



**Consolidated Health Economic Evaluation Reporting Standards (CHEERS) – Explanation and Elaboration:  
A Report of the ISPOR Health Economic Evaluations Publication Guidelines Task Force**

**Review Comments on DRAFT Task Force Report**

**General Comments**

1. The medical and behavioral health field lacks a “Cross Cultural Classification Database for Economic Cost Analysis”. In this regard, a question comes to mind - in whose interest is it to develop a database registry – e.g. international medical publisher such as Elsevier, or a public/private partnership such as WHO and World Bank, or Clinton Healthcare Initiative.
2. May I suggest writing somewhere that “it is surprising, given how important costs and outcomes are to current events, that costs remain divorced from outcomes in numerous settings. The link between costs and their corresponding outcomes underscores the real value of health economic evaluation.”
3. Although I acknowledge the complexity of the topic and agree with the level of detail reached to give recommendations, I find a bit confusing the reporting of them and would like to look at a more schematic presentation of them.
4. I would like to see in the report a more clearly distinguished section on the paper sections on which discussions and recommendations are given, to guide the reading of the report. For instance, differently reported titles/subtitles, differently coloured page, something that clarifies which are sections of the report, and which are sections reporting on the paper to be written/reviewed and under discussion.
5. My proposal would be to include an additional item: “Use of Biomarkers or Genetic Platforms to discriminate efficacy levels”. I think, this is a relevant subject which would help to differentiate Conventional Pharmacoeconomic studies and Pharmacogenomic ones (a new frontier in Economic Evaluation). If it is not possible to add up this new item, it would be worth including such information within one of the 24 items. Observe that, (243) “ITEM 4: Target Population and Subgroups” may be the right item to include this new information.
6. Reporting standards are also a ‘hot topic’ in clinical trials. In the clinical environment there is a bias regarding publication of positive results. It would be interesting to understand if the task force suggests a similar reporting bias in economic analyses and how this is reflected in the presented reporting standard
7. I really like this concept, but are the journals that will publish these guidelines prepared to change their instructions for authors to make this possible. It is hard to bring all this in 250 or 300 words, limit of most abstracts.

8. ...the appropriate reporting of health economic evaluations...my opinion is that is very difficult to report an appropriate health economic evaluations since the different view of each lens , it means that the prisma that reflect the data at the moment of the manuscript reflect the authors mental model . It means that everyone needs to relax aspects that somehow seem wrong or not totally correct.
9. My personal opinion that the lack of knowledge in this pharmaco-economic evaluation concepts need to be clearly explained by the instructor/with more examples/strong supporting modulus, in our Indian research context.
10. The Health insurance system can be a factor to determine all costs and in promoting of economic reporting standards as well improving the health care standards. So research in this helpful to avoid heterogeneity in cost effectiveness among different countries/institutions.
11. Model transparency and validation – I don't see the importance of submitting the electronic version of the model.
12. It's a well written report. However, please check for formatting and consistency throughout the report.

### **Specific Comments**

#### **Abstract**

- It would extremely valuable, within the abstract, to include information on the country that the analysis refers to and the price year (in addition to the perspective). This would rapidly speed up the critical appraisal process when undertaking systematic reviews of HE analyses.
- Use of abstracts and the suggested contents are agreeable to me. Since I would look out for similar content, I highly recommend the CHEERS abstract use to other authors.

- **Background**

- **Objective**

- **Methods**

- **Findings**

- **Conclusions**

- We hope..., I SUGGEST "We conclude ... and because the recommendation is very strong ... I SUGGEST ... BE MORE IMPERATIVE

#### **Definition of health economic evaluation (1-12)**

- (Line 4) ...of health interventions alongside their corresponding cost measurements, may differ.
- (Lines 5-12) How do these references relate to the "definition" of health economic evaluation, which is the title for that section?
- (Line 12) Economic evaluations are already standard requirement for decision making in several Countries, e.g. Germany, France

#### **Reporting challenges and shortcomings in health economic evaluations (14-33)**

- (Line 17) ...This creates \*multiple\* challenges
- (Line 19) Can I suggest the term quality assurance instead of quality control?
- (Line 23) I think this point is not fit here because misleading findings is something different than reporting. Based on your draft, this checklist is not addressing the findings.
- (Line 26) Need of health authorities to establish and optimize pricing and reimbursement strategies for drugs in development and to adopt a consistent process for evaluation and comparison of new and existing pharmaceutical products

#### **Aim and Scope (35-53)**

- (Lines 35-53) Consider moving earlier to beginning of paper

- (Line 43) This reference describes the strengths and weaknesses of checklists that have been used to evaluate best practices for reporting and conducting on economic evaluations in health care. Also check out the Ref 24, its internet address is wrong.

### **Methods (55-114)**

- The article may receive criticisms concerning how the Delphi panel was run - Potentially more explanation regarding what was done compared to what current practice is might improve the strength of the manuscript
- The article may receive criticisms concerning the choice of 24 items rather than the initial 28 resulting from the Delphi panel
- (Line 63) Ref 31 & 16 are the same. Take the 31 out.
- (Lines 66-69) How to select the participants? Randomly, or snow-ball...
- (Lines 57, 65, 66, 69, 75, 82, 88, 89, 91, 93, 98, 100, 103, 105, 107, 109, 110, 111, 112) Extra space
- (Line 96) How did you cover information bias? Knowing that a "rejected" item will be deleted unless it receives a high score could or knowing the other participants score for an item will skew the result and be a potential bias source.
- (Lines 97-98) Finally, how many participants didn't complete their survey?

### **Checklist Items (116-127)**

- (Line 127) add a comma after guidance

### **Title and Abstract (129)**

#### **• Item 1: Title (130-150)**

- (Line 131) it is good to provide suggestions how many specific items in the title could help readers search easier.
- (Line 137) What is the reference(s)?

#### **• Item 2: Abstract (152-211)**

- The abstract should also contain some (5 to 7) key words
- I really like this concept, but are the journals that will publish these guidelines prepared to change their instructions for authors to make this possible. It is hard to bring all this in 250 or 300 words, limit of most abstracts.
- (Lines 153-154) for clarity, consider the following: Provide a structured summary of objectives, methods (including study design and 153 inputs), results (including base case and uncertainty analyses), and conclusions.
- (Line 163) I would recommend specifying also which specific perspective is adopted: in case of payer, it could be the NHS, or the Insurance, Medicaid or Medicare depending on the health care system, which can make the difference in results and interpretation.
- (Line 169) The "cost-effectiveness" is reported close to "quality-adjusted life-years", because in some countries the term "cost-effectiveness" is used also for cost-utility analyses. I have noticed in the past that this combination of the two terms may generate some confusion. It may be useful giving some clarifications (I think that Drummond reports this in his bible).

### **Introduction (213)**

#### **• Item 3: Introduction (214-240)**

### **Methods – General (242)**

- I don't see any recommendations on the reporting of half cycle correction for Markov models. I feel that this should always be reported – from an industry perspective (responsible for completing NICE submissions / STA templates) this is something that is stipulated in the STA template in terms of reporting a model.
- **Item 4: Target Population and Subgroups (243-264)**
  - My proposal would be to include an additional item: "Use of Biomarkers or Genetic Platforms to discriminate efficacy levels". I think, this is a relevant subject which would help to differentiate Conventional Pharmacoeconomic studies and Pharmacogenomic ones (a new frontier in Economic Evaluation). If it is not possible to add up this new item, it would be worth including such an information within one of the 24 items. Observe that, (243) "ITEM 4: Target Population and Subgroups" may be the right item to include this new information.

- While this recommendation appears logical, it can be quite challenging if analysis is being done from a providers' perspective. It is particularly worse if resources are limited and is limited to one provider. In some instances, available provision costs may only be extracted as aggregate proxy costs from all client expenses. Hence the desired provider characteristics may become redundant or be of little use in this case.
- (Line 254) - Eligible subgroup definition is essential whether by ethnicity, age cohort, geographic, or socio-economic breakdowns as the characteristics of the subgroup often have a significant outcome on financial results.
- (Lines 257, 263) Extra space
- **Item 5: Setting and Location (266-281)**
- **Item 6: Study Perspective (283-308)**
  - Item 6 of the new standards does capture the perspective of the study. It is suggested to 'describe the perspective of the study and relate this to the costs being evaluated. From my point the description of the perspective in item 6 is too much geared toward the costs. Instead it might put more emphasis on the outcomes/ consequences being evaluated i.e I'd prefer the wording: *'Describe the perspective of the study and relate this to the costs and/or outcomes being evaluated.'*
  - Agreeable because perspectives make choosing of relevant costs more focused. But most of the available checklists for transferring references lack a universal threshold or aggregate score cut offs that authors/reviewers can follow in choosing whether to uphold references or not.
  - (Line 286) item 6: Study perspective. Especially important are the implications of the point of view/study perspective beyond the standard distinction between direct medical, direct non-medical and indirect/productivity losses costs. Perhaps one might recall from the 1984 CMAJ paper "the elements of a sound economic evaluation: was a well-defined question posed in answerable form?" (CMAJ June 15, 1984: "How to read clinical journals VII: to understand an economic evaluation (part B)").
  - (Line 300) - Societal perspective. Is it not the preferred role of the PI to seek out collaboration and methods to document costs to public health and society as a key component to any economic analysis?
- **Item 7: Comparators (310-329)**
- **Item 8: Time Horizon (331-349)**
  - (Line 340) Possibly, "used by earlier studies"
- **Item 9: Discount Rate (351-369)**
  - Need for regional discount rates

#### Methods –Outcomes (371)

- **Item 10: Choice of Outcomes (372-389)**
- **Item 11: Measurement of Effectiveness (391-434)**
  - (Line 391) ITEM 11: Measurement of Effectiveness. I think, it would be important that the manuscript be explicit as for the choice of the source of clinical data (i.e., Clinical Trial/Observational Studies/Database Analysis/Combination).
  - (Line 391) This section does not seem to discuss measurement of effectiveness, the examples provided in line 408 and 416 more likely talking about research design
  - Reference for lines 411, 412 are missing
- **Item 12: Measurement and Valuation of Preference-based Outcomes (436-465)**
  - (Line 445) - Extremely important concept for geriatric medicine. Possibly compare QALY and actuarial data.
  - (Lines 445 to 465) Several times I find a misuse of the HRQoL instruments in economic evaluations: use of translated but non validated versions, use of instruments for adults for children, use of instruments to self-completed as proxy versions etc. I would list, in this section, specific items to specify all these issues related with the use of the HRQoL instruments. The paragraph reported is informative but I perceive that it is actually helpful only for people who already know how to use the HRQoL instruments.
  - (Line 454 to 465) reference on how to best report measures QoL would be an asset (any guidelines on it?)

#### Methods – Costs (467)

- **Item 13: Estimating Resource Use and Costs (468-494)**

- **Item 14: Currency, Price Date and Conversion (496-525)**

## **Methods – Model-based Economic Evaluations (527)**

- **Item 15: Choice of Model (528-547)**

- (Line 528) ITEM 15: Choice of Model (1). I think, it is very relevant to indicate in the manuscript if the chosen model has been previously accepted or validated by a reputed Economic Evaluation Agency (e.g. NICE). Taking into consideration that, in general, mathematical models are regarded as “black boxes” becomes instrumental to indicate if this model has undergone a validation process by a relevant institution (HTA agency or University).
- (Line 528) ITEM 15: Choice of Model (2). In the case of coming up with innovative models, it would be interesting to compare the results with those from existing models (i.e. published and validated models).
- (Line 539) Explanation- “This justification might be based on references to the model structure used in well-accepted published studies of the disease of interest.” Is the reviewer expected to re-review the previously published article? What is “well-accepted published studies” mean? Do we have criteria?

- **Item 16: Model Assumptions (549-566)**

- (Line 549) ITEM 16: Model Assumptions. The use of assumptions can be regarded as an “easy” alternative for not making the effort to find the proper data or identify the proper study design. We can see EE studies that take advantage of this possibility and provide too many assumptions. I think, It would be worth specifying a limited number of assumptions than can be made in a standard EE study.
- Though item 16 is essential, I find line 564 a repetition of the characteristics about the study population and model description provided in item 15.
- (Line 565) remove the colon after “about”

## **Methods – Analytical Methods (568)**

- **Item 17: Analytic Methods (569-602)**

- (Line 591) remove the comma after “data analysis”
- (Lines 599-602) This is very important as it is often misinterpreted by non-health economics audiences
- Transparency in methods is quite essential and should be encouraged. But while bootstrapping is good for estimating 95% CIs, isn't it necessary for authors to guide readers how they choose the optimum number of bootstraps? And in situations where bootstrapping is not possible e.g. sample size may too small especially if study is being done from an institutional provider's perspective shouldn't this be acknowledged as a method limitation?

## **Results (604)**

- **Item 18: Study Parameters (605-626)**

- (Line 606) move the comma to “references and, if used, ...”
- Reference for lines 616 and 617 are missing
- Item / Recommendations 18 and the tabular presentation of parameters are okay.
- The result should be reported as mean and standard deviation (SD); as SD is important for comparison purpose.

- **Item 19: Incremental Costs and Outcomes (628-651)**

- Incremental Costs and Outcomes - item / recommendation 19 is okay

- **Item 20: Characterizing Uncertainty (653-681)**

- (Line 663) Item 20 Example (Tornado Diagram): This particular diagram does not present all useful available information, and the following would be useful to have: 1: base case value within the range; 2: color-code the horizontal bars, showing in one color the change corresponding to low end of range of parameter and another color for the upper end of the range of the parameter. I know this paper does not discuss the content of the HE evaluation, but presenting a possibility of showing complete Tornado diagram will be useful for the readers.
- Characterizing Uncertainty - Item 20/ recommendations 20a and 20b are okay but use of cost effectiveness planes and cost acceptability curves is at times problematic when data available is not patient level data. As suggested in lines 678-9, use of Tornado diagrams would remain more useful and could be emphasized.

- **Item 21: Characterizing Heterogeneity (683-709)**

- (Line 695) the table is unreadable as it is currently presented
- (Line 699) Explanation - though heterogeneity should be accounted for if present, I needed more time to make more substantial comments about controlling for differences in cost effectiveness between groups because it is a big challenge for analysts using aggregate variables to disaggregate costs of sub groups yet their studies might be using a provider or societal perspective.

## Discussion (711)

- **Item 22: Study Findings, Limitations, Generalizability, and Fit with Current Knowledge (712-780)**
  - Item 22 is good; it may discourage studies on new innovations particularly in areas like sub Saharan Africa where literature on economic evaluations is rather scarce. Differences across settings in unit prices and resource use may limit generalizability of study findings and should be acknowledged, as noted in line 771 and 779. This will help other authors and readers to take necessary pre-cautions when interpreting results.
  - (Line 772) [This line] could be better used as an illustrated effect and not an explanation of poor generalizability. Besides the precautions, often the space limitations may not permit an exhaustive discussion of all the assumptions guiding the model structure and the different methodological aspects (e.g. perspective, discount rate, choice of comparators, time horizon) of a given study as shown in line 767. Shouldn't care be taken to choose the most important aspects?
  - (Line 712) Item 22: In the Limitations, perhaps, one would add the importance of identifying known omitted variables. Omitted variables, especially in costs might skew the results. The generalizability of the results might be affected by the different pattern of care between the jurisdictions, intra- and inter-nationally. The jurisdiction for which the results might be applicable should be identified.

## Other (782)

- (Line 782) This is usually legal requirement of the journal and therefore slightly outside the scope of this document, it is useful to state here "as required by journal"
- **Item 23: Source of Funding and Support (783-799)**
  - Item 23 is agreeable without any changes suggested.
- **Item 24: Conflicts of Interest (801-820)**
  - In connection item 23, Item 24 is strongly agreeable because authors in resource limited settings are often tempted to be biased in favor of their study sponsors possibly for fear of losing additional funding. If stated upfront, this could possibly help in controlling for potential bias in given studies
  - Does the heading "Explanation" belong between lines 808 and 809?

## Conclusion (822-849)

## References (853)

- Reference 24: The correct internet address is "<http://www.ncbi.nlm.nih.gov/books/NBK114545/>"
- I propose to include the following paper as it provides a structured classification of models as suggests consistent and concise language in defining these models: "Health Econ. 2006 Dec;15(12):1295-310. A taxonomy of model structures for economic evaluation of health technologies. Brennan A, Chick SE, Davies R."

## Boxes (854-855)

## Tables (857- 862)

- Table 3 is unclear, kindly re-draw it and give the reference
- **Table 1: Published Guidelines and Reporting Checklists\* for Economic Evaluation (859)**
- **Table 2: CHEERS Checklist – Recommended items to include when reporting economic evaluations of health interventions. (863)**
  - Table 2 is useful as a quick guide of recommendations that are explained in the text, however, I did not feel comfortable while reading them

## Appendix 1: ISPOR Task Force, Delphi Panel Membership and Delphi Panel Procedure

- The selection of the Delphi panel is critical for the presented report. Further explanation of the search criteria that were applied in order to identify suitable candidates and also how the size of the expert sample was decided would be helpful
- The asset of this article is [the] number of people involved into the Delphi panel

## Appendix 2: Delphi Panel Survey Scores

- Appendix 2 displays the Scores of Delphi Round 1 & 2. Acceptance / rejection apparently was based on the mean. It would also be interesting to see the range of the score in order to identify areas of disagreement between the Delphi participant

## Compliments

1. I have gone through the whole paper and understand that the guideline will direct authors to report their result in such a way that it will persuade one to make evidence based decision and will help reviewers to work objectively.
2. Well done. I have a very few editorial comments
3. I think those documents are excellent I have no comments.
4. The topic is important and valuable
5. I looked over report #1 and have no comments.
6. CHEERS Task Force is to be highly commended. The DRAFT "Economic Evaluations" is well conceived and documented.
7. Excellent manuscript which tries to become THE point of reference for reporting EE studies.
8. This draft is well written and useful for understanding the health economics research reporting process/steps for bringing of best quality of economic research
9. CHEERS would guide researchers in appropriate way and would help to appropriately identify the research areas based on the abstract.
10. The mentioned CHEERS model will be very much useful for the researchers/scientist for understanding the methods used in economic studies.
11. I have gone through the Final draft in detail and found it up to the mark and well documented. In my opinion, no further additions and deletions are required at the moment.
12. Overall the topic is highly interesting and has been well approached and treated.
13. Excellent initiative and tremendous job done. It will be of high value for all people involved in health economic evaluation.
14. Excellent report with a precise objective, a clear methodology (2 rounds of Delphi panels), and a respective recommendation/ outcome