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Drummond, Mike orcid.org/0000-0002-6126-0944, Husereau, Don and Carswell, Chris (2021) Reporting health economic evaluations: CHEERS and beyond. Medical Writing. ISSN 2047-4806

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Reporting health economic evaluations: CHEERS and beyond



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Abstract

Health economic evaluations are relevant to those making healthcare resource allocation decisions, such as listing a new drug on the national formulary or launching a new vaccination programme. Compared with clinical studies that report only the health consequences of an intervention, economic evaluations require more space to report additional items such as resource use, costs, preference-related information, and costeffectiveness results. This creates challenges

for editors, peer reviewers, and those who wish to scrutinise a study's findings. The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) updated previous efforts to produce a single useful reporting standard. It received endorsement from, and was co-published in, 10 journals that frequently publish health economic evaluations. CHEERS provides a sound basis for improving the reporting of economic evaluations.

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Introduction

ealth economic evaluation is defined as 'the comparative analysis of alternative courses of action in terms of both their costs and their consequences.' These evaluations are increasingly used for decision-making and are an important component of health technology assessment (HTA) programmes internationally. The need for economic evaluations to report both health consequences of an intervention and additional items on resource use, costs, preference-related information, and cost-effectiveness results creates a challenge for editors,

peer reviewers, and those who wish to scrutinise a study's findings.³

There is evidence that the quality of reporting of economic evaluations varies widely and could benefit from improved quality assurance mechanisms.4,5 Transparency and structure in reporting is especially relevant for health economic evaluations because: 1. the number of published studies continues to grow;6 2. there are potentially major consequences from resource allocation decisions based on misleading study findings; and 3. unlike clinical trials, there are no widely-implemented mechanisms for registering studies or making data availa-

ble for independent interrogation or analysis.

Endorsement of reporting guidelines by journals has been shown to improve reporting of clinical research.⁷ The risk of making costly

decisions due to poor reporting combined with 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.^{3,8}

Development of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS)

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Following the recommendations of a previous task force, ⁹ the International Society for Pharma-

coeconomics and Outcomes Research (ISPOR) established the CHEERS Task Force to improve the reporting of health economic evaluations. Task Force membership consisted of health economic journal editors and content experts from around the world. The Task Force used a process consistent with that used in the development of the EQUATOR suite of guidelines, such as CONSORT (for the reporting of clinical trials) and PRISMA (for the reporting of systematic reviews). This involved consulting a Delphi group consisting of international experts representing academia, biomedical journal editors, the pharmaceutical industry, government

decision makers, and those in clinical practice.

CHEERS aimed to consolidate and update previous efforts¹⁰⁻²¹ into a single useful reporting standard. It received endorsement from, and was

co-published in, 10 journals that frequently publish economic evaluations. The CHEERS reporting standard 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 these choices are clearly reported 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 study methods (other checklists have been developed for this purpose).22 The primary audience for the CHEERS reporting standard are researchers reporting economic evaluations, journal editors, and peer reviewers of the intended journals. CHEERS consists of a 24-item checklist accompanied by recommendations on the minimum amount of information to be included when reporting economic evaluations. It has been adopted as an EQUATOR guideline.

The CHEERS checklist

The CHEERS checklist was published in 2013 and is shown in Table 1. In the full explanation and elaboration document, ²³ which can be downloaded from the ISPOR website (https://www.ispor.org/heor-resources/good-practices/article/consolidated-health-economic-evaluation-reporting-standards-(cheers)-explanation-and-elaboration), the rationale for each of the 24 items is explained and examples given. [See Table 1 on pages 62–3]

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Table 1. CHEERS checklist: Items to include when reporting economic evaluations of health interventions

Section/Item	Item No.	Recommendation	Reported on
Title and abstract			Page no. / Line No.
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed including why they were chosen.	
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	
Measurement of effectiveness	11a	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.	
	11b	Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	
Measurement and valuation of preference-based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	
Estimating resources and costs	13a	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.	
	13b	Model-base 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.	

Section/Item	Item No.	Recommendation	Reported on Page No. / Line No.
Currency, price date and conversion	14	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.	
Choice of model	15	Describe and give reasons for the specific type of decision-analytic model used. Providing a figure to show model structure is strongly recommended.	
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytic model.	
Analytic methods	17	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.	
Results			
Study parameters	18	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.	
Incremental costs and outcomes	19	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.	
Characterising uncertainty	20a	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 (e.g. discount rate, study perspective).	
	20b	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.	
Characterising heterogeneity	21	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.	
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct and reporting of the analysis. Describe other non-monetary sources of support.	
Conflicts of Interest	24	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.	

Source: Husereau et al. 23



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 shortterm 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 costeffectiveness 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 summarises the methods and results of an economic evaluation that was based on evidence from the GNOME trial (p543) 24



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 decisionmakers who need to understand the consequences of re-allocating healthcare 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 "The 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 healthcare setting. Therefore, reporting on this item needs to be considered in conjunction with that for CHEERS checklist items 4-7 (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 costeffectiveness 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".

Examples of CHEERS items #3 and #6.

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Updating CHEERS

Study methods and reporting standards may change over time, and many of the established reporting guidelines, such as CONSORT and PRISMA, have been updated periodically. In 2020, ISPOR decided to update CHEERS, and

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the Task Force was reconvened. A number of factors led to the update. First, feedback on the CHEERS checklist suggested that it was inadequate for reporting studies such as costbenefit analyses, which measure and value benefits in monetary terms.²⁷ In addition, a study of the use of the CHEERS checklist suggested that it was often used inappropriately. Specifically, it

was often used to assess the methodological quality of published studies, rather than the quality of reporting.28

Second, there have been several important developments in the methodology of economic evaluation that necessitated modification of the current checklist. These include developments in the methods for assessing individuals' preferences for health and healthcare, more complex approaches to modelling and the characterisation of uncertainty, and a growing interest in the

> distributive effects (i.e. impacts on equity) within economic evaluations.

> Third, there has been a growing interest in the contribution of patients and the general public in designing and conducting health services research studies, including economic evaluations. Patients and the general public are also increasingly important audiences for the results of econ-

omic evaluations, given their participation as stakeholders in health technology assessment (HTA) processes in many jurisdictions. Therefore, they are interested in knowing which groups of patients the study results apply to, whether outcomes relevant to patients have been assessed, and whether patients have been consulted on the design of the study.

The revision of CHEERS, which is ongoing, will respond to these developments. The Task Force includes new members with the relevant expertise in the main methodological developments and is being advised by a Patient and Public Involvement and Engagement Group with plans to report these efforts using the GRIPP2 guidelines for patient engagement.²⁹ The revised CHEERS checklist will be published in 2022 and will be endorsed by a number of journals, including those who are the largest publishers of economic evaluations.

Concluding remarks

Adequate reporting of research is crucial, especially in applied areas of research. Excellent research that is poorly reported helps no one. This has been recognised by researchers in health economic evaluation, and the CHEERS guide-

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... (p2)²⁵

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." ²⁶



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 healthcare payer's perspective (e.g. sickness fund, Medicare in the United States), a healthcare system perspective, a public health perspective, or a societal perspective. Most studies are conducted from a health system or payer

perspective (e.g. NHS in England, 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. healthcare system, societal) in terms of costs included and their associated components (e.g. direct medical costs, direct non-medical costs, 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 healthcare 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.

lines have been developed to provide an international standard for study sponsors, medical writers, authors and journals consistent with the accepted methodology for EQUATOR guidelines. The CHEERS Task Force recognises that publishing economic evaluations with sufficient information to allow interpretation and replication is quite challenging, as it requires a significant amount of text. However, the Task Force also assumes these demands are becoming easier to meet as online supplementary information can be submitted to journals, and open data sharing has become more commonplace. The Task Force anticipates the update will provide an even more useful tool for authors and medical writers in the coming years.

Conflicts of interest

The authors are members of the CHEERS Task Force. They have no other conflicts to declare.

References

1. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for

- the economic evaluation of health care programmes. 4th ed. Oxford: Oxford University Press; 2015.
- Drummond MF, Schwartz JS, Jönsson B, et al. Key principles for the improved conduct of health technology assessments for resource allocation decisions. Int J Technol Assess Health Care. 2008;24(3):244–58.
- 3. Rennie D, Luft HS. Pharmacoeconomic analyses. JAMA. 2000;283(16):2158–60.
- r4. Neumann PJ, Stone PW, Chapman RH, Sandberg EA, Bell CM. The quality of reporting in published cost-utility analyses, 1976-1997. Ann. Intern. Med. 2000 Jun 20;132(12):964–72.
- Rosen AB, Greenberg D, Stone PW, Olchanski NV, Neumann PJ. Quality of abstracts of papers reporting original costeffectiveness analyses. Med Decis Making. 2005 Aug;25(4):424–8.
- Greenberg D, Rosen AB, Wacht O, Palmer J, Neumann PJ. A bibliometric review of cost-effectiveness analyses in the

- economic and medical literature: 1976–2006. Med Decis Making. 2010;30(3):320–7.
- Turner L, Shamseer L, Altman DG, Schulz KF, Moher D. Does use of the CONSORT Statement impact the completeness of reporting of randomised controlled trials published in medical journals? A Cochrane review. Syst Rev. 2012 Nov 29;1(1):60.
- Drummond MF. A reappraisal of economic evaluation of pharmaceuticals. Science or marketing? Pharmacoeconomics. 1998;14(1):1–9.
- McGhan WF, Al M, Doshi JA, Kamae I, Marx SE, Rindress D. The ISPOR Good Practices for Quality Improvement of Cost-Effectiveness Research Task Force Report. Value in Health. 2009;12(8):1086–99.
- Task Force on Principles for Economic Analysis of Health Care Technology. Economic analysis of health care technology. A report on principles. Ann. Intern. Med. 1995;123(1):61–70.
- 11. Gold MR. Cost-effectiveness in health and



- medicine. New York: Oxford University Press; 1996.
- 12. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. BMJ. 1996;313(7052):275-83.
- 13. Siegel JE, Weinstein MC, Russell LB, Gold MR. Recommendations for reporting cost-effectiveness analyses. Panel on Cost-Effectiveness in Health and Medicine. JAMA. 1996;276(16):1339-41.
- 14. Nuijten C, Pronk MH, Brorens MJA, et al. Reporting format for economic evaluation: Part II: Focus on modelling studies. Pharmacoeconomics. 1998;14(3):259-68.
- 15. Vintzileos AM, Beazoglou T. Design, execution, interpretation, and reporting of economic evaluation studies in obstetrics. Am. J. Obstet. Gynecol. 2004;191(4):1070-
- 16. Drummond M, Manca A, Sculpher M. Increasing the generalizability of economic evaluations: recommendations for the design, analysis, and reporting of studies. Int J Technol Assess Health Care. 2005;21(2):165-71.
- 17. Ramsey S, Willke R, Briggs A, et al. Good research practices for cost-effectiveness analysis alongside clinical trials: the ISPOR RCT-CEA Task Force Report. Value Health. 2005;8(5):521-33.
- 18. Goetghebeur M, Wagner M, Khoury H,

- et al. Evidence and value: Impact on decision making - the EVIDEM framework and potential applications. BMC Health Serv Rev. 2008;8(1):270.
- 19. Davis JC, Robertson MC, Comans T, Scuffham PA. Guidelines for conducting and reporting economic evaluation of fall prevention strategies. Osteoporos Int. 2010;22(9):2449-59.
- 20. Petrou S, Gray A. Economic evaluation alongside randomised controlled trials: design, conduct, analysis, and reporting. BMJ. 2011;342:1756-1833.
- 21. Petrou S, Gray A. Economic evaluation using decision analytical modelling: design, conduct, analysis, and reporting. BMJ. 2011;342:d1766-d1766.
- 22. Walker D, Wilson R, Sharma R, et al. Best practices for conducting economic evaluations in health care: A systematic review of quality assessment tools. Agency for Healthcare Research and Quality; 2012 [cited 2012, Nov 29]. http://www.ncbi.nlm.nih.gov/books/NBK 114545/.
- 23. Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS) explanation and elaboration: a report of the ISPOR Health Economic Evaluations **Publication Guidelines Good Reporting** Practices Task Force.

- Value Health. 2013;16(2):231-50.
- 24. Petrou S, Dakin H, Abangma G, Benge S, Williamson I. Cost-utility analysis of topical intranasal steroids for otitis media with effusion based on evidence from the GNOME Trial. Value in Health. 2010;13(5):543-51.
- 25. Cobiac LJ, Vos T, Barendregt JJ. Costeffectiveness of interventions to promote physical activity: a modelling study. PLoS Med. 2009;6(7):e1000110.
- 26. Bass EB, Pitt HA, Lillemoe KD. Costeffectiveness of laparoscopic cholecystectomy versus open cholecystectomy. The American Journal of Surgery. 1993;165(4):466-71.
- 27. Sanghera S, Frew E, Roberts T. Adapting the CHEERS statement for reporting costbenefit analysis. Pharmacoeconomics. 2015; 33:5.
- 28. Caulley L, Catalá-López F, Whelan J, et al. Reporting guidelines of health research studies are frequently used inappropriately. J Clin Epidemiol. Published online March 14, 2020. doi:10.1016/j.jclinepi.2020.03.006.
- 29. Staniszewska S, Brett J, Simera I, et al. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. Res Involv Engagem. 2017;3:13. doi:10.1186/s40900-017-0062-2.



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