHL); and the Cochrane Library
Nickel et al. [3]	Systematic	Physical exercise/cognitive	Physical exercise, cognitive interventions	16	Centre for Reviews and Dissemination, EconLit, Embase, Cochrane Library, PsycInfo and PubMed

NHS National Health Service, *NHSEED* National Health Service Economic Evaluation Database

effects of the intervention on the whole of society and is often favoured by health economists [55]. The perspective taken when conducting an economic evaluation could affect the analyses and results [55].

3.2 Quality Appraisal of Economic Evaluations

Individual evaluations met between 62 and 98% of criteria items in assessment of CHEERS reporting quality (mean 81%) (Table 7). Twenty-one evaluations met over 80% of total assessed items. In terms of scores for categories of interventions, the highest was for the 'other' category, which scored 89% (mean); however, it should be noted that this category only evaluated two interventions. Exercise interventions ranked next highest with 84% (mean); training interventions scored the lowest overall, with 76% (mean).

3.3 Usefulness of Economic Evaluations to Decision Making

Scores for level of usefulness were as follows: evaluations rated as having 'strong' usefulness, $n = 8$; 'moderate', $n = 17$; and 'limited', $n = 12$. The results showed that a high CHEERS quality assessment score did not necessarily translate to a high usefulness score for aiding decision making (see Table 5).

3.4 Intervention Specific Results

3.4.1 Cognitive Interventions

Nine evaluations explored interventions focused on cognition (Table 2). Study populations comprised community dwelling PwD [19, 22, 23, 44, 47], nursing home residents [49, 50] and a combination of both populations [20, 26].

CSTs were evaluated in three papers: one evaluating cognitive stimulation for participants new to CST [22] and two evaluating maintenance cognitive stimulation therapy (MCST) [20, 26]. The D'Amico et al. evaluation reported that MCST dominated TAU, with a 40% probability of being cost-effective at a willingness-to-pay (WTP) threshold of £20,000 for cost per QALY using proxy EQ-5D ratings [20]. In the Brown et al. evaluation, MCST dominated TAU in terms of QALYs for a subgroup of people living alone [26].

Table 4 Quality assessment of systematic reviews using AMSTAR 2 [17]

Study	Alves et al. [8]	Clarkson et al. [12]	Livingston et al. [10]	Nickel et al. [3]
1. Did the research questions and inclusion criteria for the review include the components of PICO?	Met	Met	Met	Unmet
2. **Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?**	Unmet	Unmet	Met	Partial met
3. Did the review authors explain their selection of the study designs for inclusion in the review?	Unmet	Unmet	Met	Met
4. Did the review authors use a comprehensive literature search strategy?	Partial met	Partial met	Met	Partial met
5. Did the review authors perform study selection in duplicate?	Unmet	Met	Unmet	Unmet
6. Did the review authors perform data extraction in duplicate?	Met	Met	Met	Unmet
7**. Did the review authors provide a list of excluded studies and justify the exclusions?**	Unmet	Partial met	Met	Partial met
8. Did the review authors describe the included studies in adequate detail?	Met	Met	Met	Met
9. **Did the review authors use a satisfactory technique for assessing the RoB in individual studies that were included in the review?**	Met	Partial met	Met	Unmet
10. Did the review authors report on the sources of funding for the studies included in the review?	Met	Met	Met	Unmet
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?	Met	N/A	Met	N/A
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Met	N/A	Met	N/A
13. Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?	Met	Unmet	Met	Met
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Met	Met	Met	Met

Table 4 (continued)

Study	Alves et al. [8]	Clarkson et al. [12]	Livingston et al. [10]	Nickel et al. [3]
15. If they performed quantitative synthesis, did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	Met	N/A	Met	N/A
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Partial met	Partial met	Met	Met
Overall rating	**Critically low confidence**	**Critically low confidence**	**High confidence**	**Critically low confidence**

Questions with bolded text denote critical domains

AMSTAR 2 A Measurement Tool to Assess Systematic Reviews, *N/A* not applicable, *RoB* risk of bias

However, this evaluation used a small secondary dataset that may not have been representative of the general population and was not powered to detect subgroup changes; therefore, results should be interpreted with caution. The CST intervention was not evaluated as cost-effective though; it did not improve cognition or quality of life for PwD and was dominated by TAU [22].

Cognitive multicomponent interventions were evaluated in two papers [47, 50]. Sado et al. evaluated a combination of cognitive training and stimulation in a nursing home population [50], while Sogaard et al. assessed a community counselling/education and support intervention [47]. Both followed up participants for significant periods of time [47, 50]. Although the intervention Sado et al. evaluated showed significant cost savings compared to TAU [50], the non-randomised matched control design was not gold standard, and such designs risk introducing bias and confounding [56]. The intervention Sogaard et al. evaluated was not cost-effective and was dominated by TAU in terms of QALYs [47].

The remaining four cognitive papers all evaluated different types of cognitive interventions. Laakkonen et al. evaluated cognitive rehabilitation with promotion of self-management skills for people recently diagnosed [44]. Participants in the intervention group showed significantly less decline in verbal fluency scores compared with TAU, without increasing total costs [44]. Spector et al. evaluated cognitive behavioural therapy (CBT) to reduce anxiety in PwD [23]. Significant improvements in depression were reported by the intervention group; improvements in anxiety scores were also reported, but this failed to reach statistical significance [23]. Mervin et al. evaluated an intervention to improve levels of agitation using soft toys and interactive toys with artificial intelligence; no statistically significant between-group differences in agitation were found between the soft toy and the interactive toy groups, and the intervention was not cost-effective [49]. Woods et al. evaluated joint reminiscence therapy groups with carers and PwD [19]. They reported no significant difference in outcomes or service use between the intervention group and TAU [19].

3.4.2 Training Interventions

There were eight evaluations of specialised dementia training for staff caring for PwD (Table 2). Seven of the eight interventions involved nursing home staff training, with one community-based training intervention for general practitioners (GPs). The training intervention evaluation with the longest follow-up period was evaluated by Williams et al. at 36 months (mean = 15.4, SD 9.83) [39].

Four training interventions were evaluated as cost-effective in terms of QALYs [24, 27, 36, 39]. Ballard et al. reported the staff training intervention demonstrated benefits in terms of quality of life, agitation and neuropsychiatric symptoms, as well as cost savings [24]. The staff training intervention Livingston et al. evaluated was cost-effective in terms of QALYs with a 62% probability of cost-effectiveness at a WTP of £20,000/QALY [27]. The multicomponent training intervention for people with severe dementia evaluated by El Alili et al. was reported to dominate TAU in terms of QALYs [36]. Williams et al. evaluated staff communication with residents, and this intervention was found to be cost-effective; however, the evaluation lacked appropriate statistical analysis, as no incremental cost-effectiveness ratio (ICER) in terms of QALYs was reported; direct comparison with other studies is difficult [39]. A strength of this evaluation was its long time horizon of 36 months; it was limited by the small sample size, and generalisability was also limited due to the small geographical location of the nursing homes.

An evaluation of the cost-effectiveness of a programme that provided GP training in dementia care, carer counselling

Table 5 Usefulness of economic evaluations to decision making

Study	Usefulness level	Primary reasons
El Alili et al. [36]	Strong	Appropriate statistical analysis including sensitivity analysis, long time horizon
Howard et al. [29]	Strong	Appropriate statistical analysis including sensitivity analysis, long time horizon
Jutkowitz et al. [43]	Strong	Appropriate statistical analysis, model parameter uncertainty described, long time horizon
Lamb et al. [25]	Strong	Appropriate statistical analysis including sensitivity analysis, long time horizon
Meads et al. [6]	Strong	Appropriate statistical analysis including sensitivity analysis, long time horizon
Michalowsky et al. [33]	Strong	Appropriate statistical analysis including sensitivity analysis, long time horizon
Radke et al. [57]	Strong	Appropriate statistical analysis including sensitivity analysis, long time horizon
Rosenvall et al. [45]	Strong	Appropriate statistical analysis, model parameter uncertainty described, long 4-year time horizon
MacNeil Vroomen et al. [35]	Moderate	Appropriate statistical analysis including sensitivity analysis, long time horizon, study design
Mostardt et al. [32]	Moderate	Appropriate statistical analysis including sensitivity analysis, long time horizon, study design
D'Amico et al. [20]	Moderate	Appropriate statistical analysis including sensitivity analysis, short time horizon
D'Amico et al. [21]	Moderate	Appropriate statistical analysis including sensitivity analysis, short time horizon
Ghani et al. [53]	Moderate	Appropriate statistical analysis including sensitivity analysis, short time horizon
Livingston et al. [27]	Moderate	Appropriate statistical analysis including sensitivity analysis, short time horizon
Orgeta et al. [22]	Moderate	Appropriate statistical analysis including sensitivity analysis, short time horizon
Pitkäla et al. [46]	Moderate	Appropriate statistical analysis including sensitivity analysis, no ICER reported
Pizzi et al. [41]	Moderate	Appropriate statistical analysis including sensitivity analysis, no ICER reported
Romeo et al. [28]	Moderate	Appropriate statistical analysis including sensitivity analysis, short time horizon
Sogaard et al. [47]	Moderate	Appropriate statistical analysis including sensitivity analysis, no ICER reported
Sopina et al. [48]	Moderate	Appropriate statistical analysis including sensitivity analysis, short time horizon
Woods et al. [19]	Moderate	Appropriate statistical analysis including sensitivity analysis, short time horizon
Van Santen et al. [37]	Moderate	Appropriate statistical analysis including sensitivity analysis, short time horizon
Brown et al. [26]	Moderate	Boot strapping, short time horizon
Laakkonen et al. [44]	Moderate	Sensitivity analysis performed, long time horizon, no ICER reported
Williams et al. [39]	Moderate	Sensitivity analysis performed, long time horizon
Henderson et al. [54]	Limited	Appropriate statistical analysis including sensitivity analysis, short time horizon, study design
Sado et al. [50]	Limited	Appropriate statistical analysis including sensitivity analysis, no ICER reported, long time horizon, study design
Saxena et al. [52]	Limited	Long time horizon, ICER not reported for all comparison groups, study design
Ballard et al. [24]	Limited	No ICER reported, short time horizon
Davis et al. [51]	Limited	No ICER reported, short time horizon
Pizzi et al. [42]	Limited	No ICER reported, short time horizon
Spector et al. [23]	Limited	No ICER reported, short time horizon
Jennings et al. [40]	Limited	No sensitivity analysis, no ICER reported
Van de Ven et al. [38]	Limited	No sensitivity analysis, no ICER reported
Pizzo et al. [30]	Limited	Not all parameters used were reported, short time horizon
Menn et al. [31]	Limited	Statistical analysis methods not appropriate, no ICER reported
Mervin et al. [49]	Limited	No sensitivity analysis, short time horizon, no ICER reported

Appropriate statistical analysis: Deemed to be met by meeting criteria for CHEERS domain 20a—Describe the effects of sampling uncertainty for estimated incremental cost, incremental effectiveness, and incremental cost-effectiveness, together with the impact of methodological assumptions (such as discount rate, study perspective) [16]

ICER: No ICER reported – the evaluation did not present outcomes as ICER (not included if ICERs were calculated but not reported as the intervention was dominant)

Time horizon length: Economic evaluations with a longer time horizon (≥ 1 year) were rated higher than those with a short time horizon (< 1 year) as dementia is a long-term health condition

Study design: Randomised controlled trials and observational and modelling studies were rated higher than non-randomised controlled trials and quasi-experimental studies

CHEERS Consolidated Health Economic Evaluation Reporting Standards, *ICER* incremental cost-effectiveness ratio

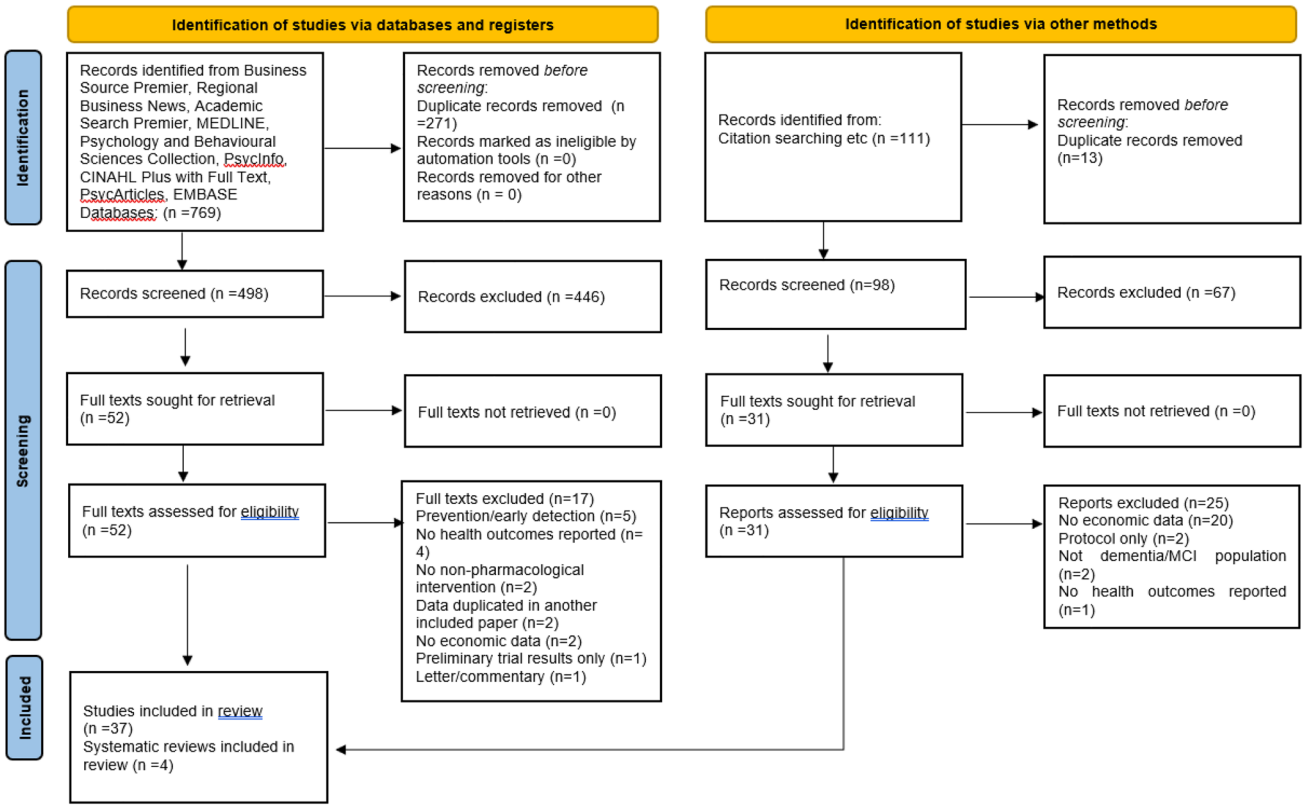

Fig. 1 PRISMA flow diagram showing inclusion process of articles in the systematic review [14]. *MCI* mild cognitive impairment, *PRISMA* Preferred Reporting Items for Systematic review and Meta-Analysis

and promotion of support groups was carried out by Menn et al. [31]. Despite having the longest of all follow-up periods at 48 months, it showed no significant reduction in time to institutionalisation [31]. Meads et al. and van de Ven et al. both evaluated dementia care mapping interventions in nursing homes; they were evaluated as not cost-effective and cost-neutral, respectively [6, 38].

3.4.3 Multicomponent Interventions

Twelve papers evaluated a range of multicomponent dementia care programmes.

Dementia care management evaluations by Jennings et al., Michalowsky et al. and Radke et al. looked at multicomponent community dementia care for assessment, management and support [33, 40, 57].

Only two of the three dementia care management interventions evaluated showed evidence of cost-effectiveness, and TAU was dominated in terms of QALYs [33, 57]. Radke et al. undertook subgroup analysis to determine which group of participants benefitted most [57]. A higher probability of cost-effectiveness was reported in those aged < 80 years compared to > 80 years; females compared to males; PwD living alone compared to those not living alone; and in people with more co-morbidity than less co-morbidity [57]. The authors suggest that the high probability of cost-effectiveness in females and those living alone could be attributed to these groups having fewer relatives or carers to provide care and support and therefore having a higher number of unmet needs, meaning that they are more likely to benefit from a multicomponent management programme [57].

Case management, supporting the person with dementia and their carer in conjunction in a multicomponent team approach, was evaluated by MacNeil Vroomen et al. and Mostardt et al. [32, 35]. Mostardt et al. reported a significant difference in average additional months spent in the home environment for intervention group participants, although no limitations were discussed in the evaluation, which also used a non-randomised matched controlled study design. MacNeil Vroomen et al. evaluated an intensive care management model that dominated TAU in terms of QALYs, with 99% WTP at €30,000/QALY [35]. However, the observational, non-randomised design may have introduced selection bias and more heterogeneity into the study population.

Three occupational therapy-based interventions were evaluated that involved PwD assessment and carer/PwD education [30, 41, 42]. While cost-benefit analysis showed

Table 6 Economic evaluation results

Author, country	INT	INT group cost[a]	Comparison group cost	INT group outcome	Comparison group outcome	Main result
Brown et al. [26], UK	Cog	Care home £18,635; lives alone £9053; lives with someone £18,853; low ADAS-Cog 18,675; high ADAS-Cog £15,266	Care home £17,485; lives alone £9155; lives with someone £15,026; low ADAS-Cog £16,398; high ADAS-Cog £13,791	0.07 QALYs (EQ-5D) lives alone		INT dominant over TAU in terms of QALYs for the subgroup living alone
D'Amico et al. [20], UK	Cog	£11,306	£11,440		Incremental effect: 0.0176 QALYs (calculated with Proxy EQ-5D)	ICER = £26,835/QALYs (calculated by Proxy EQ-5D)
Laakkonen et al. [44], Finland	Cog	€8947	€9383	− 0.03 HRQoL mean score	− 0.04 mean change in HRQoL	There was no change between the groups in HRQoL according to 15D. However, the INT had beneficial effects on cognitive function without increasing total costs
Mervin et al. [49], Australia	Cog	$13,827 (PARO, interactive toy); $12,078 (soft toy)	$6862	− 2.66 CMAI-SF mean change (PARO), −1.68 CMAI-SF mean change (soft toy)	1.22 CMAI-SF mean change	Incremental cost per unit improvement in CMAI-SF was $13.01 for the PARO group and $12.85 for the soft toy group relative to usual care
Orgeta et al. [22], UK	Cog	£4740 (HSC); £9770 (societal)	£4670 (HSC); £10,630 (societal)	ADAS-Cog 20.53, QoL-AD 37.96	21.19 ADAS-Cog, 37.71 QoL-AD	INT dominated by TAU in terms of ADAS-Cog, no differences in primary outcomes of cognition or quality of life
Sado et al. [50], Japan	Cog	$795	Not stated	68.4 CT for CNLTC mean score	83.3 mean score CT for CNLTC	INT showed $21 per month cost saving/unit of CT for CNLTC for avoiding increased long-term care costs
Sogaard et al. [47], Denmark	Cog	€84,142 per dyad	€80,741	3.26 QALYs	3.46 QALYs	INT dominated by TAU in terms of QALYs
Spector et al. [23], UK	Cog	£2344	£1259	− 4.59 mean score rating anxiety in dementia for PwD		INT was cost neutral
Woods et al. [19], UK	Cog	£5853	£4309	37.013 QoL-AD, 0.644 QALYs	36.416 QoL-AD, 0.643 QALYs	ICER = £2586/per 0.597 change in QoL-AD score (no ICER expressed in £/QALYs)

Table 6 (continued)

Author, country	INT	INT group cost[a]	Comparison group cost	INT group outcome	Comparison group outcome	Main result
Ballard et al. [24], UK	Train	£2713 (INT cost); £29,702 (total HSC costs)	£0 (INT cost); £34,442 (total HSC costs)	4.78-point improvement in DEMQOL	2.54-point improvement in DEMQOL (mean difference)	INT demonstrates benefits in terms of quality of life, agitation and neuropsychiatric symptoms, as well as cost savings
El Alili et al. [36], Netherlands	Train	£7173 (total societal costs)	£7484 (total societal costs)	Incremental effect: 0.40 QALYs	0.39 QALYs	INT dominant over TAU in terms of QALYs
Livingston et al. [27], UK	Train	£1379	£1175	0.346 QALYs	0.332 QALYs	ICER = £14,064/QALYs gained
Meads et al. [6], UK	Train	£3539	£2060	0.718 QALYs	0.708 QALYs	ICER = £64,380/QALYs gained
Menn et al. [31], Germany	Train	€80,361 (group B); €75,754 (group C)	Group A €82,745	x	x	Group B = 0.858 hazard rate on time to institutionalisation over 4 years Group C = 1.133 hazard rate on time to institutionalisation over 4 years
Romeo et al. [28], UK	Train	£32,112	£34,215	1.96 DEMQOL Proxy score (mean change)		INT dominant over TAU in terms of QALYs gained
Van de Ven et al. [38], Netherlands	Train	$0.63 per resident/day	Not stated	3.33 falls (mean annual no.), $3.50 per resident/day (total healthcare consumption), $0.13 per resident/day (psychotropic drug use)	1.81 falls (mean annual no.), $3.23 per resident/day (total healthcare consumption), $0.25 per resident/day (psychotropic drug use)	INT was cost neutral
Williams et al. [39], USA	Train	$79.69/per staff member ('elderspeak'); $39.84/per resident (resistive to care)	x	11.80% (reduction in time staff used elderspeak), 9.24% reduction in time residents resistive to care		ICER = $4/resident per 1 percentage point reduction in resistiveness to care ICER = $7/staff member per 1 percentage point reduction in elderspeak
Henderson et al. [54], Italy, Poland, UK	Multicomponent	£10,650 (total health and social care costs)	£4709 (total health and social care costs)	Incremental effect 0.40 QALYs	0.40 QALYs, mean difference 0.01 QALYs	ICER = £832,636/QALYs gained for PwD. For QALYs, the probability of C/E was 0 at WTP of £0–£350,000. For QoL-AD, the probability of C/E of INT was 50% at WTP of €5000 for a 1-point increase

Table 6 (continued)

Author, country	INT	INT group cost[a]	Comparison group cost	INT group outcome	Comparison group outcome	Main result
Jennings et al. [40], USA	Multicomponent	$317 per quarter	Not stated	Not stated	Not stated	Hazard ratio of 0.60, program participants less likely to be admitted to long-term care facility than TAU
Jutkowitz et al. [43], USA	Multicomponent					All 4 INTs showed small QALY improvements and delayed transition to long-term care
MacNeil Vroomen et al. [35], Netherlands	Multicomponent	€69,435 (ICMM); €84,155 (LM)	€107,627	1.25 QALYS (ICMM), 1.18 QALYs (LM)	1.27 QALYs	ICER (ICMM vs LM) = ICMM dominates ICER (LM vs control) = €460,135 ICER (ICMM vs control) = unstated
Michalowsky et al. [33], Germany	Multicomponent	€24,046	€24,615	1.349 QALYs	1.300 QALYs	INT dominant over TAU in terms of QALYs
Mostardt et al. [32], Germany	Multicomponent	€1409	€1292	16.4 (months in home environment)	12.2 (months in home environment)	ICER = €53 per additional month in a home environment
Pizzi et al. [41], USA	Multicomponent	$2047 mean per dyad	$0.3 mean per dyad	N/A	N/A	Mean cost savings for COPE $2354 per dyad compared to TAU
Pizzi et al. [42], USA	Multicomponent	$1707 mean per dyad	$864 mean per dyad	N/A	N/A	Mean cost savings for TAP compared with TAU: $1299 per dyad (healthcare perspective), $8611 per dyad (societal perspective)
Pizzo et al. [30], UK	Multicomponent	£2689	£1919	0.00664 QALYs	Not reported	INT was dominated by TAU
Rädke et al. [34], Germany	Multicomponent	Unavailable	Unavailable	+0.05 QALYs	Incremental effect: +0.049 QALYs	INT dominant over TAU in terms of QALYs gained
Rosenvall et al. [45], UK	Multicomponent	€527 (CM); €8,000 (rehabilitative); €341 (SFS) All costs per pt/year	N/A		N/A	Economic break-even points reached if a patient's transition to long-term care is delayed by: CM = 2.8 days; SFS = 1.8 days; rehabilitative cognitive, physical and social activation = 43.0 days

Table 6 (continued)

Author, country	INT	INT group cost[a]	Comparison group cost	INT group outcome	Comparison group outcome	Main result
Saxena et al. [52], Singapore	Multicomponent	$15,308 (MC); $13,275 (PCDC); $15,766 (other clinics)		0.78 (PCDC), 0.76 (other polyclinics clinics) (EQ-5D scores)		ICER = S$29,042/QALYs for the PCDC group when compared with the MC group
D'Amico et al. [21], UK	PE	£10,533	£7,805	N/A	Incremental effect: 0.0055 QALYs	ICER = £286,440 QALYS (calculated by DEMQOL-Proxy) Not C/E when outcomes are calculated by QALYs
Davis et al. [51], Canada	PE	$2255 (CAD) (resistance); $1417.15 (CAD) (aerobic)	$2387 (CAD) (balance and tone)	44.61 (resistance), 48.27 (aerobic) (seconds gained/lost on Stroop test)	54.69 (balance and tone) (seconds gained/lost on Stroop test)	Both the aerobic and the resistance classes dominate balance and tone classes in terms of seconds gained/lost on Stroop test
Lamb et al. [25], UK	PE	£5580	£3917	0.787 QALYs	0.826 QALYs	INT dominated by TAU in terms of QALYs
Pitkäla et al. [46], Finland	PE	$25,112 per dyad/per year (HE group); $2,066 per dyad/per year (GE group)	$34,121per dyad/per year (control group)	− 7.1 (HE group), − 10.3 (GE group) (FIM change)	−14.4 (control group) (FIM change)	HE and GE INTs had beneficial effects on the physical functioning of patients with Alzheimer's disease, without increasing the total costs of health and social services
Sopina et al. [48], Denmark	PE	£608 (including transport)	Not stated	Not stated	Not stated	ICER = €158,520/QALYs gained
Van Santen et al. [37], Netherlands	PE	€2877	€2750	0.36 QALYs	0.42 QALYs	INT dominated by TAU in terms of QALYs
Ghani et al. [53], UK	Assist tech	€8188	€8175	− 0.03 EQ-5D-3L mean change	−0.01 EQ-5D-3L mean change	INT dominated by TAU
Howard et al. [29], UK	Assist tech	£19,649 (HSC), £56,000 (societal)	£15,186 (HSC), £53,378 (societal)	1.201 QALYs	1.306 QALYs	ICER = £8635/QALYs (HSC), £33,672/QALYs (societal)

All dollar values are in US$ unless otherwise indicated

ADAS-Cog Alzheimer's Disease Assessment Scale – Cognitive subscale, *Assist tech* assistive technology, *C/E* cost-effectiveness, *CAD* Canadian dollars, *CM* care management, *CMAI-SF* Cohen-Mansfield Agitation Inventory – short form, *Cog* cognitive, *CT for CNLTC* Criterion Time for Certification of Needed Long-Term Care, *DEMQOL* Dementia Quality of Life, *EQ-5D* health-related quality-of-life measure, *FIM* Functional Independence Measure, *GE* group-based exercise, *HE* tailored home-based exercise, *HRQoL* health-related quality of life, *HSC* health and social care, *ICER* incremental cost-effectiveness ratio, *ICMM* Intensive Care Management Model, *INT* intervention, *LM* Linkage model, *MC* memory clinic, *PCDC* primary care dementia clinic, *PE* physical exercise, *PwD* person(s) with dementia, *QALY* quality-adjusted life year, *QoL-AD* Quality of Life in Alzheimer Disease, *S$* Singapore dollars, *SFS* structured family support, *TAU* treatment as usual, *Train* training interventions, *WTP* willingness to pay

[a]Mean cost per person over the length of the INT unless otherwise stated

Table 7 Quality assessment of studies using CHEERS [16]

Study	Title/abstract (2 items)	Introduction (2 items)	Methods (10[a] items)	Results (4[b] items)	Discussion (1 item)	Disclosure (2 items)	Total	% Items met
Cognitive								
Brown et al. [26]	1.5	2	6.5	3	0.5	2	15.5	74%
D'Amico et al. [20]	2	1.5	9	4	1	2	19.5	93%
Laakkonen et al. [44]	1.5	2	6.5	3.5	1	1	15.5	74%
Mervin et al. [49]	1.5	2	8	1	1	2	15.5	74%
Orgeta et al. [22]	1.5	2	9	3	2	1	18.5	88%
Sado et al. [50]	1	2	9	3	1	2	18	86%
Sogaard et al. [47]	2	2	8.5	3	1	2	18.5	88%
Spector et al. [23]	1.5	2	6	2	1	2	14.5	69%
Woods et al. [19]	1.5	2	8	4	1	2	18.5	88%
Means	1.6	1.9	7.8	2.9	0.9	1.9	17.1	81%
Training								
Ballard et al. [24]	1.5	2	4	3	1	2	13.5	64%
El Alili et al. [36]	2	1.5	8.5	3	1	2	18	86%
Livingston et al. [27]	2	2	8.5	4	1	1	18.5	88%
Meads et al. [6]	2	2	8	3	1	2	18	86%
Menn et al. [31]	1.5	2	9.5	1	1	1	16	76%
Romeo et al. [28]	1.5	2	8.5	3	0.5	1	16.5	79%
Van de Ven et al. [38]	1	2	7	1	0.5	2	13.5	64%
Williams et al. [39]	1	1.5	7	1.5	1	2	14	67%
Means	1.6	1.9	7.6	2.4	0.9	1.6	16.0	76%
Multicomponent								
Henderson et al. [54]	2	2	9.5	4	1	2	20.5	98%
Jennings et al. [40]	1.5	2	6	2	1	2	14.5	69%
Jutkowitz et al. [43]	1	1	12	3	2	1	20	83%
MacNeil Vroomen et al. [35]	1.5	2	9	3	1	2	18.5	88%
Michalowsky et al. [33]	1.5	2	9	4	1	1.5	19	90%
Mostardt et al. [32]	1	1	6.5	3	0.5	1	13	62%
Pizzi et al. [41]	2	1.5	7	3	1	2	16.5	79%
Pizzi et al. [42]	1.5	1.5	6	3	1	2	15	58%
Pizzo et al. [30]	2	2	9	2	0.5	2	17.5	65%
Radke et al. [57]	1	2	8.5	4	1	2	18.5	88%
Rosenvall et al. [45]	1	2	6.5	4	2	1	16.5	69%
Saxena et al. [52]	2	2	8.5	2	0.5	2	17	81%
Means	1.5	1.8	8.1	3.1	0.9	1.9	17.2	80%
Exercise								
D'Amico et al. [21]	1.5	1.5	9	3	1	2	18	86%
Davis et al. [51]	2	2	10	3	1	2	20	95%
Lamb et al. [25]	1.5	2	9	4	1	2	19.5	93%
Pitkälä et al. [46]	1.5	2	8.5	3	1	2	18	86%
Sopina et al. [48]	1	1.5	7.5	3	1	0	14	67%
Van Santen et al. [37]	1.5	2	7	3	0.5	2	16	76%
Means	1.5	1.8	8.5	3.2	0.9	1.7	17.6	84%
Other								
Ghani et al. [53]	2	2	8.5	4	0.5	2	19	90%
Howard et al. [29]	2	2	8.5	4	1	1	18.5	88%
Means	2.0	2.0	8.5	4.0	0.8	1.5	18.8	89%

CHEERS Consolidated Health Economic Evaluation Reporting Standards

[a]13 items assessed for Rosenvall et al. and Jutkowitz et al. modelling studies

Table 7 (continued)

[b]4 items assessed for Rosenvall et al. and Jutkowitz et al. modelling studies

cost savings for two of these interventions [41, 42], the third intervention was dominated by TAU [30].

Rosenvall et al. and Jutkowitz et al. each undertook modelling simulation evaluating interventions to delay transition to long-term care [43, 45]. Rosenvall et al. demonstrated potential cost-effectiveness through care management, family support and rehabilitation interventions to delay cognitive decline and transition to long-term care [45]. The Jutkowitz et al. modelling simulation also demonstrated potential cost-effectiveness; they modelled four interventions, including two targeting caregivers' education/support and two targeting assessment/management of PWD, and found that all showed small QALY improvements and increased time spent at home [43].

Saxena et al. undertook an evaluation comparing a primary care dementia clinic with a hospital-based memory clinic in Singapore [52]. QALYs were higher for the primary care clinic, and the ICER at 12 months was S$29,042 (Singapore dollars) per QALY (less than the assumed threshold of S$78,690). The authors concluded that the care provided by the primary care clinic had similar effectiveness to that provided by a hospital clinic, suggesting that these clinics could be cost-effectively set up elsewhere in primary care.

Henderson et al. conducted an evaluation on a non-randomised study of meeting centres providing day support [54]. The evaluation had a short 6-month time horizon; it was rated highest for reporting quality by CHEERS at 98%, but the intervention was not cost-effective in terms of QALYs.

3.4.4 Exercise Interventions

Six RCTs on the effect of physical activity on PwD were evaluated. One intervention included people living in nursing homes [21]; the rest focused on people living in the community [25, 37, 46, 48, 51]. The majority of evaluations were of group-based exercise outside of the home.

None of the interventions demonstrated cost-effectiveness in terms of QALYs; however, two showed improvements in primary outcomes [46, 51]. Davis et al. reported that resistance and aerobics dominated balance and toning in terms of seconds gained/lost on Stroop test of cognitive function and were less costly [51]. In Pitkälä et al., both home exercise and group exercise intervention groups demonstrated a significantly slower decline in functioning measured by Functional Independence Measure (FIM) (−7.1 and −10.3 FIM change, respectively) than the control group (−14.4 FIM change) without increasing the total costs of health and social services [46].

3.4.5 Assistive Technology Interventions

Howard et al. evaluated a telecare and assistive technology intervention, which was not cost-effective in terms of QALYs and did not enable PwD to live safely at home for longer [29]. Ghani et al. evaluated an app for people with MCI and their carers [53]. The results of the cost-effectiveness analysis were inconclusive but suggest the intervention may be more beneficial for carers than PwD.

4 Review of Reviews

Alves et al. undertook a systematic review of five RCTs on the efficacy and feasibility of cognitive interventions for those with Alzheimer's disease [8]. The review included cognitive stimulation, cognitive training and cognitive rehabilitation. It was rated as critically low for confidence in quality using AMSTAR 2, with several critical domains not being fully met. Only one relevant economic evaluation of cost-effectiveness was identified: in the cognitive intervention category, a programme of cognitive stimulation for PwD living either at home or in nursing homes (participant numbers not stated). The intervention was not reported as cost-effective.

Home support interventions for PwD living in the community were systematically reviewed by Clarkson et al. [12]. The review included 14 economic evaluations; six of these evaluated only carer outcomes and as such were excluded here. The economic evaluation by Pitkälä et al. [46] was reviewed by Clarkson et al.; it has already been reviewed in this paper (see Sect. 3.4.4) and will not be discussed here again to avoid duplication. The remaining seven relevant economic evaluations looked at interventions across several categories: training (dementia care mapping), cognitive (activity sessions), multicomponent (occupational therapy, dementia care management $n = 2$) and other (specialist dementia day care, home care compared to care home). Only occupational therapy was reported to show cost-effectiveness. Confidence in the Clarkson et al. review was rated as critically low for confidence in quality using AMSTAR 2 and did not fully meet all critical domains.

As part of a systematic review of interventions to reduce agitation in older adults with dementia in any setting,

Livingston et al. [10] identified an economic evaluation by Norman et al. evaluating a comparison of dementia care mapping and person-centred care [60]. Economic outcomes were measured using Cohen-Mansfield Agitation Inventory (CMAI) scores. Norman et al. reported that for person-centred care relative to usual care there were costs of A$6.43 (Australian Dollars) per CMAI point averted, for the dementia care mapping intervention, the costs were higher at A$46.89 [60]. The summary economic measure for this evaluation was cost per CMAI score change; further data on the effectiveness of this intervention were not available within the review.

Additionally, as part of the review, Livingston et al. created a simulation model using the most effective strategies identified from an effectiveness review of 30 studies of wide-ranging dementia therapies and existing patient cohort data [10]. Modelling of a multicomponent intervention for participants with mild to moderate dementia revealed 82% probability of cost-effectiveness at a maximum WTP threshold of £20,000/QALY. However, due to the multicomponent nature, it was not possible to determine which particular component of the intervention was most effective. This review rated high for confidence in quality using AMSTAR 2.

The Nickel et al. review [3] of interventions for PwD and their carers contained three evaluations in our physical activity intervention category [21, 46, 51] and three cognitive interventions [19, 20, 22] that were relevant to this systematic review. The evaluations contained in this review have already been individually identified through the literature review, and methods and results are discussed above. The review rated critically low for confidence in quality using AMSTAR 2.

5 Discussion

5.1 Summary of Main Findings

This paper reviewed economic evaluations of a wide range of interventions for dementia and MCI. These interventions took place around the world in community and nursing home settings.

Of the 37 evaluations and four reviews evaluated in this paper, 16 interventions demonstrated evidence to favour interventions, although some of these had limitations. The category with the greatest number of interventions showing evidence of cost-effectiveness was multicomponent interventions. Eight of the 16 multicomponent interventions were cost-effective in terms of QALYs gained compared to TAU. Case management showed evidence of cost-effectiveness in both evaluations; each of these evaluations rated 'moderate' for usefulness [32, 35]. However, one of these was rated 'low' in the CHEERS assessment of reporting quality and did not report cost-effectiveness in terms of QALYs [32]. Occupational therapy and dementia care management showed evidence of cost-effectiveness in over 60% of the evaluations [40, 45].

MCST demonstrated strongest evidence of cost-effectiveness, and results were reported using QALYs. Both interventions were cost-effective in terms of QALYs compared to TAU [20, 26]. They both scored 'moderate' for usefulness [20, 26], and D'Amico et al. scored highly for CHEERS reporting quality [20]. Overall conclusions should be interpreted with caution, however, as only two evaluations of MCST were available. As previously mentioned, group CST is already recommended as an intervention [7] and has been proven to be cost-effective in a large-scale study outside of the timeframe of this review [61]. However, the economic evaluation of CST was not found to be cost-effective [22], and overall, the cognitive interventions category did not demonstrate good evidence of cost-effectiveness.

There was also evidence for care home and nursing home staff training interventions. Of the training evaluations evaluated, 62% showed evidence of cost-effectiveness in terms of QALYs or showed significant patient benefits [24, 27, 28, 36, 39], and a sixth intervention was cost neutral [38].

Limitations were identified in some of the evaluations, and evidence was weakened by the small number of evaluations per intervention, small sample sizes, short timeline or reliability of evidence. Four of the evaluations reporting cost-effectiveness did not use an RCT design, and this could have led to biased estimates of effect [32, 35, 50, 52]. The generalisability of the sample to the wider population was a potential issue in two evaluations as the study population was limited to a rural community [33, 34]. Five of the cognitive evaluations took place in the same country, which may lead to a geographical bias [19, 20, 22, 23, 26].

5.2 Limitations

Despite the broad search terms used, it is possible that some economic evaluations may have been missed. There may be an element of publication bias, as it is acknowledged that authors may be less willing to publish evaluations that do not demonstrate cost-effectiveness or cost savings.

Synthesising evidence from evaluations and reviews evaluating a wide range of interventions presented challenges. Due to the variety of outcome measures used, the heterogeneity of the study methods and the variety of different interventions, it was difficult to compare the cost-effectiveness

of different interventions. The lack of WTP thresholds for different countries made it difficult to compare the ICERs between countries.

The review was also hampered by a lack of robust economic evidence generally for non-pharmacological studies. This in turn resulted in limited evidence for each category of intervention.

It is acknowledged that the revised AMSTAR 2 tool that evaluated the systematic reviews was not published until after a number of the reviews had been published, and this may have negatively impacted on the scores received.

5.3 Recommendations for Future Research

Our review excluded carer-targeted interventions; it is acknowledged that there may be interventions that improve health or quality of life of PwD in ways considered to be cost-effective, even though those consequences would be secondary to the impact on carers. Also, if carer health and costs are taken into account, this could change results.

It was noted that evaluations tended to not analyse the distribution of costs, effects and cost-effectiveness across population subgroups. Given the wide inequalities in the experiences of PwD in terms of time to diagnosis and access to dementia services, for example, future research could focus on these areas.

The results of the review demonstrate gaps in the economic evidence on non-pharmacological interventions that could benefit from further research. There was limited evidence shown for multicomponent cognitive evaluations and CBT. Additionally, economic evaluations of creative and sensory therapies were not found in the literature review. Further high-quality research would evaluate whether these interventions are cost-effective.

6 Conclusion

MCST was evaluated as having the strongest evidence of cost-effectiveness, although the number of economic evaluations was small. Case management, occupational therapy and dementia care management also showed good evidence of cost-effectiveness. More economic evidence on the cost-effectiveness of dementia care interventions is needed, with consistency of study methods and outcome measures, to inform policy and local and national decision makers future decision making. This could improve decision makers' confidence to promote cost-effective dementia interventions in the future.

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Declarations

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