



Review Article

Systematic overview of economic evaluations of health-related rehabilitation

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Abstract

Background: Health related rehabilitation is instrumental in improving functioning and promoting participation by people with disabilities. To make clinical and policy decisions about health-related rehabilitation, resource allocation and cost issues need to be considered.

Objectives: To provide an overview of systematic reviews (SRs) on economic evaluations of health-related rehabilitation.

Methods: We searched multiple databases to identify relevant SRs of economic evaluations of health-related rehabilitation. Review quality was assessed by AMSTAR checklist.

Results: We included 64 SRs, most of which included economic evaluations alongside randomized controlled trials (RCTs). The review quality was low to moderate (AMSTAR score 5–8) in 35, and high (score 9–11) in 29 of the included SRs. The included SRs addressed various health conditions, including spinal or other pain conditions ($n = 14$), age-related problems (11), stroke (7), musculoskeletal disorders (6), heart diseases (4), pulmonary (3), mental health problems (3), and injury (3). Physiotherapy was the most commonly evaluated rehabilitation intervention in the included SRs ($n = 24$). Other commonly evaluated interventions included multidisciplinary programmes (14); behavioral, educational or psychological interventions (11); home-based interventions (11); complementary therapy (6); self-management (6); and occupational therapy (4).

Conclusions: Although the available evidence is often described as limited, inconsistent or inconclusive, some rehabilitation interventions were cost-effective or showed cost-saving in a variety of disability conditions. Available evidence comes predominantly from high income countries, therefore economic evaluations of health-related rehabilitation are urgently required in less resourced settings. © 2015 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Key words: Health-related rehabilitation; Economic evaluation; Cost-effectiveness; Systematic review

Health-related rehabilitation, defined as “a set of health care measures that assist individuals, who experience or are likely to experience disability, to achieve and maintain optimal functioning in interaction with their environments,” is instrumental in improving functioning and promoting participation by people with disabilities.¹ It is extremely diverse, in terms of target population (children, adults and older people with a wide range of health conditions),

interventions (rehabilitation medicine, orthopedic surgery, physiotherapy, speech and language therapy, occupational therapy, assistive devices) and outcomes. Further development and improvement of health-related rehabilitation services are required, because they remain under-funded, under-researched, and under-provided in many contexts, particularly in low and middle income countries.¹

To make clinical and policy decisions about health-related rehabilitation interventions, resource allocation and cost issues need to be considered.^{2–4} Economic evaluations may be defined as “the comparative analysis of alternative courses of action in terms of both their costs and their consequences.”⁵ Depending on how the consequences of health care interventions are measured, full economic evaluations can be categorized as cost-effectiveness analysis (CEA), cost-utility

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analysis (CUA), and cost-benefit analysis (CBA). In cost-effectiveness analysis, the health consequences are measured in a single natural unit (e.g., life years gained, improvement in activity of daily living). For cost-utility analysis, health outcomes are measured in a comprehensive unit representing quantity and quality of life (such as QALYs or DALYs). A cost-benefit analysis converts all consequences of an intervention to their monetary equivalent, so that money units become the common currency to compare across alternatives.

By systematically identifying, assessing and synthesizing results of all relevant studies, bias could be minimized in well conducted systematic reviews (SRs).⁶ More recently, overviews of SRs have been increasingly used to summaries research evidence relevant to a wide range of health interventions.^{7,8} To support the development of the World Health Organization (WHO) Guidelines on Health-related Rehabilitation,⁹ we systematically synthesized research evidence on cost-effectiveness and cost-benefit of health-related rehabilitation. A focus for the overview was to identify research evidence from less resourced settings defined as “a geographical area with limited financial, human and infrastructural resources to provide rehabilitation (a common situation in low- and middle-income countries, but also in certain areas of high-income countries).”^{9,10} This paper presents findings from an overview of SRs of economic evaluations on health-related rehabilitation interventions.

Methods

The objectives of the overview of SRs were specified by the following:

- Population: Target population include all individuals who experience, or are likely to experience, disability.
- Interventions: Any health-related rehabilitation interventions were eligible, according to the WHO definition.¹
- Comparisons: No rehabilitation or different rehabilitation interventions.
- Rehabilitation outcomes: Decreased length of hospital stay; increased independence; decreased burden of care; return to role/occupation, other functional or physical outcome related to the specific condition; quality of life.
- Cost outcomes: Intervention costs, health resource use, and societal costs; cost-effectiveness, cost-utility or cost-benefit.

Inclusion and exclusion criteria

The overview included SRs of relevant studies which might be randomized controlled trials (RCTs), non-randomized studies (NRS), or economic modeling. To be included, an SR should have:

- Defined review question(s) and inclusion/exclusion criteria that are relevant in terms of the PICO

framework (cost-effectiveness or cost-benefits of health-related rehabilitation)

- Reported the literature search strategy
- Assessed study quality or risk of bias in results of the included economic evaluation studies
- Provided the main characteristics of the included studies

The above inclusion criteria were sometime relaxed in order to include some relevant but less rigorously conducted review articles.

We excluded:

- SRs published in languages other than English, because of resource/time restrictions.
- Conference abstracts without full reports.
- Previous versions of an SR for which a more updated version of the same review was available (for example, updated Cochrane SRs).
- A single economic evaluation based on results of SRs of effectiveness.
- SRs of interventions that focused on the general population, substance abuse and drug use, rehabilitation services delivered by different sectors i.e. vocational rehabilitation under the Ministry of Labour.
- SRs that evaluated only pharmaceutical, surgical, or behavioral interventions, in which the intervention was not explicitly described as a rehabilitation intervention.

Search strategy

We conducted a comprehensive literature search on 11th February 2014, by searching the following databases: PubMed, EMBASE, AMD, CIHAHL, PsycINFO, Web of Science (SCI and SSCI), PEDro, and NHS EED. The search strategy included “rehabilitation,” “economic evaluation,” “systematic review,” and their related terms. We also identified some relevant SRs in a previously conducted scoping literature review (September 2013). See [Online Appendix A](#) for the strategy for searching MEDLINE, EMBASE and AMED via Ovid. We also checked references of identified SRs and conducted a focused citation literature search to identify more recently published SRs when considered important.

After excluding duplicate citations from multiple databases, we screened titles and abstracts of retrieved references to identify possibly relevant SRs. We then examined full texts of possibly relevant SRs to identify studies for inclusion. Literature search and selection were carried out by two independent reviewers (SHW and LI or FS), and any disagreements were resolved through discussion between these two or by involving a third reviewer.

Quality assessment, data extraction and synthesis

We used the AMSTAR assessment tool to assess the methodological quality of included SRs.¹¹ Two

independent reviewers (SHW, LI, HF, or FS) assessed the review quality and extracted data from the included SRs, using a data extraction sheet (pre-tested using two relevant SRs). Any disagreements were resolved by discussion between two reviewers or the involvement of a third reviewer.

Study characteristics information was drawn from data extraction forms and reported separately for each SR in evidence summary tables. Findings were narratively described. In accordance with Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines,¹² we intended to provide a summary table of evidence profile for each of the rehabilitation interventions included in the overview of SRs. However, data from the included SRs of economic evaluations were generally inadequate or inappropriate to use the GRADE framework.

Results

The search of multiple bibliographic databases retrieved a total of 880 citations after excluding duplicate records. By checking titles and abstracts, we found 99 records that were potentially eligible. In addition, 15 potentially relevant records were identified from a scoping literature review we previously conducted and the bibliographies of included studies. After examining the full text of 114 records, we included 64 SRs that met the inclusion criteria (Fig. 1).^{13–76} References of excluded records and reasons for exclusion are shown in [Online Appendix B](#).

General quality of the included systematic reviews

Details on the AMSTAR quality assessment of included SRs are presented in [Online Appendix C](#). In terms of review methods used, the quality of the included SRs was generally good. Out of the 11 AMSTAR questions, the review quality was low to moderate (score 5–8) in 55% ($n = 35$), and high (score 9–11) in 45% ($n = 29$) of the

included SRs. Seven SRs scored the maximum (11), denoting excellent methodological quality in SR reporting (see [Online Appendix C](#)). [Table 1](#) shows the summary results of the AMSTAR assessment in terms of answers to each of the 11 specific questions. The probability of publication bias was considered in only 13 (21%) SRs. Study selection and data extraction were conducted independently by two reviewers in 31 (51%) of the included SRs. Only published studies were included in more than half of the included SRs (57%).

Most of the 64 SRs included randomized controlled trials (RCTs) that provided data on costs and cost-effectiveness. Tools used for the assessment of general study quality included Cochrane Collaboration checklist⁷⁷ (in 17 SRs), the Physiotherapy Evidence Database (PEDro) scale⁷⁸ (in 6 SRs), and other or unclear methods (in 24 SRs). Thirty of the 64 SRs specifically assessed the quality of economic evaluations, using Drummond's checklist⁷⁹ (in 14 SRs), Consensus on Health Economic Criteria (CHEC)⁸⁰ (in 11 SRs), or other methods (in five SRs). The GRADE tool¹² was used in only three SRs^{21,34,41} and one of the three applied the GRADE tool to effectiveness evidence only.³⁴

The main characteristics of included systematic reviews

The main characteristics of the included SRs are presented in [Online Appendix D](#). The included SRs were published from 1999 to 2013 ([Fig. 2](#)), and 52% ($n = 33$) were published since 2011.

Of the 64 SRs, 51 included studies published only in English language. Only eight included any studies from low and middle income countries (LMICs), in which a total of 13 studies in LMICs were included (11 from China and two from India).

Forty-one of the 64 included SRs focused on economic evaluations, and the remaining 23 SRs considered both clinical and cost-effectiveness. Studies of the full economic evaluation (cost-effectiveness or cost-utility analysis) were included in 40 of the 41 SRs that focused on economic evaluations. Economic evaluation was often only a small part of SRs that considered both effectiveness and costs or cost-effectiveness; only cost-analysis was reported in seven of the 23 such SRs.

The included SRs addressed various health conditions, including spinal or other pain conditions ($n = 14$), age-related problems (11), stroke (7), musculoskeletal disorders (6), heart diseases (4), pulmonary (3), mental health problems (3), and injury (3) ([Table 2](#)). Physiotherapy was the most commonly evaluated rehabilitation interventions in the included SRs of economic evaluations ($n = 24$) ([Table 3](#)). Other commonly evaluated interventions included multidisciplinary programmes (14); behavioral, educational or psychological interventions (11); home-based interventions (11); acupuncture (7); complementary

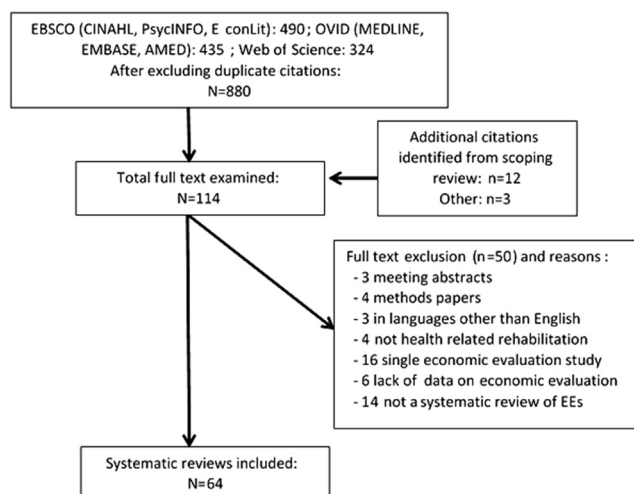


Fig. 1. Selection of relevant systematic reviews of economic evaluations of health-related rehabilitation.

Table 1
Summary results of AMSTAR assessment of included systematic reviews

AMSTAR questions	Yes	No/unclear
1. Was an <i>a priori</i> design provided?	64 (100%)	0
2. Was there duplicate study selection and data extraction?	34 (53%)	30 (47%)
3. Was a comprehensive literature search performed?	63 (98%)	1 (2%)
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	26 (41%)	38 (58%)
5. Was a list of studies (included and excluded) provided?	60 (94%)	4 (6%)
	(48 with included studies only)	
6. Were the characteristics of the included studies provided?	59 (92%)	5 (7%)
7. Was the scientific quality of the included studies assessed and documented?	49 (77%)	15 (23%)
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	48 (75%)	16 (25%)
9. Were the methods used to combine the findings of studies appropriate?	64 (100%)	0
10. Was the likelihood of publication bias assessed?	13 (20%)	51 (80%)
11. Was the conflict of interest included?	42 (66%)	22 (34%)

therapy (6); self-management (6); and occupational therapy (4). Primary care by GPs and surgical interventions were each evaluated in three and five SRs.

Economic evidence by conditions

Evidence from SRs of economic evaluations for health-related rehabilitation interventions is summarized in Table 4, in which more recently published SRs were cited when there were multiple reviews on the same topic. Findings were only briefly described for selected conditions and rehabilitation interventions, because of the large number of heterogeneous conditions and interventions included in the overview.

Pain and musculoskeletal disorders

SRs reported only limited and often inconsistent evidence on cost-effectiveness or cost-utility of different rehabilitation interventions, such as conservative treatments for neck pain,³² spinal manipulation for back or neck pain,⁵³ and interventions for ankylosing spondylitis.³⁶

An SR of guideline-endorsed interventions for lower back pain (LBP) reported that “interdisciplinary rehabilitation, exercise, acupuncture, spinal manipulation or cognitive behavioral therapies were cost-effective in people

with sub-acute or chronic LBP.”⁴⁹ However, “massage alone is unlikely to be cost-effective,” and evidence was inconsistent or insufficient for advice and spinal manipulation in acute LBP.⁴⁹

The cost-effectiveness of self-management of pain conditions was inconclusive when the effect was measured by the QALY metric.¹⁶ For patients with arthritis, self-management education (SME) interventions may improve health outcomes and many forms of SME interventions were relatively low cost to deliver.¹⁸ A few available full economic evaluations from the societal perspective, including not only health care costs but also patient out-of-pocket costs and lost productivity, were more encouraging about the cost-effectiveness of SME interventions.¹⁸

Available evidence indicated that exercise programmes were cost-effective, when QALYs were the clinical

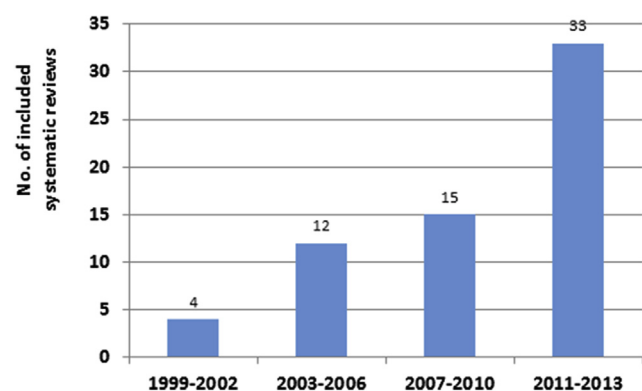


Fig. 2. Publication years of included systematic reviews.

Table 2
Main conditions of patients in the included systematic reviews (SRs)

Conditions	No. of SRs
Pain	14
Spinal/back	12
Musculoskeletal problems	6
Stroke	7
Heart diseases	4
Geriatric conditions	11
General	7
Fracture	2
Dementia	2
Pulmonary disease	3
Asthma	2
COPD	1
Mental illness	3
Dementia	2
Depression	1
Injury	3
Fracture	2
Ankle sprains	1
Multiple sclerosis	1
Hearing impairment	3
Speech/language disorders	1
Cancer	1
Variou/mixed	12

Not exclusive; more than one condition may be considered in an SR.

Table 3

Health-related rehabilitation interventions evaluated in the included SRs	No. of SRs
Rehabilitation interventions	
Physiotherapy	24
Multidisciplinary	14
Psycho-educational, behavioral	11
Home-based programme	11
Self-management	6
Occupational therapy	4
Early supported discharge	3
Tele-rehabilitation	1
General practitioner care	3
Surgery	5
Speech and language therapy	2
Complementary therapy	6
Acupuncture	7
Implementation of guidelines	1
Various/mixed	18
Lower limb prosthesis	1

More than one intervention may be evaluated in an SR.

outcome, although there was very limited evidence on patient education and conservative interventions for hip or knee osteoarthritis.⁵⁷

Stroke rehabilitation

The cost-effectiveness of early supported discharge (ESD) of stroke patients was evaluated in four SRs.^{17,65,68,74} Economic evaluations of ESD usually included costs of hospital in-patient care (length of stay and readmission), institutional or nursing home care, rehabilitation, social services, patient and informal care givers. A recently published SR found consistent evidence from six RCTs (good quality by Drummond criteria), indicating that the costs of ESD were 4%–30% lower than usual care, with similar clinical outcomes.⁶⁸ This SR also reported that home-based rehabilitation was associated with higher costs (although statistically non-significant) than usual care (such as hospital based or standard home care services) in three of the four included studies.⁶⁸ Although the costs may not be necessarily reduced, the effectiveness in terms of activities of daily living and quality of life may be improved by home-based rehabilitation programmes.⁶⁸ Another SR reported that “cost-effectiveness (direct costs) was found to be better with home-based care in two of the three studies that considered this.”⁸¹ Therefore, the cost-effectiveness of home-based stroke rehabilitation may depend on variables such as severity of disability, effectiveness and costs of the intervention and usual care services.

Cardiac rehabilitation

Exercise training is considered as a necessary component, and it is usually the main cost driver of cardiac rehabilitation (CR) programmes. For patients with myocardial infarction, heart failure, revascularization or percutaneous coronary surgery, there was evidence that supervised or

home-based CR interventions were more cost-effective than no cardiac rehabilitation.⁷⁵ However, there were no significant differences in clinical outcomes and costs between center-based and home-based cardiac rehabilitation interventions.⁷⁵

Patient education to change health behaviors is one of the three core modalities for cardiac rehabilitation (alongside exercise training and psychological support). In patients with coronary heart diseases, evidence (though inconclusive) suggested that education may improve health-related quality of life and reduce overall health care costs.¹⁹ Similar findings were reported in another review of the Heart Manual as a self-help home-based cardiac rehabilitation intervention.²⁶

Rehabilitation of older people

Older people in general

A Cochrane SR assessed the benefits and harms of physical rehabilitation interventions for older people in long-term care, and found that available evidence was insufficient to make conclusions about improvement sustainability, cost-effectiveness, or what were the most appropriate interventions.²⁸

For older people living in the community, available evidence suggested three effective and cost-saving falls prevention strategies: (1) an individually customized multifactorial programme in those with more than four out of eight targeted fall risk factors; (2) a home-based Exercise Programme in people aged over 80 years; and (3) a home safety programme in the subgroup with a previous fall.³⁰ It was concluded that targeting falls prevention strategies at high-risk groups was best value for money.

Local authority (an administrative unit of local government) based occupational therapy services in the UK (delivering interventions such as housing adaptations and equipment service) were assessed in a review.¹⁵ It was reported that occupational therapy in social care could save costs of other social care services, and was cost-effective in terms of improved quality of life for older people and their carers.¹⁵

Fracture in older people

As an overall strategy for rehabilitation after hip and other lower limb fractures, geriatric orthopedic rehabilitation units were unlikely to be cost-effective, although for some frailer patients it may reduce readmission and nursing home placement.²² Geriatric hip fracture programme and early supported discharge were probably cost-effective, by reducing length of hospital stay, and increasing rates of return to previous residential status.²² For older people with hip fracture, patients receiving multidisciplinary (MDP) rehabilitation tended to have better (though statistically non-significant) clinical outcomes, and costs were slightly increased in the intervention group compared with the usual care.³⁸

Table 4
Summary of economic evidence for health-related rehabilitation interventions from updated systematic reviews

Condition: rehabilitation intervention	Available SRs	Design and no. of included studies	Main conclusions
Pain and other musculoskeletal conditions			
Spinal/back pain: Non-operative and operative interventions	Indrakanti et al (2012) ⁴¹	27 studies (25 RCTs): Strong single-study evidence	<ul style="list-style-type: none"> • Consistent evidence indicated that operative interventions were cost-effective for treating spinal disorders involving nerve compression and instability. • For non-operative interventions, strong single-study evidence indicated that: <ul style="list-style-type: none"> - Graded activity was more cost-effective than physical therapy and pain management, - Cognitive behavioral and physiotherapy were more cost-effective than advice only, - Acupuncture, exercise and neuroreflexotherapy were more cost-effective than usual care, - Spinal manipulation was more cost-effective than exercise.
Low back pain: Various guideline-endorsed treatments	Lin et al (2011) ⁴⁹	26 RCTs with economic evaluations	<ul style="list-style-type: none"> • There was evidence supporting the cost-effectiveness of the guideline-endorsed treatments of interdisciplinary rehabilitation, exercise, acupuncture, spinal manipulation and cognitive behavioral therapy for sub-acute or chronic LBP. • There was little evidence for other treatments, advice, medication, spinal manipulation for acute LBP, and massage, yoga or relaxation for chronic LBP.
Spinal pain: Spinal manipulation	Michaleff et al (2012) ⁵³	6 RCTs with full economic evaluations	<ul style="list-style-type: none"> • Inconclusive, mostly single-study, evidence indicated that spinal manipulation was cost-effectiveness to manage back or neck pain.
Neck pain: Various conservative treatments	Driessen et al (2012) ³²	5 RCTs with economic evaluations	<ul style="list-style-type: none"> • Limited and heterogeneous evidence was insufficient to decide the cost-effectiveness of conservative treatments for non-specific neck pain.
Chronic pain-geriatric: Self-management support	Boyers et al (2013) ¹⁶	10 RCTs with economic evaluations (6 CUAs)	<ul style="list-style-type: none"> • Inconclusive evidence indicated that self-management may be cost-effective for older people with chronic pain conditions
Ankylosing spondylitis: Therapeutic interventions	Gaujoux-Viala & Fautrel (2012) ³⁶	13 RCTs or modeling studies	<ul style="list-style-type: none"> • The cost-effectiveness ratio of interventions for ankylosing spondylitis (including spa exercise, group physical therapy) remain within an acceptable range (e.g., <£30,000/QALY).
Arthritis: Self-management education	Brady (2012) ¹⁸	11 studies (8 cost analysis, 3 full cost-effectiveness analysis)	<ul style="list-style-type: none"> • Self-management education programmes may improve health outcomes at relatively low cost to deliver • Full economic evaluations from a societal perspective (including patient out-of-pocket costs and lost productivity) provided more encouraging evidence on the cost-effectiveness of the programme.
Osteoarthritis (hip/knee): Non-pharmacologic, non-surgical interventions	Pinto et al (2012) ⁵⁷	11 RCTs or quasi-RCTs with economic evaluations	<ul style="list-style-type: none"> • Exercise programmes were cost-effective when QALYs was the clinical outcome. • There was very limited economic evidence on patient education and conservative interventions for hip or knee osteoarthritis

(Continued)

Table 4
Continued

Condition: rehabilitation intervention	Available SRs	Design and no. of included studies	Main conclusions
Stroke rehabilitation			
Stroke survivors: Integrated care: Early supported discharge, home-based rehabilitation, stroke unit, and stroke service	Tummers et al (2012) ⁶⁸	12 RCTs and 3 non-randomized studies with economic evaluations	<ul style="list-style-type: none"> • Consistent evidence indicated that early supported discharge was 4–30% less costly compared with usual care, at similar clinical outcomes. • Home-based rehabilitation was unlikely to be cost-saving, but may improve health outcomes, compared with center-based rehabilitation. • Stroke unit care was more expensive but associated with improved clinical outcomes, compared with conventional inpatient stroke care. • Integrated stroke services (e.g., extended stroke unit service, stroke unit linked to continued care in geriatric units) may reduce health care costs
Stroke survivors: Inpatient rehabilitation	Brusco et al (2014) ²¹	RCTs with economic evaluations	<ul style="list-style-type: none"> • High quality evidence (from 4 RCTs with 732 patients) indicated that inpatient rehabilitation was more costly than rehabilitation in the home, for patients with moderate to severe stroke and with an appropriate home environment and adequate social support. The health outcomes were similar or in favor of rehabilitation in the home. • Moderate quality evidence (from 3 RCTs with 463 patients) indicated that stroke unit care was less costly compared with general acute care, with improved patient outcomes.
Cardiac rehabilitation			
Heart diseases: Exercise training based cardiac rehabilitation	Wong et al (2012) ⁷⁵	16 economic evaluations alongside trials or modeling studies	<ul style="list-style-type: none"> • There was evidence that supervised or home-based cardiac rehabilitation interventions were more cost-effective than no cardiac rehabilitation, for patients with myocardial infarction and heart failure. • There were no significant differences in clinical outcomes and costs between center-based and home-based cardiac rehabilitation interventions.
Dementia and Alzheimer disease			
Dementia: Various interventions	Knapp et al (2013) ⁴⁵	59 reviews and 29 primary studies	<ul style="list-style-type: none"> • Cognitive stimulation therapy, tailored activity programmes and occupational therapy were cost-effective compared with usual care. • According to data from some of the included studies, the following interventions may also be cost-effective: Respite care in day settings, psychosocial interventions for carers, coordinated care management, and personal budgets held by carers
Geriatric rehabilitation			
Older people living at home: Falls prevention strategies	Davis et al (2010) ³⁰	9 trials with economic evaluations	<ul style="list-style-type: none"> • Targeting falls prevention strategies at high-risk groups was associated with best value for money, e.g.: <ul style="list-style-type: none"> - An individually customized multifactorial programme in those with more than 4 out of 8 targeted fall risk factors - Home-based safety or exercise programmes in people > 80 years, or in those with a previous fall

(Continued)

Table 4
Continued

Condition: rehabilitation intervention	Available SRs	Design and no. of included studies	Main conclusions
Pulmonary rehabilitation			
Adults with COPD: Multi-component chronic care programmes	Steuten et al (2009) ⁶²	17 studies (14 RCTs), only 3 provided data on costs	<ul style="list-style-type: none"> • Programmes containing at least 3 components reduced hospitalization, compared with usual care. • It was unlikely that multi-component COPD programmes could be cost-saving
Injury			
Lateral ankle sprains: Diagnosis, treatment and prevention interventions	Lin et al (2013) ⁵⁰	10 economic evaluations alongside RCTs or modeling studies	<ul style="list-style-type: none"> • The available evidence indicated that the following interventions may be cost-effective: <ul style="list-style-type: none"> - Implementation of the Ottawa ankle rules (OAR) in the emergency setting - Use of anti-inflammatory medication and the plaster cast in the acute phase - Prescription of neuromuscular exercises to prevent re-injury
Mental disorders			
Workers with mental health problems: Worksite based interventions	Hamberg-van Reenen & Proper (2012) ³⁷	10 studies (6 RCTs)	<ul style="list-style-type: none"> • Worksite interventions to prevent or treat mental health problems might be cost-effective in terms of health outcomes (such as turnover, burnout and mood, hospitalization), productivity, and work performance. • Return to work interventions that included a full economic evaluation aimed at depressed employees were not cost beneficial.
Cancer rehabilitation			
Adult cancer survivors: Multidimensional cancer survivor rehabilitation	Mewes et al (2012) ⁵²	6 economic evaluations alongside RCTs, quasi-trials, and modeling studies	<ul style="list-style-type: none"> • There was no additional benefit in clinical outcomes when a multidimensional program was compared with the mono-dimensional interventions. • Available economic evaluations assessed different rehabilitation interventions, and all showed favorable cost-effectiveness ratios.
Speech and language rehabilitation			
Children with speech, language and communication needs: Various interventions	Law et al (2012) ⁴⁷	5 RCTs with economic evaluations	<ul style="list-style-type: none"> • The inclusion of parental time increased costs considerably • The home-based intervention was less expensive than the clinic-based intervention even adding in the cost of parents
Hearing impairment			
Adults with severe to profound hearing impairment: Cochlear implants	Turchetti et al (2011) ⁶⁹	4 economic evaluations (2 retrospective and 2 prospective cohort studies)	<ul style="list-style-type: none"> • Monolateral cochlear implantation is generally a cost-effective intervention • The mean direct medical costs of monolateral cochlear implantation: € 31,942 (2011 Euro) in prelingually deafened patients, and ranged from € 30,026 to € 45,770 in postlingually deafened patients. • Cochlear implantation is not cost-effective for patients with a period of over 30 years profound deafness in the ear receiving the implant, who have benefited from the use of hearing aids. • Monolateral cochlear implantation was more cost-effective than bilateral cochlear implantation in postlingually deafened patients.

(Continued)

Table 4
Continued

Condition: rehabilitation intervention	Available SRs	Design and no. of included studies	Main conclusions
Children with severe-profound hearing impairment: Cochlear implants	Turchetti et al (2011) ⁷⁰	9 economic evaluation studies (3 prospective, 3 retrospective, and 3 cross-sectional studies)	<ul style="list-style-type: none"> • The direct cost of cochlear implants ranged between € 39,507 and € 68,235 (2011 Euro). • The health care costs are high, but savings in terms of indirect and quality of life costs are also significant. • Cochlear implantation in children is cost-effective.
Multiple disability conditions Various conditions: Complementary and integrative care (CIM)	Herman et al (2012) ³⁹	31 high quality full economic evaluation studies in English, between 2001 and 2010	<ul style="list-style-type: none"> • Study quality of the cost-utility analyses (CUAs) of CIM was generally comparable to that seen in CUAs across all medicine • Of the 56 comparisons made in the higher-quality studies, 16 (29%) show a health improvement with cost savings for the CIM therapy vs. usual care. • Some complementary and integrative therapies were potentially cost-effective or cost-saving • The available evidence consistently indicated that acupuncture treatment was cost-effective for a variety of conditions, including back pain, chronic headache, osteoarthritis, stroke, dysmenorrhea, and allergic rhinitis
Various conditions: Acupuncture	Kim et al (2012) ⁴⁴	17 RCTs with full economic evaluations	<ul style="list-style-type: none"> • The available evidence consistently indicated that acupuncture treatment was cost-effective for a variety of conditions, including back pain, chronic headache, osteoarthritis, stroke, dysmenorrhea, and allergic rhinitis
Lower limb prosthesis Adult amputees: Different lower limb prosthesis	Samuelsson et al (2012) ⁶⁰	1 RCT and 1 case-control study	<ul style="list-style-type: none"> • RCT – Total surface-bearing socket (TSB) vs. conventional patellar tendon bearing socket (PTB): Cost of materials was significantly higher, manufacturing time was significantly shorter, and number of visits was significantly less in the TSB group than in the PTB group. • NRS – Microprocessor control prosthesis (MPknee) vs. mechanical control prosthesis (NMPknee): MPknee CU ratio: euro 35,971/QALY (health care costs); from societal perspective, the costs were similar.

Dementia

A comprehensive review evaluated various interventions in Alzheimer's disease.⁴⁵ There was evidence that acetylcholinesterase inhibitors were cost-effective for mild-to-moderate disease, and memantine for moderate to severe disease. Cognitive stimulation therapy, tailored activity programme and occupational therapy were cost-effective compared with usual care. According to data from some of the included studies, the following interventions may also be cost-effective: respite care in day settings, psychosocial interventions for carers, coordinated care management, and personal budgets held by carers.⁴⁵

Asthma

According to findings from a health technology assessment of psycho-educational interventions in children and adults with severe and difficult asthma,⁶¹ there would be an additional cost of achieving health gain in terms of symptom-free days. In adults the significantly increased

costs of providing an intervention were not offset by any short-term savings in use of health care resources, and neither were they associated with improvements in health outcomes.⁶¹ One SR reported that the use of self-management programs based on peak flow monitoring in patients with asthma was cost-effective or even cost saving.⁷³

Chronic obstructive pulmonary disease (COPD)

An SR evaluated the cost-effectiveness of chronic care programmes (with at least two components) for people with COPD.⁶² The multi-component COPD programmes included, for example, self-management, delivery system design, decision support, and clinical information system. The review included 17 studies (14 RCTs). Fifteen included studies reported data on resource use and only three studies provided data in monetary terms. Methodological quality of the included studies was mostly moderate, according to Drummond checklist. It was reported that programmes

containing at least three components reduced hospitalization compared with usual care, although it was unlikely that multi-component COPD programmes could be cost-saving.⁶²

Cancer rehabilitation

Effectiveness and cost-effectiveness of various cancer rehabilitation interventions were evaluated in an SR.⁵² The review included six studies that provided data on cost-effectiveness, and the study quality was moderate to good according to Drummond checklist. There was no additional benefit in clinical outcomes when a multidimensional program was compared with mono-dimensional interventions. The incremental cost-effectiveness ratios for cancer rehabilitation interventions ranged from cost-saving to €11,057 per QALY, compared with usual care control.⁵²

Children with speech-language (SL) and communication needs

According to an SR of various interventions for children with speech, language and communication needs, limited evidence indicated that the inclusion of parental time increased costs considerably, but that the home-based intervention was less expensive than clinic-based intervention even adding in the cost of parents.⁴⁷

Cochlear implant

An SR of cochlear implants in adults⁶⁹ included four economic evaluation studies. The mean direct medical cost of monolateral cochlear implants was € 31,942 (2011 Euro) in prelingually deafened patients, and it ranged from € 30,026 to € 45,770 in postlingually deafened patients.⁶⁹ A different SR provided a similar conclusion that bilateral implantation in adults is unlikely to be cost-effective.⁸² For cochlear implants in children, the direct cost of cochlear implants ranged between € 39,507 and € 68,235 (in 2011 Euro), and it was reported that “the health care costs are high, but savings in terms of indirect and quality of life costs are also significant.”⁷⁰

Complementary and alternative therapies

An SR of economic evaluations of complementary therapies and integrative care (CIM) identified a total of 338 studies, including 114 full economic evaluations published in English language between 2001 and 2010.³⁹ The review included various interventions, such as acupuncture, manipulative and body-based practices, natural products, and other CIM therapies (tai-chi, spa exercise) for patients with various disability conditions. According to data from 31 high quality full evaluations, some complementary and integrative therapies were potentially cost-effective or cost savings. Of the 56 comparisons made in the higher-quality

studies, 16 showed a health improvement with cost savings for the CIM therapy vs. usual care.³⁹ However, an earlier SR of complementary and alternative medicine (CAM) indicated that some CAM interventions might increase health care costs without further clinical benefit.²⁷

Tele-rehabilitation

Kairy and colleagues (2009) evaluated clinical outcome, health care utilization and costs of tele-rehabilitation.⁴² Tele-rehabilitation was defined as “the use of communication and information technologies to provide clinical rehabilitation services from a distance.” Available evidence indicated that tele-rehabilitation tended to be associated with improved or similar clinical outcomes compared with alternative interventions. Although data on health care utilization was insufficient, preliminary evidence indicated tele-rehabilitation is potentially cost-saving.⁴²

Worksite based disability management interventions

Tomba and colleagues (2008) evaluated the cost consequences of disability management interventions that included some work-place component.⁶⁷ The disability management interventions included occupational, physiotherapy, behavioral, psychosocial, vocational, medical, and ergonomic interventions, for various disorders such as work related injuries and spinal problems. There was strong evidence on the financial benefits of multi-sector disability management interventions, and moderate evidence for interventions with components of education, physiotherapy, and work/vocational rehabilitation.⁶⁷

Inpatient rehabilitation interventions for various conditions

An SR of economic evaluations of adult inpatient rehabilitation was conducted by Brusco and colleagues (2014), which uniquely in the present overview used the GRADE tool for economic evidence quality and quantitative pooling of data on costs.²¹ It was reported that high quality evidence indicated that home-based rehabilitation was cost-saving compared with inpatient rehabilitation for stroke survivors, with similar clinical outcomes. Home-based or community-based rehabilitation may also be less costly compared with inpatient rehabilitation in patients with orthopedic, rheumatoid arthritis, and age-related conditions. Moderate quality evidence was available indicating that stroke unit rehabilitation was associated with lower costs and improved clinical outcomes compared with general acute care interventions. Results of studies in older patients with a mix of various conditions were inconsistent.²¹

Lower limb prosthesis

An SR evaluated the effectiveness of lower limb prosthesis for adult amputees.⁶⁰ The included studies compared

total surface-bearing socket (TSB) and conventional patellar tendon bearing socket (PTB). It was found that cost of materials was significantly higher, manufacturing time was significantly shorter, and number of visits was significantly less in the TSB group than in the PTB group.

Discussion

Although the available evidence is often described as 'limited,' 'inconsistent' or 'inconclusive,' some rehabilitation interventions were cost-effective or showed cost-saving to a variety of disability conditions. For example:

- Rehabilitation interventions were associated with both additional costs and improved clinical outcomes (for example, exercise interventions additional to general practitioners' care for back pain⁴⁸).
- Rehabilitation interventions were associated with lower costs and similar clinical outcomes (for example, early supported discharge of stroke survivors,⁶⁸ and home-based vs. center-based cardiac rehabilitation⁷⁵).
- Rehabilitation interventions were cost-saving by reducing the costs of other health care services (for example, home-based programmes for preventing falls in older people³⁰), or the costs of social care services (for example, occupational therapy for older people¹⁵), or reducing the disability-related productivity loss (for example, worksite-based disability management⁶⁷).

Two specific questions were considered relevant for the development of the WHO Guidelines⁹: (1) what is the evidence for cost-effectiveness of rehabilitation with a focus on both "low cost and high volume" services and "high cost and low volume" services? (2) what would be the cost benefits of different rehabilitation outcomes for the individual, family and society? Findings from the overview may shed light on the two questions.

For the first question, the strong economic gain may result when the health condition is common (such as cardiovascular disease, back pain) and the intervention is low cost (short-term or delivered in the community). For example: self-management education programmes were relatively low cost to deliver and might be cost-effective for patients with chronic arthritis,¹⁸ and other disability conditions.⁵⁸ Tele-rehabilitation interventions may be used to deliver "low cost and high volume" services, as mobile phones have been widely available even in less resourced settings. One SR reported preliminary and inconclusive evidence indicating that tele-rehabilitation might be potentially cost-saving.⁴² Evidence on cost-effectiveness of low cost-high volume services would tend to steer governments away from investing in high technology tertiary centers, and towards solutions which are relevant to prevalent

conditions and which can be delivered in primary care or community settings. However, some speedy interventions can readily be rolled out in less resourced settings, where human resources and funding are available, and can lead to huge improvements in individual wellbeing and functioning. For example, cochlear implantation in children with profound hearing impairment was associated with initial high health care costs but could be cost-saving from societal perspective, because of improved quality of life and reduced educational costs.^{70,83}

A priori it is not possible to say which of the two extreme options, "low cost and high volume" services vs. "high cost and low volume" services, will represent better value for money. Between these two extremes there may be a middle ground of services, and it is at least conceivable that in some cases, it is those interventions that would represent most value for money. Entirely excluding this middle ground would likely miss out on a range of cost-effective interventions, apart from the difficulty of unambiguously drawing a line between, say, what is "high cost and low volume" and what is "not so high cost and not so low volume."

The second question about cost benefits focused on rehabilitation outcomes such as improved independence, reduced resource use, and return to work, although we should not ignore rehabilitation interventions (and related costs) that produce these outcomes. The commonly reported benefits of rehabilitation included a reduction in the use of health or other resources, and an increase in return to work. For example: an exercise-based comprehensive rehabilitation programme for older patients with chronic conditions improved patient's physical capacity and reduced health care utilization.⁸⁴ In adult patients with profound deafness, the economic benefits of unilateral cochlear implantation for patients and society were reported in terms of employment rates and personal income after the operation.⁸⁵ Pediatric cochlear implantation may reduce the cost of education and improve hearing impaired children's academic achievements.^{70,83} For sick listed patients with chronic lower back pain, an integrated care programme (including participatory ergonomics and a graded cognitive behavioral activity) in the Netherlands increased return to work and reduced societal costs.⁸⁶

Because of huge diversity in disability conditions and types of interventions, it is impossible to estimate the overall cost-effectiveness and cost-benefits of health-related rehabilitation services.⁸⁷ For example, in a methodologically rigorous SR, Brusco and colleagues concluded that "a single rehabilitation service may not provide health economic benefits for all patient groups and situations."²¹ The implicit acceptable thresholds for a cost-effectiveness ratio were reported to be \$US 50,000 per QALY gained for the USA, £30,000 in the UK, and €80,000 for the Netherlands.⁸⁸ Authors of several SRs explicitly mentioned that the estimated cost-effectiveness ratios for some rehabilitation interventions were within the range of

internationally acceptable cost-effectiveness ratio thresholds, or comparable with many conventional medical treatments.^{36,76} Therefore, the cost-effectiveness evidence supports the view that health-related rehabilitation services should have similar priority to conventional medical treatments in health care systems.

Quality of evidence

SRs of economic evaluation studies have more methodological challenges than SRs of effectiveness of health care interventions.^{89–91} According to the results of AMSTAR assessment, the review quality was low to moderate (score 5–8) in 55% ($n = 35$) of the included SRs, and high (score 9–11) in 45% ($n = 29$) of the included SRs. A large proportion of included SRs were satisfactory in terms of a comprehensive literature search (98%) and providing the main characteristics of included studies (92%). However, the review quality was less clear in terms of duplicate study selection and data extraction, inclusion of grey literature, and assessment of publication bias (Table 1).

Available health economic evidence is unlikely to be the theoretically most rigorous.⁹² It is generally difficult, if not impossible, to appropriately assess the validity of decision analytic models that were based on data from multiple sources and numerous subjective assumptions. Hill and colleagues (2012) considered that economic evaluations alongside clinical trials may be an “alternative standard of evidence,” and recommended SRs of cost and resource utilization data from direct comparison RCTs.² SRs identified by the overview included mainly economic evaluations alongside RCTs, although data from other sources and subjective assumptions are still usually necessary.⁹¹

Randomized controlled studies are required to detect uncertain, small to moderate but clinically meaningful, treatment effects between competing interventions. Evidence from studies other than RCTs may be used to confirm the cost-effectiveness of some interventions with a large treatment effect.⁹³ In addition, randomized comparison may not be feasible to evaluate complex rehabilitation processes under certain circumstances. Therefore, evidence from observational studies and other sources should not be dismissed without careful consideration of their usefulness.

Applicability of evidence

The available evidence comes predominantly from high income countries. Results of economic evaluations are of questionable applicability even among different settings within high-income countries or regions. It may be more problematic to apply results of economic evaluations in high income countries to less resourced settings in LMICs. Costs included in economic evaluations may vary greatly depending on economic evaluation perspectives, health and social welfare systems. For the purpose of guideline

development, cost-effectiveness or cost-benefit ratios are generally considered less informative, compared to disaggregated data on costs and resource utilization for an intervention.^{2,91} It has been recommended that SRs should focus on the identification of key variables that may be used to estimate the cost and affordability of relevant interventions in different settings.^{2,91}

Limitations

Some relevant SRs may have not been included in the overview. Because of the restriction of time and other resources, we only included SRs published in English, and the literature search may not be sufficient sensitive to identify some SRs that did not describe the intervention as a health-related rehabilitation. In addition, some recently published economic evaluation studies may have not been included in SRs.

We intended but failed to summaries evidence profile for each of the rehabilitation interventions according to the GRADE guidelines. This is because the huge number of relevant studies and diversity in population, interventions and outcomes addressed. Only two of the 64 SRs attempted to use GRADE tool to assess the quality of economic evidence, and none presented data according to the recommended table of evidence profile.

Overviews of SRs have been usually used to synthesize results of multiple SRs of different interventions on a specified clinical condition.⁷ The current overview of SRs was more complex as it included different health-related rehabilitation interventions for diverse disability conditions. Given the breadth and comprehensiveness of studies, compromise was necessary to reduce depth of coverage for relevance and validity assessment. We were able only to provide a broad but rough summary of findings from economic evaluations of health-related rehabilitation. However, findings from this overview may indicate the need for further and more detailed research.

Summary

Physiotherapy was the most commonly evaluated rehabilitation intervention in the included SRs. Other commonly evaluated interventions included multidisciplinary programmes; behavioral, educational or psychological interventions; home-based interventions; complementary therapy; self-management; and occupational therapy. Although the available evidence is often described as limited, inconsistent or inconclusive, some rehabilitation interventions were cost-effective or showed cost-saving to a variety of disability conditions. As available evidence comes predominantly from high income countries, economic evaluations in less resourced settings are required.

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Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.dhjo.2015.08.009>.

References

1. WHO. *World Report on Disability 2011*. Geneva: The World Health Organization. Accessed 06.07.15, http://www.who.int/disabilities/world_report/2011/report.pdf; 2011.
2. Hill SR, Olson LG, Falck-Ytter Y, et al. Incorporating considerations of cost-effectiveness, affordability, and resource implications in guideline development: article 6 in integrating and coordinating efforts in COPD guideline development. An official ATS/ERS workshop report. *Proc Am Thorac Soc*. 2012;9:251–255. <http://dx.doi.org/10.1513/pats.201208-059ST>.
3. Matchar DB, Mark DB. Strategies for incorporating resource allocation and economic considerations: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). *Chest*. 2008;133:132S–140S. <http://dx.doi.org/10.1378/chest.08-0671>.
4. Woolf S, Schunemann HJ, Eccles MP, Grimshaw JM, Shekelle P. Developing clinical practice guidelines: types of evidence and outcomes; values and economics, synthesis, grading, and presentation and deriving recommendations. *Implement Sci*. 2012;7:61. <http://dx.doi.org/10.1186/1748-5908-7-61>.
5. Drummond MF, Sculpher M, Torrance G, O'Brien J, Stoddart GL. *Methods for the Economic Evaluation of Health Care Programmes*. 3rd ed. Oxford University Press; 2005.
6. Dijkers MP, Bushnik T, Heinemann AW, et al. Systematic reviews for informing rehabilitation practice: an introduction. *Arch Phys Med Rehabil*. 2012;93:912–918. <http://dx.doi.org/10.1016/j.apmr.2011.10.032>.
7. Hartling L, Vandermeer B, Fernandes RM. Systematic reviews, overviews of reviews and comparative effectiveness reviews: a discussion of approaches to knowledge synthesis. *Evid Based Child Health*. 2014;9:486–494. <http://dx.doi.org/10.1002/ebch.1968>.
8. Thomson D, Russell K, Becker L, Klassen T, Hartling L. The evolution of a new publication type: steps and challenges of producing overviews of reviews. *Res Synth Methods*. 2010;1:198–211. <http://dx.doi.org/10.1002/jrsm.30>.
9. WHO. *Concept Paper: WHO Guidelines on Health-related Rehabilitation (Rehabilitation Guidelines)*. Geneva: The World Health Organization. Accessed 23.06.15, http://who.int/disabilities/care/rehabilitation_guidelines_concept.pdf; 2013.
10. Country and Lending Groups. *The World Bank*. Accessed 22.06.15, http://data.worldbank.org/about/country-and-lending-groups#Lower_middle_income; 2015.
11. Shea BJ, Grimshaw JM, Wells GA, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Med Res Methodol*. 2007;7:10. <http://dx.doi.org/10.1186/1471-2288-7-10>.
12. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011;64:383–394. <http://dx.doi.org/10.1016/j.jclinepi.2010.04.026>.
13. Alves J, Magalhaes R, Thomas RE, Goncalves OF, Petrosyan A, Sampaio A. Is there evidence for cognitive intervention in Alzheimer disease? A systematic review of efficacy, feasibility, and cost-effectiveness. *Alzheimer Dis Assoc Disord*. 2013;27:195–203. <http://dx.doi.org/10.1097/WAD.0b013e31827bda55>.
14. Bachmann S, Finger C, Huss A, Egger M, Stuck AE, Clough-Gorr KM. Inpatient rehabilitation specifically designed for geriatric patients: systematic review and meta-analysis of randomised controlled trials. *BMJ (Online)*. 2010;340:1230. <http://dx.doi.org/10.1136/bmj.c1718>.
15. Boniface G, Mason M, Macintyre J, Synan C, Riley J. The effectiveness of local authority social services' occupational therapy for older people in Great Britain: a critical literature review. *Br J Occup Ther*. 2013;76:538–547. <http://dx.doi.org/10.4276/030802213X13861576675240>.
16. Boyers D, McNamee P, Clarke A, et al. Cost-effectiveness of self-management methods for the treatment of chronic pain in an aging adult population: a systematic review of the literature. *Clin J Pain*. 2013;29:366–375. <http://dx.doi.org/10.1097/AJP.0b013e318250f539>.
17. Brady BK, McGahan L, Skidmore B. Systematic review of economic evidence on stroke rehabilitation services. *Int J Technol Assess Health Care*. 2005;21:15–21. <http://dx.doi.org/10.1017/S0266462305050026>.
18. Brady TJ. Cost implications of self-management education intervention programmes in arthritis. *Best Pract Res Clin Rheumatol*. 2012;26:611–625. <http://dx.doi.org/10.1016/j.berh.2012.09.001>.
19. Brown JPR, Clark AM, Dalal H, Welch K, Taylor RS. Effect of patient education in the management of coronary heart disease: a systematic review and meta-analysis of randomized controlled trials. *Eur J Prev Cardiol*. 2013;20:701–714. <http://dx.doi.org/10.1177/2047487312449308>.
20. Brusco NK, Paratz J. The effect of additional physiotherapy to hospital inpatients outside of regular business hours: a systematic review. *Physiother Theory Pract*. 2006;22:291–307. <http://dx.doi.org/10.1080/09593980601023754>.
21. Brusco NK, Taylor NF, Watts JJ, Shields N. Economic evaluation of adult rehabilitation: a systematic review and meta-analysis of randomized controlled trials in a variety of settings. *Arch Phys Med Rehabil*. 2014;95:94–116.e114. <http://dx.doi.org/10.1016/j.apmr.2013.03.017>.
22. Cameron I, Crotty M, Currie C, et al. Geriatric rehabilitation following fractures in older people: a systematic review. *Health Technol Assess*. 2000;4:i–iv. 1–111.
23. Canter PH, Coon JT, Ernst E. Cost-effectiveness of complementary therapies in the United Kingdom – a systematic review. *Evid Based Complement Alternat Med*. 2006;3:425–432. <http://dx.doi.org/10.1093/ecam/nel044>.
24. Carroll C, Rick J, Pilgrim H, Cameron J, Hillage J. Workplace involvement improves return to work rates among employees with back pain on long-term sick leave: a systematic review of the effectiveness and cost-effectiveness of interventions. *Disabil Rehabil*. 2010;32:607–621. <http://dx.doi.org/10.3109/09638280903186301>.
25. Cheng AK, Niparko JK. Cost-utility of the cochlear implant in adults: a meta-analysis. *Arch Otolaryngol Head Neck Surg*. 1999;125:1214–1218.
26. Clark M, Kelly T, Deighan C. A systematic review of the heart manual literature. *Eur J Cardiovasc Nurs*. 2011;10:3–13. <http://dx.doi.org/10.1016/j.ejcnurse.2010.03.003>.
27. Coon JT, Ernst E. A systematic review of the economic evaluation of complementary and alternative medicine. *Perfusion*. 2005;18:202–214.
28. Crocker T, Forster A, Young J, et al. Physical rehabilitation for older people in long-term care. *Cochrane Database Syst Rev*; 2013. <http://dx.doi.org/10.1002/14651858.CD004294.pub2>.

29. Dagenais S, Roffey DM, Wai EK, Haldeman S, Caro J. Can cost utility evaluations inform decision making about interventions for low back pain? *Spine J*. 2009;9:944–957. <http://dx.doi.org/10.1016/j.spinee.2009.07.007>.
30. Davis JC, Robertson MC, Ashe MC, Liu-Ambrose T, Khan KM, Marra CA. Does a home-based strength and balance programme in people aged > or =80 years provide the best value for money to prevent falls? A systematic review of economic evaluations of falls prevention interventions. *Br J Sports Med Online*. 2010;44:80–89. <http://dx.doi.org/10.1136/bjsm.2008.060988>.
31. Demaerschalk BM, Hwang HM, Leung G. Cost analysis review of stroke centers, telestroke, and rt-PA. *Am J Manag Care*. 2010;16:537–544.
32. Driessen MT, Lin CWC, Van Tulder MW. Cost-effectiveness of conservative treatments for neck pain: a systematic review on economic evaluations. *Eur Spine J*. 2012;21:1441–1450. <http://dx.doi.org/10.1007/s00586-012-2272-5>.
33. Farag I, Sherrington C, Ferreira M, Howard K. A systematic review of the unit costs of allied health and community services used by older people in Australia. *BMC Health Serv Res*. 2013;13:69. <http://dx.doi.org/10.1186/1472-6963-13-69>.
34. Furlan AD, Yazdi F, Tsertsvadze A, et al. *Complementary and Alternative Therapies for Back Pain II*. Evidence Report/Technology Assessment (no. 194). AHRQ Publication No. 10(11)-E007. Accessed 06.07.15. <http://www.ahrq.gov/research/findings/evidence-based-reports/backcam2tp.html>; 2010.
35. Garrett S, Elley CR, Rose SB, O'Dea D, Lawton BA, Dowell AC. Are physical activity interventions in primary care and the community cost-effective? A systematic review of the evidence. *Br J Gen Pract*. 2011;61. <http://dx.doi.org/10.3399/bjgp11X561249>.
36. Gaujoux-Viala C, Fautrel B. Cost effectiveness of therapeutic interventions in ankylosing spondylitis: a critical and systematic review. *Pharmacoeconomics*. 2012;30:1145–1156. <http://dx.doi.org/10.2165/11596490>.
37. Hamberg-van Reenen HH, Proper KI. Worksite mental health interventions: a systematic review of economic evaluations. *Occup Environ Med*. 2012;69:837–845. <http://dx.doi.org/10.1136/oemed-2012-100668>.
38. Handoll HH, Cameron ID, Mak JC, Finnegan TP. Multidisciplinary rehabilitation for older people with hip fractures. *Cochrane Database Syst Rev*; 2009. <http://dx.doi.org/10.1002/14651858.CD007125.pub2>.
39. Herman PM, Poindexter BL, Witt CM, Eisenberg DM. Are complementary therapies and integrative care cost-effective? A systematic review of economic evaluations. *BMJ Open*. 2012;2. <http://dx.doi.org/10.1136/bmjopen-2012-001046>.
40. Hillier S, Inglis-Jassiem G. Rehabilitation for community-dwelling people with stroke: home or centre based? A systematic review. *Int J Stroke*. 2010;5:178–186. <http://dx.doi.org/10.1111/j.1747-4949.2010.00427.x>.
41. Indrakanti SS, Weber MH, Takemoto SK, Hu SS, Polly D, Berven SH. Value-based care in the management of spinal disorders: a systematic review of cost-utility analysis. *Clin Orthop Relat Res*. 2012;470:1106–1123. <http://dx.doi.org/10.1007/s11999-011-2141-2>.
42. Kairy D, Lehoux P, Vincent C, Visintin M. A systematic review of clinical outcomes, clinical process, healthcare utilization and costs associated with telerehabilitation. *Disabil Rehabil*. 2009;31:427–447. <http://dx.doi.org/10.1080/09638280802062553>.
43. Khan F, Amatya B, Ng L, Drummond K, Olver J. Multidisciplinary rehabilitation after primary brain tumour treatment. *Cochrane Database Syst Rev (Online)*. 2013;1:CD009509. <http://dx.doi.org/10.1002/14651858>.
44. Kim S, Lee H, Chae Y, Park H, Lee H. A systematic review of cost-effectiveness analyses alongside randomised controlled trials of acupuncture. *Acupunct Med*. 2012;30:273–285. <http://dx.doi.org/10.1136/acupmed-2012-010178>.
45. Knapp M, Iemmi V, Romeo R. Dementia care costs and outcomes: a systematic review. *Int J Geriatr Psychiatry*. 2013;28:551–561. <http://dx.doi.org/10.1002/gps.3864>.
46. Kollen BJ, Lennon S, Lyons B, et al. The effectiveness of the Bobath concept in stroke rehabilitation: what is the evidence? *Stroke*. 2009;40:e89–97. <http://dx.doi.org/10.1161/STROKEAHA.108.533828>.
47. Law J, Zeng B, Lindsay G, Beecham J. Cost-effectiveness of interventions for children with speech, language and communication needs (SLCN): a review using the Drummond and Jefferson (1996) 'Referee's Checklist'. *Int J Lang Commun Disord*. 2012;47:1–10. <http://dx.doi.org/10.1111/j.1460-6984.2011.00084.x>.
48. Lin CW, Haas M, Maher CG, Machado LA, van Tulder MW. Cost-effectiveness of general practice care for low back pain: a systematic review. *Eur Spine J*. 2011;20:1012–1023. <http://dx.doi.org/10.1007/s00586-010-1675-4>.
49. Lin CWC, Haas M, Maher CG, MacHado LAC, Van Tulder MW. Cost-effectiveness of guideline-endorsed treatments for low back pain: a systematic review. *Eur Spine J*. 2011;20:1024–1038. <http://dx.doi.org/10.1007/s00586-010-1676-3>.
50. Lin C-WC, Uegaki K, Kerkhoffs GM. Economic evaluations of diagnostic tests, treatment and prevention for lateral ankle sprains: a systematic review. *Br J Sports Med Online*. 2013;47:1144–1149. <http://dx.doi.org/10.1136/bjsports-2012-090319>.
51. Maund E, Craig D, Suekarran S, et al. Management of frozen shoulder: a systematic review and cost-effectiveness analysis. *Health Technol Assess*. 2012;16:1–264. <http://dx.doi.org/10.3310/hta16110>.
52. Mewes JC, Steuten LMG, IJ MJ, van Harten WH. Effectiveness of multidimensional cancer survivor rehabilitation and cost-effectiveness of cancer rehabilitation in general: a systematic review. *Oncologist*. 2012;17:1581–1593. <http://dx.doi.org/10.1634/theoncologist.2012-0151>.
53. Michaleff ZA, Lin CWC, Maher CG, van Tulder MW. Spinal manipulation epidemiology: systematic review of cost effectiveness studies. *J Electromyogr Kinesiol*. 2012;22:655–662. <http://dx.doi.org/10.1016/j.jelekin.2012.02.011>.
54. Moffa-Trotter ME, Anemaet WK. Cost effectiveness of home rehabilitation: a literature review. *Top Geriatr Rehabil*. 1999;14:1–33.
55. Palmer KT, Harris EC, Linaker C, et al. Effectiveness of community- and workplace-based interventions to manage musculoskeletal-related sickness absence and job loss: a systematic review. *Rheumatology*. 2012;51:230–242. <http://dx.doi.org/10.1093/rheumatology/ker086>.
56. Papadakis S, Oldridge NB, Coyle D, et al. Economic evaluation of cardiac rehabilitation: a systematic review. *Eur J Cardiovasc Prev Rehabil*. 2005;12:513–520.
57. Pinto D, Robertson MC, Hansen P, Abbott JH. Cost-effectiveness of nonpharmacologic, nonsurgical interventions for hip and/or knee osteoarthritis: systematic review. *Value Health*. 2012;15:1–12. <http://dx.doi.org/10.1016/j.jval.2011.09.003>.
58. Richardson G, Gravelle H, Weatherly H, Ritchie G. Cost-effectiveness of interventions to support self-care: a systematic review. *Int J Technol Assess Health Care*. 2005;21:423–432.
59. Roine E, Roine RP, Rasanen P, Vuori I, Sintonen H, Saarto T. Cost-effectiveness of interventions based on physical exercise in the treatment of various diseases: a systematic literature review. *Int J Technol Assess Health Care*. 2009;25:427–454. <http://dx.doi.org/10.1177/s0266462309990353>.
60. Samuelsson KAM, Toytari O, Salminen AL, Brandt A. Effects of lower limb prosthesis on activity, participation, and quality of life: a systematic review. *Prosthet Orthot Int*. 2012;36:145–158. <http://dx.doi.org/10.1177/0309364611432794>.
61. Smith JR, Mugford M, Holland R, et al. A systematic review to examine the impact of psycho-educational interventions on health outcomes and costs in adults and children with difficult asthma. *Health Technol Assess*. 2005;9:iii–iv. 1–167.
62. Steuten LM, Lemmens KM, Nieboer AP, Vrijhoef HJ. Identifying potentially cost effective chronic care programs for people with COPD. *Int J Chron Obstruct Pulmon Dis*. 2009;4:87–100.

63. Tappenden P, Campbell F, Rawdin A, Wong R, Kalita N. The clinical effectiveness and cost-effectiveness of home-based, nurse-led health promotion for older people: a systematic review. *Health Technol Assess*. 2012;16:1–71. <http://dx.doi.org/10.3310/hta16200>.
64. Taylor RS, Buyten JPV, Buchser E. Spinal cord stimulation for complex regional pain syndrome: a systematic review of the clinical and cost-effectiveness literature and assessment of prognostic factors. *Eur J Pain*. 2006;10:91–101. <http://dx.doi.org/10.1016/j.ejpain.2005.02.004>.
65. Teasell RW, Foley NC, Bhogal SK, Speechley MR. Early supported discharge in stroke rehabilitation. *Top Stroke Rehabil*. 2003;10:19–33. <http://dx.doi.org/10.1310/QLFN-M4MX-XEMM-2YQC>.
66. Thomsen AB, Sorensen J, Sjogren P, Eriksen J. Economic evaluation of multidisciplinary pain management in chronic pain patients: a qualitative systematic review. *J Pain Symptom Manage*. 2001;22:688–698. [http://dx.doi.org/10.1016/s0885-3924\(01\)00326-8](http://dx.doi.org/10.1016/s0885-3924(01)00326-8).
67. Tompa E, de Oliveira C, Dolinschi R, Irvin E. A systematic review of disability management interventions with economic evaluations. *J Occup Rehabil*. 2008;18:16–26. <http://dx.doi.org/10.1007/s10926-007-9116-x>.
68. Tummers JF, Schrijvers AJ, Visser-Meily JM. Economic evidence on integrated care for stroke patients; a systematic review. *Int J Integr Care*. 2012;12:e193.
69. Turchetti G, Bellelli S, Palla I, Berrettini S. Systematic review of the scientific literature on the economic evaluation of cochlear implants in adult patients. *Acta Otorhinolaryngol Ital*. 2011;31:319–327.
70. Turchetti G, Bellelli S, Palla I, Forli F. Systematic review of the scientific literature on the economic evaluation of cochlear implants in paediatric patients. *Acta Otorhinolaryngol Italica*. 2011;31:311–318.
71. van der Roer N, Goossens M, Evers S, van Tulder MW. What is the most cost-effective treatment for patients with low back pain? A systematic review. *Best Pract Res Clin Rheumatol*. 2005;19:671–684. <http://dx.doi.org/10.1016/j.berh.2005.03.007>.
72. Wieland D. The effectiveness and costs of comprehensive geriatric evaluation and management. *Crit Rev Oncol Hematol*. 2003;48:227–237. <http://dx.doi.org/10.1016/j.critrevonc.2003.06.005>.
73. Willems DC, Joore MA, Hendriks JJ, Wouters EF, Severens JL. Cost-effectiveness of self-management in asthma: a systematic review of peak flow monitoring interventions. *Int J Technol Assess Health Care*. 2006;22:436–442.
74. Winkel A, Ekdahl C, Gard G. Early discharge to therapy-based rehabilitation at home in patients with stroke: a systematic review. *Phys Ther Rev*. 2008;13:167–187.
75. Wong WP, Feng J, Pwee KH, Lim J. A systematic review of economic evaluations of cardiac rehabilitation. *BMC Health Serv Res*. 2012;12:243. <http://dx.doi.org/10.1186/1472-6963-12-243>.
76. Zhang F, Kong LL, Zhang YY, Li SC. Evaluation of impact on health-related quality of life and cost effectiveness of traditional Chinese medicine: a systematic review of randomized clinical trials. *J Altern Complement Med*. 2012;18:1108–1120. <http://dx.doi.org/10.1089/acm.2011.0315>.
77. Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]*. The Cochrane Collaboration. Accessed 06.07.15, <http://handbook.cochrane.org/>; 2011.
78. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther*. 2003;83:713–721.
79. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. *BMJ*. 1996;313:275–283.
80. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: consensus on health economic criteria. *Int J Technol Assess Health Care*. 2005;21:240–245.
81. Hirneiss C, Neubauer AS, Niedermeier A, Messmer EM, Ulbig M, Kampik A. Cost utility for penetrating keratoplasty in patients with poor binocular vision. *Ophthalmology*. 2006;113:2176–2180.
82. Crathorne L, Bond M, Cooper C, et al. A systematic review of the effectiveness and cost-effectiveness of bilateral multichannel cochlear implants in adults with severe-to-profound hearing loss. *Clin Otolaryngol*. 2012;37:342–354. <http://dx.doi.org/10.1111/coa.12011>.
83. Barton GR, Stacey PC, Fortnum HM, Summerfield AQ. Hearing-impaired children in the United Kingdom, II: Cochlear implantation and the cost of compulsory education. *Ear Hear*. 2006;27:187–207.
84. Smith TP, Kennedy SL, Smith M, Orent S, Fleshner M. Physiological improvements and health benefits during an exercise-based comprehensive rehabilitation program in medically complex patients. *Exerc Immunol Rev*. 2006;12:86–96.
85. Monteiro E, Shipp D, Chen J, Nedzelski J, Lin V. Cochlear implantation: a personal and societal economic perspective examining the effects of cochlear implantation on personal income. *J Otolaryngol Head Neck Surg*. 2012;41(suppl 1):S43–S48.
86. Lambeek LC, Bosmans JE, Van Royen BJ, Van Tulder MW, Van Mechelen W, Anema JR. Effect of integrated care for sick listed patients with chronic low back pain: economic evaluation alongside a randomised controlled trial. *BMJ*. 2010;341:c6414. <http://dx.doi.org/10.1136/bmj.c6414>.
87. Cardenas DD, Haselkorn JK, McElligott JM, Gnatz SM. A bibliography of cost-effectiveness practices in physical medicine and rehabilitation: AAPM&R white paper. *Arch Phys Med Rehabil*. 2001;82:711–719. <http://dx.doi.org/10.1053/apmr.2001.24814>.
88. Eichler HG, Kong SX, Gerth WC, Mavros P, Jonsson B. Use of cost-effectiveness analysis in health-care resource allocation decision-making: how are cost-effectiveness thresholds expected to emerge? *Value Health*. 2004;7:518–528. <http://dx.doi.org/10.1111/j.1524-4733.2004.75003.x>.
89. CRD. *Systematic Review of Economic Evaluations. CRD's Guidance for Undertaking Reviews in Health Care*. Centre for Reviews and Dissemination, University of York; 2009.
90. Edejer TT. Improving the use of research evidence in guideline development: 11. Incorporating considerations of cost-effectiveness, affordability and resource implications. *Health Res Policy Syst*. 2006;4:23. <http://dx.doi.org/10.1186/1478-4505-4-23>.
91. Brunetti M, Shemilt I, Pregno S, et al. GRADE guidelines: 10. Considering resource use and rating the quality of economic evidence. *J Clin Epidemiol*. 2013;66:140–150. <http://dx.doi.org/10.1016/j.jclinepi.2012.04.012>.
92. Johnston MV, Dijkers MP. Toward improved evidence standards and methods for rehabilitation: recommendations and challenges. *Arch Phys Med Rehabil*. 2012;93:S185–S199. <http://dx.doi.org/10.1016/j.apmr.2011.12.011>.
93. Glasziou P, Chalmers I, Rawlins M, McCulloch P. When are randomised trials unnecessary? Picking signal from noise. *BMJ*. 2007;334:349–351. <http://dx.doi.org/10.1136/bmj.39070.527986.68>.