ABSTRACT

Background: Economic evaluations of health interventions pose a particular challenge for reporting because substantial information must be conveyed to allow scrutiny of study findings. Despite a growth in published reports, existing reporting guidelines are not widely adopted. There is also a need to consolidate and update existing guidelines and promote their use in a user-friendly manner. A checklist is one way to help authors, editors, and peer reviewers use guidelines to improve reporting. Objective: The task force’s overall goal was to provide recommendations to optimize the reporting of health economic evaluations. The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement is an attempt to consolidate and update previous health economic evaluation guidelines into one current, useful reporting guidance. The CHEERS Elaboration and Explanation Report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force provides explanation and elaboration, as well as an example for each recommendation. The primary audiences for the CHEERS statement are researchers reporting economic evaluations and the editors and peer reviewers assessing them for publication. Methods: The need for new reporting guidance was identified by a survey of medical editors. Previously published checklists or guidance documents related to reporting economic evaluations were identified from a systematic review and subsequent survey of task force members. A list of possible items from these efforts was created. A two-round, modified Delphi Panel with representatives from academia, clinical practice, industry, and government, as well as the editorial community, was used to identify a minimum set of items important for reporting from the larger list. Results: Out of 44 candidate items, 24 items and accompanying recommendations were developed, with some specific recommendations for single study-based and model-based economic evaluations. The final recommendations are subdivided into six main categories: 1) title and abstract, 2) introduction, 3) methods, 4) results, 5) discussion, and 6) other. The recommendations are contained in the CHEERS statement, a user-friendly 24-item checklist. The task force report provides explanation and elaboration, as well as an example for each recommendation. The ISPOR CHEERS statement is available online via the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force webpage (http://www.ispor.org/TaskForces/EconomicPubGuidelines.aspx). Conclusions: We hope that the ISPOR CHEERS statement and the accompanying task force report guidance will lead to more consistent and
translucence, and ultimately, better health decisions. To facilitate wider dissemination and uptake of this guidance, we are copublishing the CHEERS statement across 10 health economics and medical journals. We encourage other journals and groups to consider endorsing the CHEERS statement. The author team plans to review the checklist for an update in 5 years.

**Background to the Task Force**

The ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force was approved by the ISPOR Board of Directors in 2009 to develop guidance to improve the reporting of health economic evaluations. Task force membership was comprised of health economic journal editors and content experts from around the world.

The task force met bimonthly via teleconference and in person at ISPOR annual meetings and congresses to develop reporting guidance based on a modified Delphi Panel process. A group of international experts representing academia, biomedical journal editors, the pharmaceutical industry, government decision makers, and those in clinical practice were invited to participate. Forty-seven participants, including task force members, completed the two-round Delphi Panel. See Appendix 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2013.02.002 for composition of the task force and Delphi Panel participants, as well as the Delphi Panel process.

The task force submitted their first draft to the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force Review Group. Written comments were submitted by 24 reviewers. The report was revised and re-titled Consolidated Health Economic Evaluation Reporting Standards (CHEERS) at a face-to-face meeting of the task force in May 2012. The revised CHEERS report was presented at the ISPOR 17th Annual International Meeting in Washington, DC. Oral comments were considered, the report revised again, and a final draft was submitted to ISPOR's membership for comments in January 2013. All comments were considered by the task force and addressed as appropriate for a consensus statement and report. Collectively, the task force received a total of 179 written comments submitted by 48 ISPOR members. All written comments are published on the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force – CHEERS webpage on the ISPOR website: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp that can also be accessed via the Research menu on ISPOR’s home page: http://www.ispor.org. Reviewers who submitted written comments are acknowledged in a separate listing on this webpage as well. The ISPOR CHEERS Statement was endorsed and simultaneously published by 9 journals in late March 2013.

**Definition and Use of Health Economic Evaluation**

Health economic evaluations are conducted to inform health care resource allocation decisions. Economic evaluation has been defined as “the comparative analysis of alternative courses of action in terms of both their costs and their consequences” [1]. All economic evaluations assess costs, but approaches to measuring and valuing the consequences of health interventions may differ (Box 1). Economic evaluations have been widely applied in health policy, including the assessment of prevention programs (such as vaccination, screening, and health promotion), diagnostics, treatment interventions (such as drugs and surgical procedures), organization of care, and rehabilitation. Structured abstracts of published economic evaluations can be found in a number of publicly available databases, such as the Health Economic Evaluations Database (HEED) [2], the National Health Service Economic Evaluation Database (NHS EED) [3], and the Tufts Cost-Effectiveness Analysis Registry [4]. Economic evaluations are increasingly used for decision making and are an important component of health technology assessment programs internationally [5].

**Reporting Challenges and Shortcomings in Health Economic Evaluations**

Compared with clinical studies that report only the consequences of an intervention, economic evaluations require more reporting space for additional items, such as resource use, costs, benefits, and health outcomes. Economic evaluations, which are focused on the comparative analysis of alternative courses of action in terms of both their costs and their consequences, must consider as many types of outcomes as possible (Box 1). Costs are measured in units of money, whereas consequences may be measured in terms of quality-adjusted life-years gained, quality-adjusted life-years avoided, additional disability-adjusted life-years, or quality-adjusted life-years.

**Box 1 – Forms of economic evaluation.**

Specific forms of analysis reflect different approaches to evaluating the consequences of health interventions. Health consequences may be estimated from a single analytic (experimental or nonexperimental) study, a synthesis of studies, mathematical modeling, or a combination of modeling and study information. Cost-consequences analyses examine costs and consequences, without attempting to isolate a single consequence or aggregate consequences into a single measure. In cost-minimization analysis (CMA), the consequences of compared interventions are required to be equivalent and only relative costs are compared. Cost-effectiveness analysis (CEA) measures consequences in natural units, such as life-years gained, disability days avoided, or cases detected. In a variant of CEA, often called cost-utility analysis, consequences are measured in terms of preference-based measures of health, such as quality-adjusted life-years, or disability-adjusted life-years. Finally, in cost-benefit analysis, consequences are valued in monetary units [1].

Readers should be cautioned that an economic evaluation might be referred to as a “cost-effectiveness analysis” or “cost-benefit analysis” even if it does not strictly adhere to the definitions above. Multiple forms may also exist within a single evaluation. Different forms of analysis provide unique advantages or disadvantages for decision making. The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement can be used with any form of economic evaluation.
preference-related information, and cost-effectiveness results. This creates challenges for editors, peer reviewers, and those who wish to scrutinize a study’s findings [6]. There is evidence that the quality of reporting of economic evaluations varies widely, and could potentially benefit from improved quality assurance mechanisms [7,8].

Transparency and structure in reporting is especially relevant for health economic evaluations because 1) the number of published studies continues to grow [9]; 2) there are significant opportunity costs from decisions based on misleading study findings; and 3) outside of economic evaluations conducted alongside clinical trials, there are no widely implemented mechanisms for warehousing data to allow for independent interrogation, such as ethics review proceedings, regulator dossiers, or study registries. Instead, independent analysis may rely on the record keeping of individual investigators.

Even with existing measures to promote transparency for other study types, such as trial registries, biomedical journal editors have increasingly promoted and endorsed the use of reporting guidelines and checklists to improve reporting. Endorsement of guidelines by journals has been shown to improve reporting [10]. The combination of the risk of making costly decisions due to poor reporting and the lack of mechanisms that promote accountability makes transparency in reporting economic evaluations especially important and a primary concern among journal editors and decision makers [6,11].

**Aim and Scope**

The aim of the ISPOR Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement is to provide recommendations in a checklist to optimize reporting of health economic evaluations. The need for contemporary reporting guidance for economic evaluations was recently identified by researchers and biomedical journal editors [12]. The CHEERS statement attempts to consolidate and update previous efforts [13–24] into a single useful reporting standard. The CHEERS statement is not intended to prescribe how economic evaluations should be conducted; rather, analysts should have the freedom to innovate or make their own methodological choices. Its objective is to ensure that these choices are clear to reviewers and readers. Therefore, the CHEERS statement could be used to examine the quality of reporting, but it is not intended to assess the quality of conduct. Other checklists have been developed for this purpose [25].

The primary audiences for the CHEERS statement are researchers conducting economic evaluations and the editors and peer reviewers of the journals in which they intend to publish. We hope the CHEERS statement, which consists of a 24-item checklist and accompanying recommendations on the minimum amount of information to be included when reporting economic evaluations, is a useful and practical tool for these audiences and will improve reporting and, in turn, health and health care decisions.

**Methods**

The task force’s approach in developing this report was based on recommendations for developers of reporting guidelines [26] and was modeled after other similar efforts [27–29]. First, the need for new guidance was identified by a task force examining priorities for quality improvement of economic evaluations and a survey of members of the World Association of Medical Editors. Of the 965 members surveyed, 55 journals with a largely (72%) international readership responded [12]. Ninety-one percent of the respondents indicated that they would use a standard if one were widely available [12]. Second, previously published checklists or guidance documents related to reporting economic evaluations were identified from a systematic review and discussion among task force members [30]. Table 1 provides a list of those published guidelines identified, including some developed through a similar consensus approach [13–15].

Items identified in these reports were used to create a preliminary list of items. The task force, consisting of 10 members with considerable experience in journal editorship, reporting guideline

<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Description</th>
<th>Checklist?</th>
<th>Main items (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drummond [15]</td>
<td>1996</td>
<td>Consensus panel—Instructions for authors to BMJ</td>
<td>Yes</td>
<td>35</td>
</tr>
<tr>
<td>Gold/Siegel [14,16]</td>
<td>1996</td>
<td>Consensus panel—US Public Health Service Appointed</td>
<td>Yes</td>
<td>37</td>
</tr>
<tr>
<td>Nuijten [17]</td>
<td>1998</td>
<td>Specific to modeling studies</td>
<td>No</td>
<td>12</td>
</tr>
<tr>
<td>Vintzileos [18]</td>
<td>2004</td>
<td>Economic evaluation in obstetrics</td>
<td>Yes</td>
<td>33</td>
</tr>
<tr>
<td>Drummond [19]</td>
<td>2005</td>
<td>Suggestions for improving generalizability and uptake of studies</td>
<td>No</td>
<td>10</td>
</tr>
<tr>
<td>Ramsey [20]</td>
<td>2005</td>
<td>ISPOR Task Force guidance for economic evaluation alongside clinical trials</td>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>Goetghebeur [21]</td>
<td>2008</td>
<td>Suggestions for structured reporting to improve decision making</td>
<td>Yes</td>
<td>11</td>
</tr>
<tr>
<td>Davis [22]</td>
<td>2010</td>
<td>Economic evaluation of fall prevention strategies</td>
<td>Yes</td>
<td>10</td>
</tr>
<tr>
<td>Petrou [23,24]</td>
<td>2011</td>
<td>General guidance for economic evaluation alongside modeling and clinical trials</td>
<td>No</td>
<td>7</td>
</tr>
</tbody>
</table>

* Readers will note that checklists and guidance for the conduct of economic evaluations (e.g., The Consensus on Health Economic Criteria (CHEQ) List, The Quality of Health Economic Studies (QHES) List, and The Pediatrics Quality Appraisal Questionnaire (PQAQ)) are not included in this review.
development, decision modeling, and conducting health economic evaluation, was asked to review and finalize the list. Task force members were then asked to nominate a purposive sample of possible candidates for a Delphi Panel with a focus on finding participants representative of different primary work environments and geographic locations. The ten task force members and 37 participants taking the survey (n = 47) included a broad international representation from academia, clinical practice, industry, and government, with many holding editorial positions at health economic, outcomes research, and other medical journals (see Appendix 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2013.02.002). Panelists were invited to participate by e-mail and directed to a Web-based survey.

The survey consisted of an instructions page and three separate sections: the first for personal information, the second to score candidate reporting items, and the third to comment on the survey or to suggest additional items. Items were numbered and arranged according to typical article sections (e.g., title, abstract, and introduction). Task force members piloted the Delphi survey process.

In total, 44 items were circulated to participants in round 1 of the Delphi Process. Each item was accompanied by a description and suggested direction(s). For example, with the item “Discount Rate and Rationale,” the following description was included: “If applicable, report and justify the discount rate used to calculate present values of costs and/or health outcomes.”

In round 1, participants scored the importance of items by using a 10-point Likert scale (anchored from 1, not important, to 10, very important). They could also provide a rationale or provide information for their score in text. In addition, they rated their ability to judge the importance of each item on the basis of their current knowledge (1, not confident, to 3, very confident). Participant responses were recorded in an electronic spreadsheet. One author (DH) then collated comments and initiated a second survey round with additional information about item ranks, averages weighted by rater confidence, nonweighted averages, median scores, and associated distributions.

In round 2 of the survey, items with a weighted average score of more than 8 were labeled “included.” Items with a weighted average score of more than 6 were labeled “possible.” Cutoff thresholds for the selection of items were based on previous reporting guideline efforts. While all items were included in the second round of the survey, participants were informed that items labeled “possible” would be candidates for the final checklist only if they received a higher score. Items with a score of 6 or less after round 2 were labeled “rejected” and not considered for the final checklist. Items appeared in order of ranked importance, based on the weighted average scores. Respondents were asked to revisit their scores and revise or provide a reason if necessary. Item-specific comments from round 1 were included below each ranked item in the second survey round so that participants could see all the comments an item received. Participants could also see additional statistics (i.e., nonweighted scores, ranks, and interquartile ranges) as well as the score that the participant gave the item in the first round. Thirty-five participants completed round 2.

Participants were given 14 days each to complete the survey’s first and second rounds. An e-mail reminder was sent to those who had not completed the survey round. At the task force face-to-face consensus meeting held in early May 2012 in Boston, MA, task force members reviewed all comments submitted by the Delphi Panel participants on items not rejected after two rounds. Although 28 items were initially considered “included,” and another 12 considered “possible,” it was decided, on the basis of the opinion of the task force members and qualitative feedback on the survey, that some overlap and consolidation was required to shorten the checklist to a more user-friendly 24 items. Comments and the survey score results were made available to task force members in advance of this meeting.

Based on these deliberations, a consensus list of recommendations was developed. A first draft of the CHEERS checklist was presented at the ISPOR 17th Annual International Meeting held in June 2012 in Washington, DC. The checklist was subsequently revised on the basis of comments.

The revised draft was circulated to the 200+ member ISPOR Health Economic Evaluation Publication Guidelines Task Force - CHEERS Review Group and to the Delphi Panel participants surveyed in the research project. Written comments were submitted by 24 reviewers. All comments were reviewed by the task force and addressed as appropriate. The final product is the explanation and elaboration report prepared by task force members.

How to Use This Report

The examples and explanations in this report are intended to facilitate an understanding of the checklist items and recommendations. In the section below, each item from the CHEERS statement checklist (Table 2) is given along with its accompanying recommendation. An illustrative example of the recommendation follows along with an explanation as to the importance of the item, including empirical evidence to support the claim if available. Items and recommendations are subdivided into six main categories: 1) title and abstract, 2) introduction, 3) methods, 4) results, 5) discussion, and 6) other. A copy of the checklist can be found on the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force - CHEERS webpage (http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp).

Checklist Items

The CHEERS statement assumes that the amount of information required for adequate reporting will exceed conventional space limits of most journal reports. Therefore, in making our recommendations, we assume that authors and journals will make some information available to readers by using online appendices and other means where required.

To encourage dissemination and use of a single international standard for reporting, the CHEERS statement is being simultaneously published in biomedical journals endorsing the recommendations including BMC Medicine, BMJ, BJOG: An International Journal of Obstetrics and Gynaecology, Clinical Therapeutics, Cost-effectiveness and Resource Allocation, The European Journal of Health Economics, International Journal of Technology Assessment in Health Care, Journal of Medical Economics, Pharmacoeconomics, and Value in Health. These journals were solicited by the task force and represent the largest publishers of economic evaluations and those widely read by the medical community. To facilitate wider dissemination and uptake of this reporting guidance, we encourage other journals, and groups, to consider endorsing CHEERS.

Title and Abstract

Item 1: Title

Recommendation: Identify the study as an economic evaluation, or use more specific terms such as “cost-effectiveness analysis,” and describe the interventions compared.

Example: Economic Evaluation of Endoscopic Versus Open Vein Harvest for Coronary Artery Bypass Grafting [31].

Explanation: There are at least 1 million research articles published annually [32]. These articles are indexed in various electronic databases, such as Medline, HEED, and NHS EED. These databases contain journal citations and abstracts for biomedical literature from around the world and are indexed by using a
<table>
<thead>
<tr>
<th>Section/item</th>
<th>Item no.</th>
<th>Recommendation</th>
<th>Reported on page no./line no.</th>
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</thead>
<tbody>
<tr>
<td><strong>Title and abstract</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Title</strong></td>
<td>1</td>
<td>Identify the study as an economic evaluation, or use more specific terms such as “cost-effectiveness analysis” and describe the interventions compared.</td>
<td></td>
</tr>
<tr>
<td><strong>Abstract</strong></td>
<td>2</td>
<td>Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base-case and uncertainty analyses), and conclusions.</td>
<td></td>
</tr>
<tr>
<td><strong>Introduction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Background and objectives</strong></td>
<td>3</td>
<td>Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.</td>
<td></td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Target population and subgroups</strong></td>
<td>4</td>
<td>Describe characteristics of the base-case population and subgroups analyzed including why they were chosen.</td>
<td></td>
</tr>
<tr>
<td><strong>Setting and location</strong></td>
<td>5</td>
<td>State relevant aspects of the system(s) in which the decision(s) need(s) to be made.</td>
<td></td>
</tr>
<tr>
<td><strong>Study perspective</strong></td>
<td>6</td>
<td>Describe the perspective of the study and relate this to the costs being evaluated.</td>
<td></td>
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<tr>
<td><strong>Comparators</strong></td>
<td>7</td>
<td>Describe the interventions or strategies being compared and state why they were chosen.</td>
<td></td>
</tr>
<tr>
<td><strong>Time horizon</strong></td>
<td>8</td>
<td>State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.</td>
<td></td>
</tr>
<tr>
<td><strong>Discount rate</strong></td>
<td>9</td>
<td>Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.</td>
<td></td>
</tr>
<tr>
<td><strong>Choice of health outcomes</strong></td>
<td>10</td>
<td>Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.</td>
<td></td>
</tr>
<tr>
<td><strong>Measurement of effectiveness</strong></td>
<td>11a</td>
<td>Single study–based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11b</td>
<td>Synthesis-based estimates: Describe fully the methods used for the identification of included studies and synthesis of clinical effectiveness data.</td>
<td></td>
</tr>
<tr>
<td><strong>Measurement and valuation of preference-based outcomes</strong></td>
<td>12</td>
<td>If applicable, describe the population and methods used to elicit preferences for outcomes.</td>
<td></td>
</tr>
<tr>
<td><strong>Estimating resources and costs</strong></td>
<td>13a</td>
<td>Single study–based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>13b</td>
<td>Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.</td>
<td></td>
</tr>
<tr>
<td><strong>Currency, price date, and conversion</strong></td>
<td>14</td>
<td>Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.</td>
<td></td>
</tr>
<tr>
<td><strong>Choice of model</strong></td>
<td>15</td>
<td>Describe and give reasons for the specific type of decision-analytic model used. Providing a figure to show model structure is strongly recommended.</td>
<td></td>
</tr>
<tr>
<td><strong>Assumptions</strong></td>
<td>16</td>
<td>Describe all structural or other assumptions underpinning the decision-analytic model.</td>
<td></td>
</tr>
<tr>
<td><strong>Analytic methods</strong></td>
<td>17</td>
<td>Describe all analytic methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (e.g., half-cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.</td>
<td></td>
</tr>
</tbody>
</table>
variety of simple and more advanced terms. Once each article is indexed, databases can be searched. To help the indexers provide the best cataloguing and indexing terms, titles should be precise and describe the content of the report. If authors clearly state in their title that the report provides an economic evaluation and describe the interventions, there is a greater likelihood that the article will be catalogued by using these terms. Authors are encouraged to use more specific terms that describe the form of analysis, such as “cost-effectiveness analysis” or “cost-benefit analysis” to better inform the reader and clearly identify the report as an economic evaluation. Vague or ambiguous titles run the risk of being inappropriately indexed, making identification more difficult for database searchers. It has been suggested that there is a need to improve methods to better identify economic evaluations because current search approaches lack specificity [33].

Example:

**BACKGROUND:** The best strategies to screen postmenopausal women for osteoporosis are not clear.

**OBJECTIVE:** To identify the cost-effectiveness of various screening strategies.

**DESIGN:** Individual-level state-transition cost-effectiveness model.

**DATA SOURCES:** Published literature.

**TARGET POPULATION:** U.S. women aged 55 years or older.

**TIME HORIZON:** Lifetime.

**PERSPECTIVE:** Payer.

**INTERVENTION:** Screening strategies composed of alternative tests (central dual-energy x-ray absorptiometry [DXA], calcaneal quantitative ultrasonography [QUS], and the Simple Calculated Osteoporosis Risk Estimation [SCORE] tool) initiation ages, treatment thresholds, and rescreening intervals. Oral bisphosphonate treatment was assumed, with a base-case adherence rate of 50% and a 5-year on/off treatment pattern.


**RESULTS OF BASE-CASE ANALYSIS:** At all evaluated ages,

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### Table 2 – continued

<table>
<thead>
<tr>
<th>Section/item</th>
<th>Item no.</th>
<th>Recommendation</th>
<th>Reported on page no./line no.</th>
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</thead>
<tbody>
<tr>
<td><strong>Results</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study parameters</td>
<td>18</td>
<td>Report the values, ranges, references, and if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.</td>
<td></td>
</tr>
<tr>
<td>Incremental costs and outcomes</td>
<td>19</td>
<td>For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.</td>
<td></td>
</tr>
<tr>
<td>Characterizing uncertainty</td>
<td>20a</td>
<td>Single study–based economic evaluation: Describe the effects of sampling uncertainty for estimated incremental cost, incremental effectiveness, and incremental cost-effectiveness, together with the impact of methodological assumptions (such as discount rate, study perspective).</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20b</td>
<td>Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.</td>
<td></td>
</tr>
<tr>
<td>Characterizing heterogeneity</td>
<td>21</td>
<td>If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.</td>
<td></td>
</tr>
<tr>
<td><strong>Discussion</strong></td>
<td></td>
<td></td>
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<tr>
<td>Study findings, limitations, generalizability, and current knowledge</td>
<td>22</td>
<td>Summarize key study findings and describe how they support the conclusions reached. Discuss limitations and the generalizability of the findings and how the findings fit with current knowledge.</td>
<td></td>
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<tr>
<td><strong>Other</strong></td>
<td></td>
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<tr>
<td>Source of funding</td>
<td>23</td>
<td>Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other nonmonetary sources of support.</td>
<td></td>
</tr>
<tr>
<td>Conflicts of interest</td>
<td>24</td>
<td>Describe any potential for conflict of interest among study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors’ recommendations.</td>
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</tbody>
</table>

Note. For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement checklist.
screening was superior to not screening. In general, quality-adjusted life-days gained with screening tended to increase with age. At all initiation ages, the best strategy with an incremental cost-effectiveness ratio (ICER) of less than $50,000 per QALY was DXA screening with a T-score threshold of −2.5 or less for treatment and with follow-up screening every 5 years. Across screening initiation ages, the best strategy with an ICER less than $50,000 per QALY was initiation of screening at age 55 years by using DXA −2.5 with rescreening every 5 years. The best strategy with an ICER less than $100,000 per QALY was initiation of screening at age 55 years by using DXA with a T-score threshold of −2.0 or less for treatment and then rescreening every 10 years. No other strategy that involved treatment of women with osteopenia had an ICER less than $100,000 per QALY. Many other strategies, including strategies with SCORE or QUS prescreening, were also cost-effective, and in general the differences in effectiveness and costs between evaluated strategies was small.

RESULTS OF SENSITIVITY ANALYSIS: Probabilistic sensitivity analysis did not reveal a consistently superior strategy.

LIMITATIONS: Data were primarily from white women. Screening initiation at ages younger than 55 years were not examined. Only osteoporotic fractures of the hip, vertebrae, and wrist were modeled.

CONCLUSION: Many strategies for postmenopausal osteoporosis screening are effective and cost-effective, including strategies involving screening initiation at age 55 years. No strategy substantially outperforms another.

PRIMARY FUNDING SOURCE: National Center for Research Resources. [34]

Explanation: We recommend the use of structured abstracts when a summary of the economic evaluation is required. Structured abstracts provide readers with a series of headings pertaining to the background, objectives, type of study, perspective, form of analysis, study population, benefit and costs measures, discount rate(s), key findings, and analyses of uncertainty. Some journals may have this information reported under specific headings, and authors may need to use these headings. Some studies have found that structured abstracts are of higher quality than the more traditional descriptive abstracts [35] and that they allow readers to find information more easily [36].

A complete, transparent, and sufficiently detailed abstract is important because readers often assess the relevance of a report or decide whether to read the full article on the basis of information provided in the abstract. In some settings, readers have access only to a title and abstract and may be forced to make judgments or decisions on the basis of this information. Abstracts will also contain key words, helpful for indexing and later article identification and can also help editors and peer reviewers quickly assess the relevance of the findings.

A journal abstract should contain sufficient information about an economic evaluation to serve as an accurate record of its conduct and findings, providing optimal information about the evaluation within the space constraints and format of a journal. The abstract should not include information that does not appear in the body of the article. Studies comparing the accuracy of information reported in a journal abstract with that reported in the text of the full publication have found claims that are inconsistent with, or missing from, the body of the full article [37–40]. There is evidence that abstracts of published economic evaluations frequently omit information critical to proper interpretation of their methods or findings [8].

Introduction

Item 3: Introduction

Recommendation: Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.

Example:

Many nonsurgical treatments, such as decongestants, antihistamines, antibiotics, mucolytics, steroids, and autoinflation, are currently used in the UK National Health Service (NHS) as short-term treatments for otitis media (OME) in an attempt to avoid unnecessary secondary referral and costly surgery. However, there is little evidence that these nonsurgical options are beneficial. "...further evaluation should aim to estimate the cost-effectiveness of topical intranasal corticosteroids in order to provide decision-makers with evidence on whether the considerable resources currently being invested in this area represent an efficient use of scarce public resources...." This paper summarizes the methods and results of an economic evaluation that was based on evidence from the GNOME trial. [41, p. 543]

Explanation: Economic evaluations may examine whether a new intervention should be reimbursed or may assess existing health interventions. Sometimes, a resource allocation question will be researcher- or consumer-driven. Increasingly, however, economic evaluations are being conducted to meet the needs of decision makers who need to understand the consequences of reallocating health care resources. If the study was conducted for a decision maker, this should be stated. Otherwise, a description of the importance of the question should be given.

It is not enough to state that "[t]he purpose of the study was to assess the cost-effectiveness of treatment X." Correct specification of the study question requires details of the study (patient) population, the intervention of interest, the relevant comparator(s), and the health care setting. Therefore, reporting on this item needs to be considered in conjunction with that for CHEERS checklist items 4 to 7 (i.e., target population and subgroups, setting and location, study perspective, and comparators) described below. A good example of a study question would be "We assessed the cost-effectiveness of etanercept, as compared with infliximab, in patients whose rheumatoid arthritis was inadequately controlled by methotrexate, within the context of the UK National Health Service."

Methods—General

Item 4: Target population and subgroups

Recommendation: Describe characteristics of the base-case population and subgroups analyzed including why they were chosen.

Example:

Participants were men and women who presented at 40-80 years with total cholesterol concentrations of at least 3.5 mmol/l (135 mg/dl) and a medical history of coronary disease, cerebrovascular disease, other occlusive arterial disease, diabetes mellitus, or (if a man aged ≥ 65) treated hypertension .... Participants were divided into five similar sized groups of estimated five-year risk of a major vascular event, with average risks in the groups ranging from 12% to 42% (which correspond to risks of 4% to 12% for non-fatal myocardial infarction or coronary death). [42, p. 1]

Explanation: The eligible population group is important to define because in numerous cases, cost-effectiveness will vary by population characteristics [43]. In many instances, the studies, from which effectiveness estimates are taken, will define baseline population characteristics for a decision-analytic model. Subgroups may relate to univariate risk factors (e.g., presence or absence of a particular genotype or phenotype) or multivariate risk factors (e.g., cardiovascular risk factors in the example for item 4).

There is considerable evidence to suggest that subgroup analyses are often poorly conducted, reported, and interpreted [44–49]. Therefore, authors should report or provide a reference to...
factors that may support their interpretation of results, such as biological plausibility of hypotheses and prespecification of subgroup testing (see Sun et al. [50] for example of current reporting guidance). Sufficient information should be provided to support assumptions about subgroup differences.

Item 5: Setting and location
Recommendation: State relevant aspects of the system(s) in which the decision(s) needs to be made.

Example: In Australia, a standardised approach to assessing cost-effectiveness (ACE) has been developed ... [51]
Explanation: An economic evaluation addresses a question relevant to the place and setting in which the resource allocation decision is being contemplated. This includes the geographical location (country or countries) and the particular setting of health care (i.e., primary, secondary, tertiary care, or community/public health interventions), as well as any other relevant sectors, such as education or legal systems [1]. A clear description of the location, setting, or other relevant aspects of the system in which the intervention is provided is needed so that readers can assess external validity, generalizability, and transferability of study results to their particular setting. Authors can subsequently interpret findings in light of system-specific factors in the “Discussion” section (see Item 22).

Item 6: Study perspective
Recommendation: Describe the perspective of the study and relate this to the costs being evaluated.

Example (1):
The cost of implementing each intervention is derived from an Australian health sector perspective. This includes costs to both government and patients, including time and travel costs, but excluding patient time costs associated with changes in physical activity. Intervention start-up costs (e.g., costs of research and development of intervention materials for GP prescription) are excluded so that all interventions are evaluated and compared as if operating under steady-state conditions... [51, p. 2]

Example (2): Estimates of direct costs associated with each type of surgery were derived from the perspective of the payer and included hospital charges and professional fees for the initial operation as well as those for any subsequent services or procedures that might be necessary to manage postoperative complications. [52]

Explanation: The study perspective is the viewpoint from which the intervention’s costs and consequences are evaluated. A study could be conducted from one or more perspectives, including a patient perspective, an institutional perspective (e.g., hospital perspective), a health care payer’s perspective (e.g., sickness fund, Medicare in the United States), a health care system perspective, a public health perspective, or a societal perspective. Most studies are conducted from a health system or payer perspective (e.g., National Health Service in England and Medicare in the United States) or from a societal perspective. The health system and payer’s perspectives typically include direct medical care costs, including the cost of the intervention itself and follow-up treatment costs. A societal perspective will also estimate broader costs to society (e.g., productivity losses resulting from poor health or premature death, family costs, or costs to other sectors such as the criminal justice system). Because these perspectives lack standard definitions, authors should describe the perspective (e.g., health care system, societal) in terms of costs included and their associated components (e.g., direct medical costs, direct nonmedical costs, and indirect/productivity costs), and how this fits the needs of the target audience(s) and decision problem. When a societal perspective is used, reporting the results from a health care system or payer perspective, where only direct medical costs are reported, should also be considered. References to jurisdiction-specific guidelines or documents describing local economic evaluation methods can also be provided, along with a reason for why these were chosen.

Item 7: Comparators
Recommendation: Describe the interventions or strategies being compared and state why they were chosen.

Example:
Given that both increases in invasive disease caused by non-vaccine serotypes and absence of herd protection may considerably affect the cost effectiveness of the current Dutch vaccination programme, we set out to update cost effectiveness estimates for the current four dose schedule of PCV-7 ... Also, we investigate the cost effectiveness of reduced dose schedules and vaccine price reductions combined with the implementation of 10 valent and 13 valent pneumococcal vaccines (PCV-10 and PCV-13). [53, p. 2]

Explanation: Economic evaluations based on single studies compare only the interventions in the study concerned, while model-based evaluations allow all relevant comparators to be assessed [54]. Interventions and delivery of technologies may differ among countries or settings, making it important to describe the relevant characteristics of studied interventions. This includes intensity or frequency of treatment (for behavioral or nondrug interventions), drug dosage schedule, route, and duration of administration. Relevant comparators may include “do nothing,” “current practice,” or “the most cost-effective alternative.” Authors should describe why the particular comparators were chosen. Authors should consider listing all potentially relevant comparators or explaining why a more common, lower priced, or more effective comparator was not considered.

Item 8: Time horizon
Recommendation: State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.

Example:
... we compared the progress of a hypothetical cohort of women with heavy menstrual bleeding when they are treated by four alternative interventions... The starting age of women in the model is 42, as this is the mean age of women in all the ablation randomised controlled trials, and the period covered is a total of 10 years. We assume that all women will become menopausal at the age of 52, the average age of menopause in the UK. ... These are also the assumptions used by earlier authors. [55, p. 2]

Explanation: The time horizon refers to the length of time over which costs and consequences are being evaluated. The relevant time horizon reflects the long-term consequences of a decision and is typically longer than the length of follow-up in trials. Many countries’ economic evaluation guidelines recommend a specific time horizon to be followed for local decision making. Often, economic evaluations based on individual patient data from a clinical trial have truncated time horizons even if patient-relevant outcomes are longer-term, such as mortality [54]. Some interventions, such as preventive interventions, and some study designs, such as evaluations based on dynamic transmission models, will be particularly sensitive to the choice of the time horizon [56]. The time horizon and reasons for its choice should be reported.
Item 9: Discount rate
Recommendation: Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.

Example: Both costs and health outcomes were discounted at an annual rate of 5%, as recommended by Brazilian guidelines. [57]

Explanation: Discount rates allow analysts to adjust for time preference for the costs and consequences of a decision, by providing present values. Discount rates are not universal—they will vary according to the setting, location, and perspective of the analysis [58]. Some health jurisdictions have recommended rates, often in economic evaluation guidelines, while others do not. In addition, some jurisdictions may recommend a common rate for both costs and consequences, while others prescribe differential rates.

Reporting discount rates is important because the findings of an economic evaluation, specifically those in which costs or consequences of an intervention are not realized for several years, may be particularly sensitive to the choice of the discount rate [59]. Authors are encouraged to relate the chosen rate to the decision maker by citing local economic evaluation guidelines or treasury reports. Although it is common practice not to apply discount rates for economic evaluations with short (e.g., <1 year) time horizons, analysts should report this rate as 0% for clarity.

Methods—Outcomes

Item 10: Choice of outcomes
Recommendation: Describe what outcomes were used as the measure(s) of benefit in the economic evaluation and their relevance for the type of analysis performed.

Examples:

1. The health outcomes of each intervention are evaluated in disability-adjusted life-years (DALYs), the measure favoured by the World Health Organization... and the alternative to the quality-adjusted life-year (QALY) measure used in some cost-effectiveness analyses of physical activity interventions. [51]

2. We then developed a stochastic simulation model to determine the incremental per-case cost of radial versus femoral catheterization. The model outcome, the incremental cost of radial versus femoral catheterization, is shown in Equation 1... [60]

Explanation: Outcomes used in economic evaluation might include, but are not limited to, outcomes expressed in natural units (e.g., myocardial infarctions avoided, life-years gained); outcomes based on preferences for health (e.g., quality-adjusted life-years [QALYs] or disability-adjusted life-years); or outcomes expressed in monetary terms for the purpose of cost-benefit analysis. Because the findings of an economic evaluation may be sensitive to the choice of outcome, the reason for choosing one measure of outcome over another should be provided.

Item 11: Measurement of effectiveness

Item 11a: Single study–based estimates.
Recommendation: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.

Example:

Methods for the Magpie Trial [ISRCTN86938761] are described elsewhere [61]. In brief, women with pre-eclampsia were eligible for trial entry if there was uncertainty about whether to use magnesium sulphate and they had not given birth or were within 24 hours of delivery. Women were randomised to either magnesium sulphate or placebo. The treatment regimen was an intravenous bolus followed by a 24-hour maintenance therapy. Each centre chose whether to use the intramuscular or intravenous route for maintenance. Clinical monitoring of urine output, respiratory rate and tendon reflexes were used for both regimens. All other aspects of care were according to local clinical practice. Primary outcomes were eclampsia and, for women randomised before delivery, death of the baby (including stillbirths). Follow-up was until discharge from hospital after delivery, or death. Overall, 10,141 women were randomised from 33 countries between 1998 and 2001. Follow-up data were available for 10,110. [62, p. 145]

Item 11b: Synthesis-based estimates
Recommendation: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.

Example:

We conducted systematic reviews to answer 32 questions to inform model parameters. We used published studies to answer 14 questions, primary datasets for 24 questions, and expert opinion for five questions. One question (vaccine efficacy) relied solely on expert opinion. Details of each review and data sources are given in the full report. [63]

We used multi-parameter evidence synthesis [64,65] to simultaneously estimate each model parameter using all relevant data inputs that directly or indirectly informed the parameters. The model parameters for infection outcomes and treatment effectiveness are summarised in tables 1 and 2. Further details are in the full report [63]. [66, p. 2]

Explanation: Economic evaluations of health interventions are underpinned by assessments of their clinical effectiveness. It may be helpful for analysts to first describe the source(s) of clinical data, whether from one or more studies, and the study design(s). If the economic evaluation is based on a single experimental or nonexperimental study with patient-level data, the design features of that source study or reference should be provided.

If this is the first time the source study is reported, attention should be paid to fulfilling other applicable reporting requirements (e.g., Consolidated Standards of Reporting Trials, CONSORT for randomized trials [27]; Strengthening the Reporting of Observational Studies in Epidemiology, STROBE for observational studies [67]). It is important to report why the single study was a sufficient source of clinical effectiveness data. Furthermore, if the time horizon of the economic evaluation is longer than that for the source study, the long-term extrapolation approach should be described as well as why it is appropriate.

Synthesis-based economic evaluation will require adequate information (i.e., conforming with Preferred Reporting Items for Systematic Reviews and Meta-Analyses [28]) or a reference to a report. This includes the strategy adopted to search and select relevant evidence, as well as information related to potential bias arising from study selection and synthesis methods. In addition, it may require reporting of long-term extrapolation methods.

Item 12: Measurement and valuation of preference-based outcomes

Recommendation: If applicable, describe the population and methods used to elicit preferences for outcomes.
Example: We used the EuroQol EQ-5D social tariff, estimated from a representative sample of the UK population, to convert patients’ responses to the EuroQol EQ-5D questionnaire at baseline, six, 12, and 24 months into single utility levels [68] ... We then constructed patient-specific utility profiles, assuming a straight-line relation between each of the patient’s utility levels. [69]

Explanation: In many jurisdictions, the preferred outcome measure in economic evaluation is the QALY, a preference-based measure of health outcome that combines length of life and health-related quality of life in a single metric. The methods for measuring changes in health-related quality of life that contribute to QALYs or other preference-based measures should be described. This may involve the use of a multiattribute utility measure—a generic health-related quality-of-life instrument with preexisting preference weights (utility values) that can be attached to each health state [70–72]. The format and timing(s) of these measurements should be described. Authors should consider recent guidance for reporting health-related quality-of-life measures in clinical trials [73]. When patients are either too ill or do not have the cognitive competencies to describe their own health-related quality of life, authors should describe the sources of proxy measurements and why these are appropriate.

The values placed on health-related quality of life may be derived from different sources and estimated by using a number of alternative preference-elicitation techniques. Consequently, authors should describe the population from which valuations were obtained in terms of size and demographic characteristics, for example, a representative sample of the general population, patients, providers, and expert opinion. This population may differ from the study population for the economic evaluation. Authors should also outline the preference elicitation technique used to value descriptions of health-related quality of life, for example, time trade-off approach, standard gamble approach, and discrete choice experiment. Methods for converting utility values at each time point of assessment into QALY profiles, for example, linear interpolation between measurements, should be described. If utility values are derived from non-preference-based measures of health-related quality of life, the empirical data and the statistical properties of the mapping function underpinning this derivation should be described.

Methods—Costs

Item 13: Estimating resource use and costs

Item 13a: Single study–based economic evaluation.
Recommendation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.

Item 13b: Model-based economic evaluation.
Recommendation: Describe approaches and data sources used to estimate resource use and costs associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.

Example: Costs in the first year were estimated from the REFLUX trial. The trial collected data on the use of health service resources up to one year.... These resources were costed using routine NHS costs and prices. [74]

Explanation: Costing involves two related, but separate, processes: estimation of the resource quantities in natural units and the application of prices (unit costs) to each resource item. The sources for the estimation of resource quantities and the date(s) they were collected should be outlined. These could be derived from a single clinical study, an existing database, routine sources, or the broader literature. Economic evaluations typically use prices from a wide range of sources, and so it is important to describe these sources so that they can be verified. In some settings, there may be multiple prices for the same resource item. This should be noted if the different cost estimates are to be used in a sensitivity analysis. On some occasions, especially when a societal perspective is being adopted, it may be relevant to report in detail how the unit costs used in the study were calculated. For example, are they approximations to social opportunity costs? Or merely charges? Do they include capital costs or exclude them? Do they include sales taxes or not? These issues are explored more fully, in the context of drug costs, in the six ISPOR Good Research Practices for Measuring Drug Costs in Cost-Effectiveness Analysis Task Force Reports [75–80].

Item 14: Currency, price date, and conversion.
Recommendation: Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.

Example: In the case of single-country studies, currency conversions (to US$) were usually required, as these reported results in different local currencies, perhaps also for different years. In these situations the conversion was made using the general purchasing power parity (PPP) for the most appropriate year. Where the studies reported results for different years, the mid-year PPP was used. All results are reported in US$. [81, p. 12]

Explanation: Because prices change over time, it is important to include the date with the price. Although prices for most resource items will be available for the current year, some may be available only for previous years. In these cases, the method of price adjustment, for example, by applying a specific price index, should be reported. The currency used should be clearly reported, especially when more than one jurisdiction has a currency with the same name (e.g., dollars and pesos). Depending on journal requirements, authors should consider using the convention described in ISO 4217 (e.g., USD for US dollars and ARS for Argentinian pesos) to aid reporting. Some studies may include currency adjustments, specifically when prices of a resource item are not available in the country of interest or if analysts prefer to report findings in a widely used currency (e.g., USD), or if the study reports results from several countries simultaneously.

If currency conversions are performed, the method used (e.g., through purchasing power parities) should be reported. For example, an algorithm for adjusting costs to a specific target currency and price year [82] outlines a two-stage computation: first, costs are converted from their original currencies to the target price year by using a gross domestic product deflator index for the jurisdiction concerned; then, in the second step, the price year–adjusted cost estimates are converted to the target currency by using purchasing power parities. The reporting of studies from different countries in a widely used currency, such as USD, may facilitate comparisons of the cost-effectiveness of different interventions. However, there are caveats, outlined in the Transferability of Economic Evaluations Across Jurisdictions: ISPOR Good Research Practices Task Force Report [83].

Methods—Model-Based Economic Evaluations

Item 15: Choice of model
Recommendation: Describe and give reasons for the specific type of model used. Providing a figure to show model structure is strongly recommended.
Example (1):

An area under the curve partitioned survival Markov-type model ... was developed to model disease progression in CML and treatment effectiveness of all drugs. In this type of model, the number of patients in each health state at any time is determined directly from the underlying survival curves. This was preferred to a conventional Markov approach for two reasons. First, it bypassed the need to estimate transition probabilities and second, it avoided the need for additional assumptions, such as whether death was permitted from all health states. [84, p. 1058]

Example (2):

We constructed a Markov decision model for the natural history of [pelvic inflammatory disease, PID], with the ability to vary PID development time... Figure 1 is a schematic representation of the model. [83] (See Fig. 1, adapted from [85])

Explanation: The article should describe the model structure used for analysis and explain why it is appropriate for use in the study. For consistency, analysts may want to use recent guidance for describing model types [86,87]. This explanation might refer to the similarity of the model structure used for analysis to the model structure used in previous studies of the disease of interest where this is available [87,88]. Alternatively, if an innovative modeling approach is being used, this approach might be related to the outcomes needed for decision makers or how the chosen model structure better reflects disease natural history, current treatment practice, and efficacy and safety compared with previous models in the disease area. The use of an innovative approach might also be related to the extent to which credible data are available to populate the model. In most cases, a figure illustrating the model structure and patient flows through the model should be provided.

Item 16: Model assumptions

Recommendation: Describe all structural or other assumptions underpinning the decision-analytic model.

Example:

...short-term outcomes were modeled by assuming, for all immunomodulatory therapies, a single percentage reduction for relapse and disease progression in the first 2 years of therapy. This assumption was based on data from several published review papers... the point at which patients transformed from RRMS....to SPMS...assumed that this transformation took place between EDSS 3.0-5.5 and EDSS 6.0-7.5... the model assumed that non-relapse-related EDSS scores do not improve over time. [89]

Explanation: In addition to the model’s input parameter values, assumptions make up a critical set of information needed to understand the model structure and dynamics. The report should present a listing of all the assumptions needed for a reader with the necessary expertise to potentially program and run the model [88]. The basis for each assumption should be presented whether the assumption is based on a specific data source or based on expert opinion or standard practice or even convenience. Assumptions may include information about the characteristics of the modeled population, disease natural history, and disease management patterns including choice of comparator(s) and treatment pathways.

Methods—Analytical Methods

Item 17: Analytic methods

Recommendation: Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.

Example:

Monthly costs for inpatient care, outpatient care, and non-study medications were calculated for each of the four clinical phases for subjects with complete data. If subjects were missing all costs for any month, the median costs for each clinical phase, clinical trajectory, and treatment group for that month were used to impute missing costs. Costs were then summed across clinical phases to calculate total costs for subjects in each clinical trajectory. Mean total costs for both treatment groups were calculated by summing total costs for subjects across all trajectories and dividing by the total number of subjects in both treatment groups... Sensitivity analyses were undertaken to assess variation in mean estimates resulting from changes in costing methods. ... Patients who died during the study period were included in the denominator for calculations of mean costs per treatment group and mean costs per clinical trajectory. Subject characteristics for both treatment groups were summarized using descriptive statistics. ... Continuously distributed variables were compared using t-tests, and categorical variables were compared using χ2 tests. We used the nonparametric bootstrap method to assess differences in mean costs between groups, and we used the bias-adjusted percentile method to compute 95% confidence intervals (CIs)... [90, p. 207]
Explanation: The analytic strategy should be fully explained as part of the "Methods" section of the article. The exact methods used will be dependent on the study design (e.g., a patient-level data analysis or an evidence synthesis decision model). The general principle is that only by reporting all the methods used can the appropriateness of the methods and the corresponding results be judged. For single-study-based economic evaluations, authors should report the methods and results of regression models that disentangle differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients. A study by Mihaylova et al. [91] provides a template.

For model-based economic evaluations, authors should describe and report how they estimated parameters, for example, how they transformed transition probabilities between events or health states into functions of age or disease severity. Regardless of study design, the handling of uncertainty and the separation of heterogeneity from uncertainty should be consistent themes, even if the methods used (e.g., statistical analysis of patient-level data or probabilistic sensitivity analysis of decision model parameters) vary by study type.

Results
Item 18: Study parameters
Recommendation: Report the values, ranges, references, and if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.

Example: Table [3] shows the use of health service resources and cost for GORD-related causes during the first year of follow-up in the REFLUX trial. (see Table 3) [74]

Explanation: To aid interpretability, present a tabulated listing of each of the parameters required to calculate overall costs and consequences and their associated values. This includes all clinical parameters, such as health outcomes, and economic parameters, such as resource use, unit costs, and utility values, that would be needed by a reader to replicate the findings or interpret their validity. Where appropriate, the distributions used to characterize uncertainty in study parameters should be documented and justified. The relevant values related to the uncertainty surrounding study parameters should be provided. Authors should describe why data sources were used as sources of values.

Item 19: Incremental costs and outcomes
Recommendation: For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios (ICERs).

Example:
On the basis of the exponential survival models, total life expectancy for the TAVR group was estimated to be 3.1 years compared with 1.2 years for the control group, a difference of 1.9 years (95% CI, 1.5–2.3 years). This difference decreased to 1.6 years (95% CI, 1.3–1.9 years) after the 3% discount rate was applied. On the basis of these life expectancy projections and the empirical cost data from the last 6 months of follow-up (TAVR $22, 429/year; control $35, 343/year), lifetime medical care costs beyond the trial were estimated at $43, 664 per patient for the TAVR group and $16, 282 per patient for the control group... On the basis of the empirical data for the first 12 months of follow-up and our trial-based survival and cost projections, we estimated a difference in discounted lifetime medical care costs of $79,837 per patient (95% CI, $67,463–$92,349) and a gain in discounted life expectancy of 1.6 years, which resulted in a lifetime incremental cost-effectiveness ratio (ICER) of $50,212 per life-year gained (95% CI, $41,392–$62,591 per life-year gained). [97, p. 1105]

Explanation: Authors should report mean values for the main categories of costs, including total costs, report outcomes of interest for each comparator group, and report on a pairwise basis mean differences between the comparator groups (i.e., incremental costs and incremental outcomes). Differences in costs between alternative interventions (incremental cost) should be divided by differences in outcomes (incremental effectiveness) to produce ICERs. Reporting ICERs may not be applicable when an intervention is either dominant or dominated or is not considered relevant for decision making.

Item 20: Characterizing uncertainty
Item 20a: Single study–based economic evaluation
Recommendation: Describe the effects of sampling uncertainty for estimated incremental cost, incremental effectiveness, and incremental cost-effectiveness, together with the impact of methodological assumptions (such as discount rate, study perspective).

Example: See Table 4.

Item 20b: Model-based economic evaluation
Recommendation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.

Example:
Univariate sensitivity analyses are displayed in a tornado diagram of the most influential variables (Figure 2). In this diagram, each bar represents the impact of uncertainty in an individual variable on the ICER... Additional File 2 provides the results for univariate analyses for all model parameters. [99, p. 6] (see Fig 2)

Explanation: Statistical uncertainty associated with cost-effectiveness analysis undertaken with patient-level data can be reflected by using standard confidence intervals or Bayesian credibility intervals on incremental costs and incremental effects. Because confidence or credible intervals can be problematic to estimate, cost-effectiveness planes and cost-effectiveness acceptability curves may be appropriate presentational tools. These presentational devices are more consistent with a decision-making rather than an inferential approach to interpreting uncertainty in cost-effectiveness analysis. Nevertheless, other types of sensitivity analysis may still be required to capture uncertainty that is not related to sampling variability, such as choice of discount rates, unit cost vectors, and study perspective.

For model-based economic evaluations, parameter uncertainty may be represented for individual parameters in a deterministic sensitivity analysis or across all parameters simultaneously with probabilistic analysis. If deterministic analyses are performed, tornado diagrams are useful presentational tools. For probabilistic sensitivity analyses, a list of parameters included in the probabilistic sensitivity analysis and use of a cost-effectiveness plane and cost-effectiveness acceptability curves are suggested to present results. Authors can report structural, methodologic, and other nonparametric uncertainty as separate analyses.

Item 21: Characterizing heterogeneity
Recommendation: If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.

Example:
The discounted incremental cost of statin allocation ranged from £630 (SE 126) in the highest risk quintile to £1164 (45) in the lowest. Overall, the cost of avoiding a major vascular event was estimated
<table>
<thead>
<tr>
<th>Unit cost (£)</th>
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<th>Unit of measure</th>
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<td>264</td>
<td>b Days</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>High</td>
<td>657</td>
<td>b Days</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>High dependency</td>
<td></td>
<td></td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total surgery</td>
<td></td>
<td></td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Visit to GP</td>
<td>36</td>
<td>c Visits</td>
<td>44</td>
<td>1.16</td>
</tr>
<tr>
<td>Visit from GP</td>
<td>58</td>
<td>c Visits</td>
<td>1</td>
<td>0.01</td>
</tr>
<tr>
<td>Outpatient</td>
<td>88</td>
<td>b Visits</td>
<td>14</td>
<td>0.30</td>
</tr>
<tr>
<td>Day case</td>
<td>896</td>
<td>b Admit</td>
<td>10</td>
<td>0.14</td>
</tr>
<tr>
<td>Inpatient</td>
<td>1259</td>
<td>b Admit</td>
<td>3</td>
<td>0.03</td>
</tr>
<tr>
<td>Subsequent</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>costs</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Medication costs</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total costs</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Note. Adapted from BMJ, 339, Epstein D, Bojke L, Sculpher MJ, Laparoscopic fundoplication compared with medical management for gastro-oesophageal reflux disease: cost effectiveness study, b2576, Table 2, 2009, with permission from BMJ Publishing Group Ltd.

GP, general practitioner.

* Sources of unit costs used in the analysis: (a) Mean unit costs of a survey of five participating centers, 2003, updated for inflation [92], (b) mean hospital costs for England and Wales, 2006/07 [93], (c) Curtis and Netten [94], (d) British Medical Association and the Royal Pharmaceutical Society of Great Britain [95], and Grant et al. [96].
to be £11,600 (95% CI 8,500–16,300), but this result masks substantial variation between the risk subgroups. Corresponding results for vascular deaths ranged from £21,400 (10,700–46,100) in the highest risk quintile to £296,300 (178,000–612,000) in the lowest. [91, p. 1782] (see Table 5)

**Explanation:** Heterogeneity may be important if particular patient subgroups differ with respect to observed or unobserved characteristics, such as age or sex, or differ systematically in ways that affect the results of an economic evaluation, for example, through their treatment costs or their capacity to benefit from an intervention [100]. If heterogeneity is important, authors should report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients.

Where it is clear that there are subgroup effects in cost-effectiveness, either driven through differential treatment effects for patients of differing characteristics or because a homogeneous relative treatment effect applies to patients at differential baseline risk, then the general reporting recommendations for cost-effectiveness should apply to each subgroup. Where baseline risk varies continuously, it may be appropriate to present results for patient quartile or quintile risk groups.

---

**Table 4 – Example of reporting the effects of sampling uncertainty and methodologic assumptions from a single study for estimated incremental cost, incremental effectiveness, and incremental cost-effectiveness.**

<table>
<thead>
<tr>
<th></th>
<th>N Placebo (95% CI)</th>
<th>N FP (95% CI)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life-years</td>
<td>370 2.74 (2.68–2.80)</td>
<td>372 2.81</td>
<td>0.06 (–0.01 to 0.14)</td>
</tr>
<tr>
<td>QALYs</td>
<td>370 1.74 (1.67–1.80)</td>
<td>372 1.86</td>
<td>0.11* (0.04–0.20)</td>
</tr>
<tr>
<td>Cost (£)</td>
<td>370 1509 (1,286–1,879)</td>
<td>372 2530 (2,341–2,774)</td>
<td>1,021 (619–1,338)</td>
</tr>
<tr>
<td>Cost per life-year (£)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undiscounted</td>
<td>16,300 (6,400–∞)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discounted</td>
<td>17,700 (6,900–∞)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost per QALY (£)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undiscounted</td>
<td>9,600 (4,200–26,500)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discounted</td>
<td>9,500 (4,300–26,500)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


*A After controlling for baseline utility.

---

**Fig. 2 – Example of tornado diagram to describe the effects of uncertainty for important model parameters.** Reprinted from BMC Health Serv Res, 9, Moore SG, Shenoy PJ, Fanucchi L, et al., Cost-effectiveness of MRI compared to mammography for breast cancer screening in a high risk population, 9, Figure 2, 2009, with permission from BioMed Central Ltd [99]. Ca., cancer; Mammo, mammography; MRI, magnetic resonance imaging; Neg, negative; Pos, positive; Pt, patient; QALY, quality-adjusted life-year.
Table 5 – Example of reporting heterogeneous findings: costs, effects, and cost-effectiveness based on subgroups of patients with characteristics or observed variability not reducible by more information.

<table>
<thead>
<tr>
<th>Risk group (5-y MVE risk)</th>
<th>Incremental cost* (£) (SE)</th>
<th>MVE avoided per 1,000 persons (SE)</th>
<th>Cost (£) per MVE avoided (95% CI)</th>
<th>Vascular deaths avoided per 1,000 persons (SE)</th>
<th>Cost (£) per vascular death avoided (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (12%)</td>
<td>1,164 (45)</td>
<td>37 (5)</td>
<td>31,100 (22,900–42,500)</td>
<td>4 (1)</td>
<td>296,300 (178,000–612,000)</td>
</tr>
<tr>
<td>2 (18%)</td>
<td>1,062 (61)</td>
<td>58 (7)</td>
<td>18,300 (13,500–25,800)</td>
<td>7 (2)</td>
<td>147,800 (92,000–292,200)</td>
</tr>
<tr>
<td>3 (22%)</td>
<td>987 (71)</td>
<td>80 (9)</td>
<td>12,300 (8,900–17,600)</td>
<td>13 (3)</td>
<td>78,900 (48,800–157,400)</td>
</tr>
<tr>
<td>4 (28%)</td>
<td>893 (83)</td>
<td>93 (11)</td>
<td>9,600 (6,700–13,900)</td>
<td>18 (5)</td>
<td>49,600 (30,800–100,700)</td>
</tr>
<tr>
<td>5 (42%)</td>
<td>630 (126)</td>
<td>141 (16)</td>
<td>4,500 (2,300–7,400)</td>
<td>29 (7)</td>
<td>21,400 (10,700–46,100)</td>
</tr>
<tr>
<td>Overall</td>
<td>947 (72)</td>
<td>82 (9)</td>
<td>11,600 (8,500–16,300)</td>
<td>14 (4)</td>
<td>66,600 (42,600–135,800)</td>
</tr>
</tbody>
</table>

Note. Adapted from The Lancet, 365(9473), Mihaylova B, Briggs A, Armitage J, et al., Cost-effectiveness of simvastatin in people at different levels of vascular disease risk: economic analysis of a randomised trial in 20,536 individuals, 1779-85, Web Table 1, 2005, with permission from Elsevier.

CI, confidence interval; MVE, major vascular event; SE, standard error.
* Discounted at 3.5% per annum.

Discussion

Item 22: Study findings, limitations, generalizability, and fit with current knowledge

Recommendation: Summarize key study findings and describe how they support the conclusions reached. Discuss limitations and the generalizability of the findings and how the findings fit with current knowledge.

Example (Study Findings):

Initiating asthma controller therapy with [a leukotriene receptor antagonist] or [inhaled corticosteroid] in this 2-year pragmatic trial yielded no significant differences between treatment groups in QALYs gained in the imputed adjusted analysis; however, over 2 months and 2 years, from both [UK] NHS and societal perspectives, patients prescribed LTRAs incurred significantly higher costs than those prescribed ICS (societal costs at 2 years, £711 vs £433). Therapy with ICS dominated therapy with LTRAs in terms of cost effectiveness, and the results of the analyses suggest there is a very low probability of LTRAs being cost effective compared with ICS for first-choice initial asthma controller therapy at 2005 values. [101, p. S91]

Example (Limitations):

As with any model, our analysis has limitations, which are governed by data availability and our assumptions. Our model has not stratified the results by sex and we have not modelled other possible [herpes zoster] sequelae such as ocular and cutaneous manifestations. By exclusion of those complications, we have likely underestimated the benefits of vaccination strategy. Lack of evidence on the length of vaccine protection and the actual vaccine cost in Canada are also ... In the absence of any study that measured EQ-5D utility among the general population excluding only [herpes zoster] patients, we may have double counted the effect of [herpes zoster] and [post-herpetic neuralgia] on the [quality of life] weights. However, overall we believe that the effect of double counting is not large and, if present, results in an overestimation of current ICERs. Therefore, the current estimation of the ICER can be considered slightly conservative and biased against the vaccination strategy. [102, p. 1002]

Example (Generalizability):

The current decision model has a number of limitations that need to be considered when assessing its relative generalizability. First, the perspective was that of a third-party payer and not a societal one and as such we excluded indirect costs or out-of-pocket direct costs incurred by the patient. Taking such costs into account would likely increase the cost efficacy/dominance of the esomeprazole IV strategy given the associated shorter admission time in patients without rebleeding. Second, even though the resulting internal validity of the estimates is heightened the data used in our analysis were derived from a single clinical trial, representing a potential limitation in the generalizability of our findings for a variety of reasons. However, the study was adequately powered to demonstrate a reduction of the risk of rebleeding and in addition primarily recruited Caucasians, thus making it applicable to Western European and North American populations. [103, p. 227]

Example (Fit with Current Knowledge):

The cost-effectiveness estimate from this model is similar to a number of previously performed economic evaluations. [104–111] Our central estimate for the ICER is below the often quoted upper limit for the WTP threshold in the UK of £30 000 per QALY. The only previous analysis from a UK perspective was a decision model that was submitted by the manufacturer to NICE in 2006. After independent assessment, their estimate for the ICER was £18 449 per QALY (year 2006 values) [112]. This is somewhat lower than our estimate, but we believe that this difference can be attributed to two factors: (i) reliance on the hazard ratio for DFS of 0.54 from the 1-year analysis of the HERA trial; and (ii) an assumed duration of benefit of 5 years. Two model-based cost-effectiveness analyses from Canadian [113] and Japanese [114] perspectives considered the implications of using the updated 2-year HERA analysis. Their conclusions were similar to our own: an increase in the ICER, which does not exceed the assumed WTP threshold. When we make the same modelling assumptions about the treatment effect as were taken in the NICE appraisal, our ICER is in fact lower (£14 288); this may be due to more accurate modelling of baseline recurrence risk or the later base year for analysis. [115]

Explanation: Failure to provide a concise summary of the study findings, limitations, generalizability, and how findings fit with current knowledge hinders transparency, makes critical review more difficult, and may perpetuate perceptions that all economic evaluations are a “black box” [116]. A succinct and objective summary of the analysis’s key findings should include the base-
case values, mention of the perspective, interventions, and patient population(s). Authors should also indicate the degree and main areas of uncertainty and the main drivers of cost-effectiveness and discuss any notable subgroup effects. With respect to limitations, health economic evaluations, particularly model-based analyses, require a number of simplifying assumptions (e.g., model structure) and methodological choices (e.g., perspective, discount rate, choice of comparators, and time horizon). It is important that these assumptions and choices are made explicit to the reader and that their possible effects on the base-case results are fully discussed [1].

Economic evaluations are often designed with a particular setting or jurisdiction in mind. This can limit their generalizability is a commonly cited barrier to the use of health economic evaluations in decision making [117]. Authors should discuss the potential applicability of their results to other settings. There are a number of parameters that can limit generalizability, including differences across settings in unit prices and resource use, baseline risk of disease, clinical practice, and availability of health care resources [83,118].

Finally, providing comparisons with previous knowledge provides the reader with an understanding and appreciation of potential sources of bias, the major drivers of study results, and provides the reader with an understanding and appreciation of potential sources of bias, the major drivers of study results, and availability of health care resources [83,118].

Explanation: Studies show that authors' financial connections may be associated with the findings of economic evaluations [120,122,124–126]. Our recommendations for disclosure are modeled on those of the International Committee of Medical Journal Editors [127]. Authors should report relevant financial and non-financial associations with commercial, academic, or other entities that are associated with the work reported in the submitted manuscript. This includes entities that have a general interest in the subject of the work or who may benefit as a result of the work. Relevant financial and nonfinancial associations should also be reported for each author's spouse or children younger than 18 years. Competing interests should be disclosed, even if not specifically required by a journal or publisher.

As a general rule, reporting may be limited to associations within 5 years of the article's publication or to a time period specified by an individual journal's policy. In cases in which associations outside this 5-year window are likely to be deemed relevant by knowledgeable readers, authors should err on the side of more extensive disclosure.

Concluding Remarks

As the number of published health economic evaluations continues to grow, we believe that standard reporting of methods and findings will be increasingly important to facilitate interpretation and provide a means of comparing studies. We hope the ISPOR CHEERS statement, consisting of recommendations in a 24-item checklist, will be viewed as an effective consolidation and update of previous efforts and serve as a starting point for standard reporting going forward.

We believe that the CHEERS statement represents a considerable expansion relative to previous efforts [13–24]. The strength of our approach is that it was developed in accordance with current recommendations for the development of reporting guidelines, using an international and multidisciplinary team of editors, and content experts in economic evaluation and reporting. Similar to other widely accepted guideline efforts, we have defined a minimum set of criteria though a modified Delphi technique and have translated these into recommendations, a checklist, and an explanatory document. Unlike some previous reporting guidance for economic evaluation, we have also made every effort to be neutral about the conduct of economic evaluation, allowing analysts the freedom to choose different methods.

There may be some limitations to our approach that deserve mention. First, there is evidence that a different panel composition could lead to different recommendations [128]. This suggests that a more robust process with a larger Delphi Panel could lead to differences in the final set of recommendations. Some less-common approaches and contexts (e.g., public health, developing countries, and system dynamic models) for conducting cost-effectiveness analysis may not be well represented by the sample of experts. In addition, like many Delphi Panel processes, decisions to reject or accept criteria were based on arbitrary levels of importance. However, the sample used to create the statement is sufficiently knowledgeable of the more common applications of economic evaluation and the rules used to select criteria were created a priori and are consistent with previous efforts.

It will be important to evaluate the effect of implementation of the ISPOR CHEERS statement on reporting in future economic evaluations in a manner similar to other reporting guidelines [10]. As methods for the conduct of economic evaluation continue to evolve, it will also be important to revisit or extend these recommendations. The authors plan to review the checklist for an update in five years.

Explanation: Authors should explain factors that contribute to discrepant findings.

Other

Item 23: Source of funding and support

Recommendation: Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other nonmonetary sources of support.

Example: The study was funded by the Medical Research Council, as part of the North West Hub in Trial Methodological Research (NWHTMR). The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report [119].

Explanation: Authors should identify and report all sources of funding for an economic evaluation so that the study's credibility can be assessed. Studies suggest that economic analyses funded by pharmaceutical companies are more likely to report favorable results than studies funded by noncommercial sources [120–126]. All sources of funding includes funds received indirectly, for example, grants to an author's academic institution or to a professional society where they are then used to fund author or staff salaries or research. Any in-kind or other sources of support for the analysis, such as secretarial, statistical, research, or writing assistance, provided by outside sources or by contributors who do not meet criteria for authorship should also be reported. Depending on individual journal policies, sources of funding and contributions of named individuals may be listed in an "Acknowledgments" section.

Item 24: Conflicts of interest

Recommendation: Describe any potential for conflict of interest among study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors' recommendations.

Example: JP and DAH have support from the Medical Research Council for the submitted work; no relationships that might have an interest in the submitted work in the previous three years; no non-financial interests that may be relevant to the submitted work... [119]
Acknowledgments

The ISPOR Task Force for Health Economic Evaluation Publication Guidelines acknowledges the support of Elizabeth Molsen. The task force also acknowledges Donna Rindress who provided the initial leadership for this effort.


We thank the following reviewers for their helpful comments on earlier drafts of this report: Bhagwan Aggarwal, Jon Kim Andrus, Olatunde Aremu, Mamdouh Ayad, Ali Bonakdar Tehrani, Hélène Chevré-Séverac, Hsinying Hung, Doug Coyle, Kristen Downs, Heather Edin, Linda Goe Martin, Richa Goyal, Alastair He´ lAndrus, Olatunde Aremu, Mamdouh Ayad, Ali Bonakdar Tehrani, on earlier drafts of this report: Bhagwan Aggarwal, Jon Kim

Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.jval.2013.02.002 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

REFERENCES


