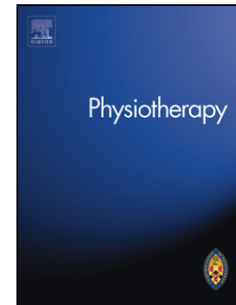


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PII: S0031-9406(22)00002-5

DOI: <https://doi.org/10.1016/j.physio.2022.01.002>

Reference: PHYST 1287

To appear in: *Physiotherapy*

Please cite this article as: Fatoye F, Tadesse G, Clara F, Mbada C, A Systematic Review of Economic Models for Cost Effectiveness of Physiotherapy Interventions Following Total Knee and Hip Replacement, *Physiotherapy* (2022), doi: <https://doi.org/10.1016/j.physio.2022.01.002>

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A Systematic Review of Economic Models for Cost Effectiveness of Physiotherapy Interventions Following Total Knee and Hip Replacement

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Contribution of the paper:

- This paper presents model based CE of physiotherapy interventions for patients with TKHR.
- This paper provides valuable information that physiotherapy interventions were CE and cost saving for patients with TKHR.
- This review could be a source of information for researchers developing new economic model to assess the cost-effectiveness of physiotherapy intervention for TKHR.
- **Abstract**
- **Background:** Osteoarthritis is a primary cause of pain and disability, and it places a considerable economic burden on individuals and the society. In the management of total knee or hip replacement

(TKHR), the long-term effectiveness of physiotherapy interventions may slowly accumulate over a period.

- **Objectives:** To evaluate all the model-based cost- effectiveness (CE) of physiotherapy interventions for patients with (TKHR).
- **Data sources:** A literature search was carried out on AMED, MEDLINE, CINAHL, DARE, HTA, NHSEED and Cost- Effectiveness registry databases from inception to May 2021.
- **Study selection:** Studies that assessed model-based CE of physiotherapy interventions following TKHR and were published in English language. The methodological quality of the included studies were assessed using the Philips Checklist criteria.
- **Data extraction/data synthesis:** Two reviewers, using a predefined data extraction form, independently extracted data. A descriptive synthesis was used to present the results.
- **Result:** Eight hundred eighty-six studies were identified, and the only 3 that met the inclusion criteria were included. Different model structures and assumptions were used in the included studies. The included studies were conducted in the United States of America (n = 1), Singapore (n= 1) and Italy (n = 1). The societal (n = 2) and healthcare (n = 1) perspective were adopted in the studies. The included studies reported an incremental cost effectiveness ratio (ICER) of \$57,200 and 27,471 Singapore dollar (SGD) per quality-adjusted life years in a time horizon of lifetime and three months, respectively. Physiotherapy (hydrotherapy) interventions were potentially cost-effective.
- **Conclusion:** Based on the best available evidence, the findings of this review suggest that physiotherapy interventions were CE and cost saving. However, it is important to note that among others the CE of the interventions was a function of the healthcare system, duration of interventions, patient compliance and price.
- **Systematic review registration number CRD:** CRD42019151214.

Introduction

Osteoarthritis (OA) is a primary cause of pain and disability, and it places a considerable clinical and economic burden on individuals and the society. The annual direct costs of OA per patient in United States of America (USA), Canada, Spain, Italy and Hong Kong in 2010 were estimated £1526, £3162, £1292, £981 and £6561, respectively [1]. The annual cost for oral and topical nonsteroidal anti-inflammatory drugs for patients with OA in the United Kingdom (UK) were £19.2 million and £25.65 million, respectively [2]. The non-healthcare related costs due to OA per patient also ranged from €432 to €11,956 per year globally [3]. Pain and functional

impairment are the key clinical outcomes that significantly affect the quality of life of people with OA [4]. Although the prevalence of OA varies according to the geographical areas, sex and age, over 26 million people in the USA [5] and 10 million in the UK [6] had some form of OA.

Evidence suggests that 40% of men and 57% of women with knee OA are inactive and would therefore benefit from physiotherapy [7]. After total knee or hip replacement (TKHR), physiotherapy interventions are used to alleviate pain and improve function for people with OA [8]. Most patients report positive health outcomes following total knee replacement between 3 and 6 months [9]. However, the implementation of these physiotherapy interventions are expensive. For example, in 2005, rehabilitation costs around €158 million to the national health system of Italy [10]. In order to decide whether or not to accept a new intervention, information on its cost-effectiveness is needed [11]. A recent systematic review found difficulty reaching a conclusion on the cost-effectiveness of physiotherapy interventions based on the small number of studies available [12].

Other than clinical trial-based cost-effectiveness analyses, an analytical framework that helps to understand the cost-effectiveness of new treatments is model-based economic evaluation [13]. Model-based economic evaluation enables researchers and policy makers to inform complex policy decisions by integrating multiple factors into a single decision analytical model [14]. To date, no literature review has been published summarising model-based cost-effectiveness of physiotherapy interventions for patients with TKHR. The objective of this study was to summarise the literature evaluating the model-based cost-effectiveness of physiotherapy interventions for patients with TKHR.

Methods

Search protocol and registration

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA), a technique that addresses the eligibility, data sources, selection of studies, data extraction and data analysis as a reporting guideline [15]. This review was registered on PROSPERO, with registration number, CRD: CRD42019151214.

Data sources

A literature search was conducted through using multiple databases including AMED, MEDLINE, CINAHL, DARE, HTA, NHSEED and Cost- Effectiveness registry databases from inception to May 2021. The search terms used were 'total hip replacement or total hip arthroplasty', 'hip arthroplasty or 'hip replacement', 'hydrotherapy', 'strength', 'strength training', 'exercise or physical activity or fitness', 'training', 'physiotherapy', 'physical therapy', 'tele-rehabilitation', 'total knee arthroplasty', 'knee arthroplasty', 'total knee replacement', 'knee replacement', 'economic model', 'model', 'long term', 'decision analysis', 'economic evaluation', and 'cost utility analysis'. These search terms were combined using conjunctions such as "AND" and "OR". Further, the snowball technique was used to identify other articles by searching for relevant papers listed in reference lists of the initially selected articles.

Search strategy

We identified articles that used model-based economic evaluation of physiotherapy interventions for patients with TKHR. The inclusion criteria were model-based economic evaluation studies that assessed the cost-effectiveness of physiotherapy interventions, studies meeting with explicit analysis of both costs and effects of an intervention, studies with at least one comparator, all age groups, and published in the English language. The exclusion criteria were abstract unavailable, studies not yet fully completed, conference papers, and clinical trial-based cost-effectiveness studies. Duplicates were removed electronically and manually. Two independent researchers (TG & CF) were involved in screening the title and abstract of each study. Full-text articles were obtained and were excluded if they did not meet the inclusion criteria. Any disagreement in study selection was resolved through discussion and consultation with other members of the team (FF) where necessary.

Data extraction and study quality assessment

After screening based on title and abstract, full papers were retrieved and key data were extracted by two reviewers (TG & CF). The key components extracted from each study include author, country of the study, population, intervention type, comparator, model type, health states, study perspective, time horizon, discount rate, outcome measure and costs. Incremental cost-effectiveness ratio (ICER) and sensitivity analysis were also

extracted. The model structures used in the included articles were assessed. We identified the important clinical events and/or health states included in the model.

Philips et al.'s quality assessment checklist was used to assess the quality of the included studies [13]. It provides the best practice guidelines in decision modelling for cost-effectiveness analysis and contains all the key attributes for critical assessment. These key attributes are categorised into three broad dimensions namely structure, data and consistency. The quality of included studies was appraised by two independent reviewers (TG and CF) and disagreements were further assessed by a third reviewer (FF), where necessary.

Results

Study selection

Eight hundred and eighty-six studies were identified using the search strategy. Screening of the titles and abstracts led to the selection of thirty-four publications for full-text reading. After full-text reading, three articles met the inclusion criteria and were included in the review. The study flow diagram indicates the selection process (Figure 1).

-----**Figure 1**-----

General characteristics

The included studies were published between January 2016 and 26 July 2018 (Table 1). They were conducted in the United States of America (n = 1), Singapore (n= 1) and Italy (n = 1). The included studies were carried out from the healthcare [16] and societal perspective [17, 18]. Two of the included studies were cost-utility analysis (CUA) expressing outcomes in QALYs [16, 17] and one study was CUA and cost-effectiveness analysis [18]. The types of interventions included in the studies were telephone health coaching & financial incentives to promote physical activity [16], hydrotherapy [17] and standard rehabilitation and tele-rehabilitation [18]. All of the included studies declared their source of funding.

-----**Table 1**-----

Model structure and outcomes

The results of cost-effectiveness of the included studies are presented in Table 2. Osteoarthritis Policy (OAPol) model developed by Holt and colleague [20] was used to evaluate the cost-effectiveness of telephonic health coaching and financial incentives [16]. The OAPol model is a validated microsimulation model of knee OA natural history and treatment that runs on an annual cycle. The disease states which were defined by OA severity include: normal radiograph (no OA), questionable osteophytes (pre-radiographic OA), definite osteophytes (early OA), < 50% narrowing of knee joint space (advanced OA), and \geq 50% narrowing of joint space (end-stage OA). A decision-analytic model in the form of a decision tree was used to evaluate the cost-effectiveness of hydrotherapy versus land-based therapy; the model duration was set as 3 months [17]. The third study that evaluated the cost-effectiveness and cost-utility of tele-rehabilitation adopted a Markov model and the cycle length considered was 1 year [19]. The health states included in the Fusco & Tuchetti [19] were successful TKR, revision, successful revision and death.

-----**Table 2**-----

Methodological quality of the included studies

Very limited comparability between the studies was observed due to use of different model structures, model assumptions and input parameter estimates. Most of the studies did not perform consistently well on the items from the Philips' checklist. Details of individual study performance against the Philips checklist is shown in Appendix 1.

Structure

The decision problem and the objective of the included studies were clearly stated. None of the studies stated the sources of data used to inform their model structure, nor did they provide justification for the scope of the model. Two studies [16, 19] used a lifetime time horizon and one study justified a three-month time horizon [17]. The disease states were described in all the included studies.

Data

Clear and transparent modelling methodologies were presented in all the included studies. The sources of data used to calculate the transition probabilities were indicated in two studies [16, 19]. Neither the sources nor the

calculation of the transition probabilities were presented in one of the studies [17]. The sources and derivation of utilities used for the health states were transparent in all the included studies. All the included studies performed probabilistic sensitivity analysis. One study [17] carried out a subgroup analyses whereas the remaining two studies did not.

Discussion

This is the first study that summarised literature evaluating model-based cost-effectiveness analyses of physiotherapy interventions for patients with TKHR. All the included studies used a decision analytic model to assess the cost-effectiveness of physiotherapy interventions. The inclusion criteria were economic evaluation of physiotherapy based on decision analytic model published in English language. We included three model-based studies which assessed the cost-effectiveness of telephonic health coaching and financial incentives, hydrotherapy and tele-rehabilitation. The effectiveness data used in the model were derived from studies carried out using randomised controlled trials and were associated with a substantial improvement in physical activity and fitness following TKHR. It is well understood that healthcare programmes are accompanied with improved health outcomes but also with large direct and indirect costs [18]. The incremental cost-effectiveness ratio estimate for telephonic health coaching & financial incentives, tele-rehabilitation, and hydrotherapy were \$93,300, -€960, and SGD 27,471 per QALY gained, respectively. Although the comparisons of the results of the review were constrained by methodological differences such as evaluation perspectives, types of interventions, types of cost included, countries and demographics, the results indicated that physiotherapy interventions were cost-effective. However, due to the uncertainty arising from the assumption of the model input parameters, the cost-effectiveness of physiotherapy interventions for patients with TKHR should be interpreted with caution. For example, the findings of a systematic review published recently suggested that there are some trial-based studies, which reported physiotherapy interventions for TKHR was not cost effective [12].

Our review has some strengths and limitations. To our knowledge, this is the first review to address the model-based cost-effectiveness of physiotherapy interventions. One of the main limitations of this study is the low number of studies that met the inclusion criteria. We did not consider cost effectiveness studies that had been carried out alongside randomised controlled trials as a previous review has already addressed this question [12]. The current review included only peer-reviewed model based economic evaluations published in the English

languages. We did not collect information on validation of the included studies and consideration was not given to parametric and structural uncertainty. Moreover, the different estimate of costs may have impacted on the cost-effectiveness of physiotherapy programmes. Further, the lack of reporting details of modelling methodology in the included studies could lead to drawing wrong conclusion from the review.

Overall, regardless of these limitations, the current review offers some evidence that physiotherapy interventions are likely to be cost-effective. However, cost-effectiveness evidence is one element that needs to be taken in to account in healthcare decision-making (i.e. it compares the relative costs and health benefits of different programmes). Further, different assumptions such as the course of disease progression, the duration of the treatment effect and the changes of treatment effect over time could be introduced when evaluating the cost-effectiveness of physiotherapy interventions for TKHR.

In conclusion, model based cost-effectiveness analysis requires information from a variety of different sources. It is thus necessary that readers should understand how the information derived from different sources interplay in the model based economic evaluation to produce the cost-effectiveness results. Based on the best available evidence, the findings of this review suggest that physiotherapy interventions were cost effective and cost saving. However, it is important to note the cost effectiveness of the interventions was a function of the healthcare system, duration of intervention, patient adherence and price. The authors hope that this review can be a source of information for researchers developing new economic models to assess the cost-effectiveness of physiotherapy interventions for TKHR.

Ethical Approval: Ethical approval was not required for this study as it was a systematic review based on published papers.

Funding: There was no funding received in support of this study.

Conflict of Interest: None of the authors have any conflicts of interest to disclose.

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Table**Table 1:** General characteristics of the included model-based economic evaluations.

Study	Country	Population	Intervention	Comparator	Model type	Perspective	Time horizon	Discount rate	Outcome measure	Sensitivity analysis
Smith et al. [16]	USA	TKR	THC & FI	Usual care	Markov model	Healthcare perspective	Lifetime	3%	QALY	Yes
Teng et al. [17]	Singapore	TKHR	Hydrotherapy	Land-based physiotherapy	Decision tree	Societal perspective	3 months	N/A	QALY	Yes
Fusco & Turchetti, [19]	Italy	TKR	SR and TR	20 face-to-face rehabilitation sessions in the following 3 months	Markov model	Societal & Italian-NHS	lifetime	3%	QALY	Yes

Note: THC = Telephone health coaching; FI = Financial incentives; SR = Standard rehabilitation; TR = tele rehabilitation; TKHR = Total knee and hip rehabilitation; QALY = Quality adjusted life years; USA = United States of America; N/A = Not available; NHS = National health system; TKR = Total knee replacement; ICER = Incremental cost-effectiveness ratio; SGD = Singapore dollar

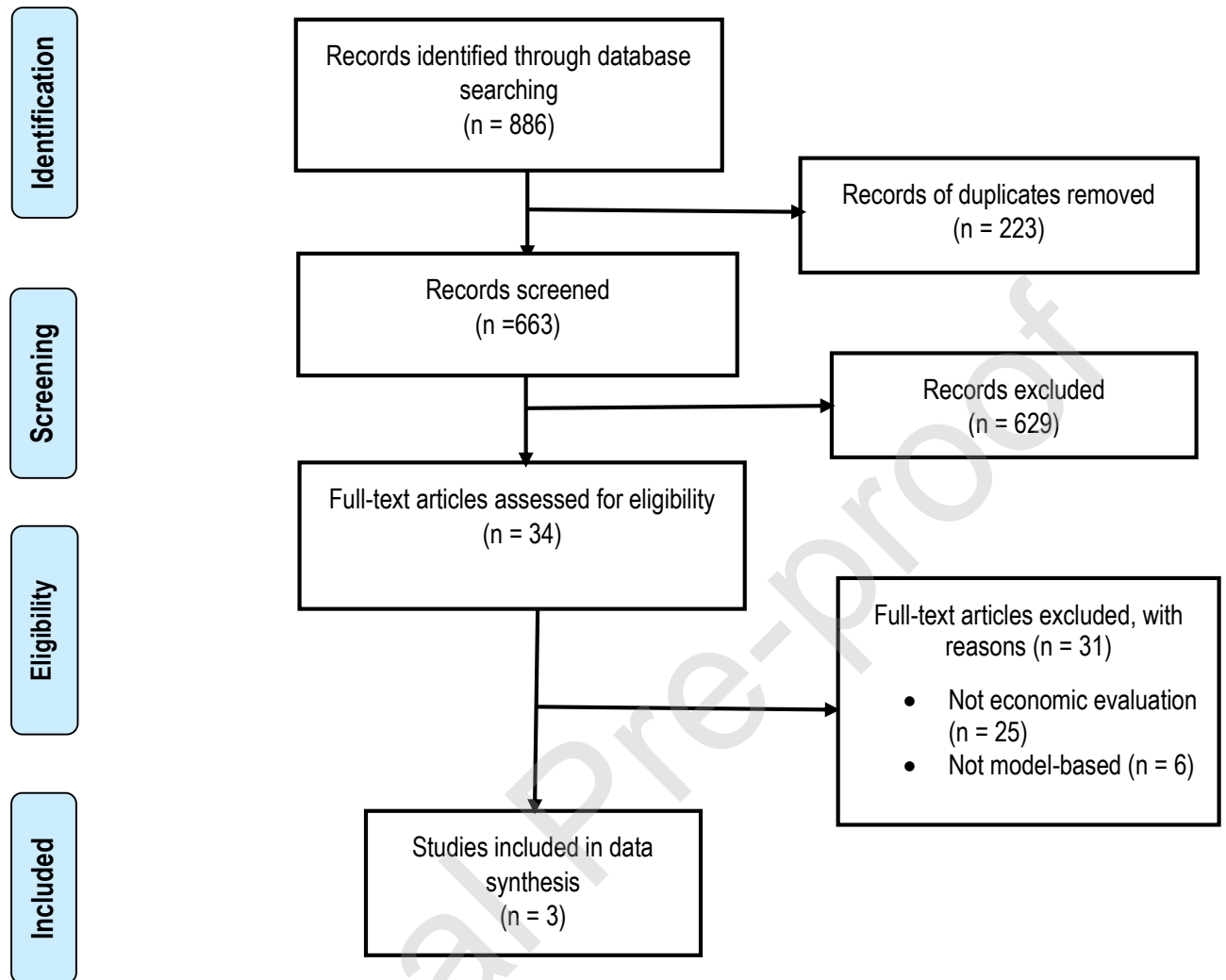
Table 2: Summary of results

Study	Total costs	Total QALYs	ICER (Cost/QALY)
Smith et al. [16]	Usual care = \$140,700 THC & FI = \$141,000	Usual care = 9.783 THC & FI = 9.788	#THC & FI intervention was cost-effective (ICER <\$100,000/QALY) with an ICER of \$57,200/QALY. #THC and FI might be a cost-effective alternative to usual care.
Teng et al. [17]	Land-based therapy (THR) = SGD 16,532; Land-based therapy (TKR) = SGD 11,373 Hydrotherapy (THR) = SGD 16,425 Hydrotherapy (TKR) = SGD 11,267	Land-based therapy (THR) = 0.177 Land-based therapy (TKR) = 0.177 Hydrotherapy (THR) = 0.179 Hydrotherapy (TKR) = 0.179	#Hydrotherapy was associated with an incremental cost-effectiveness ratio (ICER) of SGD 27 471 per QALY. #Hydrotherapy was dominant (more effective and less costly)
Fusco & Turchetti, [19]	Italian-NHS Standard rehabilitation = €904 Telerehabilitation = €840 Societal Standard rehabilitation = €1095 Telerehabilitation = €955	Italian NHS Standard rehabilitation = 13.02 Telerehabilitation = - Societal Standard rehabilitation = 13.02 Telerehabilitation = -	Italian NHS #Mixed SR-TR service was cost-effective (with an ICER of -€117/ROM gained) #Assuming that TR would increase health-related quality of life (HRQOL) utilities by 2.5%, the ICER is -€960/QALY Societal #Mixed SR-TR service was cost-effective (with an ICER of -€152/ROM gained) #Assuming that TR would increase health-related quality of life (HRQOL) utilities by 2.5%, the ICER is -€1245/QALY #SR-TR was dominant

Note: THC = Telephone health coaching; FI = Financial incentives; SGD = Singapore dollar; ROM = Range of motion; SR = Standard rehabilitation; THR = Total hip replacement; TKR = Total knee replacement; SR-TR = Standard rehabilitation and telerehabilitation; TR = Telerehabilitation; HRQOL = Health related quality of life; Italian-NHS = Italian National Health System

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Figure

**Figure 1.** Flow diagram of publications included and excluded in the review

Appendix 1: Philips *et al.*'s quality assessment checklist for studies that include an economic model

Criteria	Smith <i>et al.</i> , 2018	Teng <i>et al.</i> , 2018	Fusco & Turchetti, 2016
1 Is there a clear statement of the decision problem?	Y	Y	Y
2 Is the objective of the model specified and consistent with the stated decision problem?	Y	Y	Y
3 Is the primary decision maker specified?	Y	Y	Y
4 Is the perspective of the model stated clearly?	Y	Y	Y
5 Are the model inputs consistent with the stated perspective?	N	N	N
6 Has the scope of the model been stated and justified?	Y	Y	N
7 Are the outcomes of the model consistent with the perspective, scope and overall objective of the model?	Y	Y	Y
8 Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	Y	Y	Y
9 Are the sources of the data used to develop the structure of the model specified?	Y	UNC	Y
10 Are the causal relationships described by the model structure justified appropriately?	Y	Y	Y
11 Are the structural assumptions transparent and justified?	Y	Y	Y

Note: N= No; NA = Not applicable; UNC = Unclear; Y = Yes.

Appendix 1: Philips et al.'s quality assessment checklist for studies that include an economic model

Criteria	Smith et al., 2018	Teng et al., 2018	Fusco & Turchetti, 2016
12 Are the structural assumptions reasonable given the overall objective, perspective and scope of the model?	Y	Y	Y
13 Is there a clear definition of the options under evaluation?	Y	Y	Y
14 Have all feasible and practical options been evaluated?	N	Y	Y
15 Is there justification for the exclusion of feasible options?	NA	NA	NA
16 Is the chosen model type appropriate given the decision problem and specified casual relationships within the model?	Y	Y	Y
17 Is the time horizon of the model sufficient to reflect all important differences between the options?	Y	Y	Y
18 Are the time horizon of the model and the duration of treatment described and justified?	Y	Y	Y
19 Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological process of the disease in question and the impact of interventions?	Y	Y	Y
20 Is the cycle length defined and justified in terms of the natural history of disease?	Y	Y	Y
21 Are the data identification methods transparent and appropriate given the objectives of the model?	UNC	Y	UNC
22 Where choices have been made between data sources are these justified appropriately?	UNC	UNC	UNC
23 Has particular attention been paid to identifying data for the important parameters of the model?	Y	Y	Y
24 Has the quality of the data been assessed appropriately?	UNC	UNC	UNC

Note: N = No; NA = Not applicable; UNC = Unclear; Y = Yes.

Appendix 1: Philips et al.'s quality assessment checklist for studies that include an economic model

Criteria	Smith et al., 2018	Teng et al., 2018	Fusco & Turchetti, 2016
25 Where expert opinion has been used are the methods described and justified?	NA	NA	NA
26 Is the data modelling methodology based on justifiable statistical and epidemiological techniques?	Y	Y	Y
27 Is the choice of baseline data described and justified?	Y	Y	Y
28 Are transition probabilities calculated appropriately?	Y	Y	Y
29 Has a half-cycle correction been applied to both costs and outcomes?	N	N	N
30 If not, has the omission been justified?	N	N	N
31 If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques?	NA	NA	NA
32 Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified?	NA	NA	NA
33 Have alternative extrapolation assumptions been explored through sensitivity analysis?	NA	NA	NA
34 Have assumptions regarding the continuing effect of treatment once treatment is complete been documented and justified?	NA	NA	NA
35 Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis	NA	NA	NA
36 Are the costs incorporated into the model justified?	Y	Y	Y
37 Has the source for all costs been described?	Y	Y	Y

Criteria	Smith et al., 2018	Teng et al., 2018	Fusco & Turchetti, 2016
38 Have discount rates been described and justified given the target decision maker?	Y	Y	Y

Note: N = No; NA = Not applicable; UNC = Unclear; Y = Yes.

Appendix 1: Philips et al.'s quality assessment checklist for studies that include an economic model

Criteria	Smith et al., 2018	Teng et al., 2018	Fusco & Turchetti, 2016
39 Are the utilities incorporated into the model appropriate?	Y	Y	Y
40 Is the source of utility weights referenced?	Y	Y	Y
41 Are the methods of derivation for the utility weights justified?	UNC	UNC	UNC
42 Have all data incorporated into the model been described and referenced in sufficient detail?	Y	Y	Y
43 Has the use of mutually inconsistent data been justified (i.e. are assumptions and choices appropriate)?	Y	Y	Y
44 Is the process of data incorporation transparent?	Y	Y	Y
45 If data have been incorporated as distributions, has the choice of distributions for each parameter been described and justified?	N	N	N
46 If data have been incorporated as distributions, is it clear that second order uncertainty is reflected?	UNC	UNC	UNC
47 Have the four principal types of uncertainty been addressed?	N	N	N
48 If not, has the omission of particular forms of uncertainty been justified?	N	N	N
49 Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?	N	N	N

Note: N = No; NA = Not applicable; UNC = Unclear; Y = Yes.

Appendix 1: Philips et al.'s quality assessment checklist for studies that include an economic model

Criteria	Smith et al., 2018	Teng et al., 2018	Fusco & Turchetti, 2016
50 Is there evidence that structural uncertainties have been addressed via sensitivity analysis?	N	N	N
51 Has heterogeneity been dealt with by running the model separately for different subgroups?	Y	Y	Y
52 Are the methods of assessment of parameter uncertainty appropriate?	Y	Y	Y
53 If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified?	Y	Y	Y
54 Is there evidence that the mathematical logic of the model has been tested thoroughly before use?	UNC	UNC	UNC
55 Are any counterintuitive results from the model explained and justified?	NA	NA	NA
56 If the model has been calibrated against independent data, have any differences been explained and justified?	NA	NA	NA
57 Have the results been compared with those of previous models and any differences in results explained?	Y	Y	Y

Note: N = No; NA = Not applicable; UNC = Unclear; Y = Yes.