

A practical instrument for assessing the quality of pharmacoeconomic studies: how to use it



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Since pharmacoeconomic evaluations are having an increasing impact on evidence-based pharmaceutical decision-making, it is clear that pharmacists need at least a basic knowledge of pharmacoeconomics in order to assess the quality of the available reports. This will enable them to make better choices for budgets, formularies, projects and so on. Those involved in research also need to consider proper techniques of economic evaluation in their studies and reports in order to obtain the necessary funding for their work.

By providing a validated, structured, easy-to-use scorecard a pharmacist can be guided through the process of pharmacoeconomic assessment. Nevertheless, a basic understanding of terminology and methodology is essential. An introduction to the questionnaire used in the scorecard, with guidance upon how to use it is described.

Mastering these techniques requires training and experience, however, there is little time spent on these topics in most pharmacy undergraduate or post-graduate curricula. As a consequence, it is difficult for the individual pharmacist to critically assess the quality of an economic evaluation of a health technology.

Therefore, in order to help less experienced pharmacists, an international, multidisciplinary panel of experts has developed a validated, practical scorecard which can be used to assess pharmacoeconomic studies by simply answering a questionnaire about the paper.

Content of the questionnaire

The methodology of the development of the questionnaire used in the scorecard has been described in the previous article in detail. The questionnaire was based on an extensive literature review, which revealed that two issues should be distinguished in the assessment of economic evaluations; first, the methodological quality and validity of data and secondly, the transferability to a specific setting, relevant for the assessor.

The methodological quality of economic evaluations is independent of the setting where the data of the study will be applied, leading to an objective score which should not differ between users throughout the world. The quality issues are surveyed in the first part of the scorecard's questionnaire (categories 1–4); transferability is evaluated in the second part (category 5). The transferability score

may differ between assessors and thus cannot be copied between different settings [1, 2].

An economic evaluation is deemed to be transferable if it can be adapted to apply to another setting or area of practice [3]. The terms are used to indicate where a local health technology assessment or economic evaluation is carried out. This may refer to a country, or a region within a country, but could also relate to a more specific setting such as a local hospital or even a specific healthcare payer. However, adapting research conducted in one setting or area of practice to another entails various degrees of complexity. Recently, an adaptation scale has been proposed which ranges from no adaptation to impossible adaptation [4]. The ISPOR Task Force on Transferability of Economic Evaluations has developed good research practices for dealing with aspects of transferability [2]. The degree of adaptation required depends on a number of issues, including the objectives of the analysis, availability of data, methodological rigour, time and budgetary constraints.

Categories in the questionnaire

In the first category of the scorecard's questionnaire the clarity of the research question is evaluated. This information has to be clearly stated and understandable to the reader and is relevant to its perspective, e.g. patient, hospital, government, caregiver, etc. As a pharmacoeconomic study always compares at least two alternatives, these should be fully described and, for each, both costs and outcomes should be evaluated. No

relevant alternative health technology should be omitted from the study. Even a 'do-nothing' scenario or placebo therapy can be considered valid treatments.

The second category in the questionnaire is divided into sections. The first section asks if the study is demonstrating efficacy or effectiveness. Efficacy is defined as the maximum effect under ideal circumstances, e.g. laboratory data, while effectiveness measures the effect in real life daily practice, e.g. dealing with patients' lack of compliance. Since the aim is to know the effect in a real population, effectiveness is granted a higher value in the scorecard than efficacy. If the report demonstrates effectiveness the relevant section should be completed. For efficacy (the subject of the majority of studies) the questions are different than for a single study, e.g. a controlled clinical trial, a systematic review of trials and an expert opinion, with each having its own set of questions. There is no valuation of the type of trial included; as a randomised clinical trial (RCT) or a systematic review of RCTs has no inheritable higher quality than a systematic review of non-randomised trials or a descriptive study.

The section on single studies mainly focuses on the challenge of identifying the different types of hidden bias, as defined by the Cochrane collaboration [5]. These are:

- Selection bias: when selecting the study population there can be systematic differences between, for example, patients, groups and caregivers, which can influence the results.
- Performance bias: systematic differences regarding the care provided, apart from the interventions being evaluated, can have an impact on the outcome.
- Attrition bias (formerly known as exclusion bias): when patients are excluded from the study or when they drop out or are withdrawn the characteristics of the sampled population can change, leading to a different result.
- Other biases are related to the method of evaluation of outcome (detection

bias) or the interpretation of objective measures and gathered information by the investigator (information bias).

It is impossible to always avoid every kind of bias but this is not a problem when the intrinsic risk or even a transparent correction is discussed. These questions are also applicable to reports on effectiveness studies. Of course, prospectively gathered evidence is rated higher than retrospective data.

In the case of a systematic review the search strategy has to be clearly outlined and reproducible. The relevant differences and similarities between the individual studies should be discussed. Outcome parameters should be comparable and have the possibility to be



extrapolated to a comparable time frame while financial data should be discounted to a reference year and currency; otherwise data in different currencies or from different years will lead to an artifact while comparing the values [6].

In a paper which makes use of expert opinion the validity of the assumptions made by the author or an expert panel must be checked. As in the case of a single study there can be different kinds

of bias, mainly on the methodology used or reasoning. Clearly the composition of an expert panel must be relevant for all aspects of the research domain and justifications are required for all of the assumptions made.

An assessment of costs and consequences is the purpose of the third category. Both must be relevant, well selected, clearly defined and justified. Costs such as labour costs, operating costs and capital costs are frequently forgotten in financial equations and only a few studies assess indirect costs, such as loss of productivity. The type of analysis is indirectly subject to ranking also. A cost-utility analysis is difficult to achieve but is considered the better method in comparison with the frequently used cost-effectiveness analysis. Cost-benefit analysis is the least preferred method in pharmacoeconomics since the outcomes are not so easily comparable because they do not have the same parameters.

The methodological quality and the validity of the conclusions are examined in category four. As with previous sections of the questionnaire attention is paid to clear definitions, transparency and possible bias. Moreover, there are questions with regard to interpretation, generalisability, ethical issues, feasibility, constraints and even redeployment of freed resources.

Uncertainty and sensitivity analysis

A major issue in economic evaluations is the uncertainty of data; quite often it is not possible to pinpoint an exact number, but a confidence interval in which the real value is situated. Take, for instance, an example of an Intravenous-Per Oral (IV-PO) switch intervention by a clinical pharmacist, with a cost saving due to the lower price of the oral alternative. The total saving will be calculated as the cost per day multiplied by the number of days the patient is switched to oral medication. In this case, there is no certainty that the physician shall notice the opportunity to do the IV-PO switch during one of the following

days, resulting in a lesser cost saving for the intervention (cost per day multiplied by the number of days between the day the pharmacist noticed the opportunity and the day switch was made by the physician).

A good pharmacoeconomic evaluation identifies such uncertain data and discusses the possible effects, or even risks, in reaching a valid conclusion. A commonly used technique to monitor the impact of uncertain data is a sensitivity analysis. In simple terms this method calculates the result for the outer ranges of the uncertain parameters, e.g. the number of days in the IV-PO switch is situated between one and the number of days until the planned stop of the specific therapy. Besides correct identification of the uncertain data it is important to define and justify the proper range for the analysis. Recently more authors are including a sensitivity analysis in their publications but only in a few reports is this uncertainty of data also reflected in the conclusion.

Power Analysis

Some authors base their general conclusions on a rather small data set (due to the collection of data over a short period in time), or on a small population of patients or on a wrong statistical technique. Calculating the power of a study is one way to justify the conclusions but requires essential statistic knowledge and is possible overkill. In most cases a critical attitude of the representativeness of the studied population and the time frame can show the difference between study designs of high and low quality.

When differences in costs and outcomes are known, an incremental cost ratio, defined as the differences in costs compared to the differences in outcome, e.g. $\Delta \text{cost} / \Delta \text{avoided Adverse Drug Events}$, can be calculated. Such a ratio has to be interpreted intelligently and with common sense rather than just numerically. In the case of dominance of a specific health technology (more effective and less costly than the comparator) mechanistic interpretation can lead to wrong conclusions [1]. When other studies, investigat-

ing the same question, are available the author should compare the research as part of a simple cross-check.

A score for a declaration of conflict of interest included in a paper is not given in the scorecard since it gives no further added value. An author with a declaration of conflict of interest can write an objective (even negative) report and vice versa. In fact, it will not necessarily influence the intrinsic quality of the study.



Transferability

Finally, in category five, the transferability of a study to the setting or area of practice of the assessor is examined by questioning the variations between populations and settings, differences in law and legislation and availability of local alternatives. Three questions assess the relevance of the research question and the perspective to the intended setting or decision-making context. In order to check the transferability of financial outcomes and conclusions all calculations and key values should be transparent so they can be used with data from the setting of destination. Therefore, it is necessary that prices and numbers are mentioned separately. This score is assessor and setting-specific and, therefore, is not transposable to others and does not judge the intrinsic methodological quality of the publication.

Use of the scorecard and its outcomes

In ideal circumstances the results of sections one to four should be independent from the assessors' setting or area of practice, while section five will be, more often than not, different for every assessor because it questions the transferability to a very specific context and setting. When reporting the outcome of the assessment of a paper it is necessary to mention at least the results of sections one to four as they quantify the quality of the reported study. Although the result of section five quantifies the transferability to a very specific setting, it can also be an indicator of the overall transferability. The combined score can also be used to rank different pharmacoeconomic evaluations according to their degree of usefulness to the assessor.

Theoretically, a web-based version of the scorecard, which calculates the scores for a publication and is linked to an international database, could lead to an important source of information on the quality of pharmacoeconomic reports. This would be a useful reference source for pharmacists and their work in the pharmacy and therapeutics committees. Results from earlier assessments could also be retrieved. It would be possible to detect bias by statistical analysis of the answers from the various assessors of each economic evaluation.

Conclusion

The assessment of pharmacoeconomic evaluations by pharmacists without specific expertise in the field cannot be taken for granted. By providing a validated, structured, practical scorecard the assessor can be guided through the process. Nevertheless, a basic knowledge of the terminology and methodology is necessary. Therefore, it is advisable to read and understand these, or have them explained by an experienced colleague, before entering the world of pharmacoeconomic assessment. The scorecard provided is self-explanatory, since clarification of possible ambiguous questions is also given. Together with the accompanying article this should enable

the modern pharmacist to critically assess pharmaco-economic studies, thus contributing to the quality of decision-making in the hospital setting.

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References

1. Drummond M, Sculpher M, Torrance G, et al. Methods for the economic evaluation of health care programmes. 3rd Edition. 2005 Oxford university press. ISBN 019-852945-7.
2. Sculpher M, Pang F, Manca A, et al. Generalisability in economic evaluation studies in healthcare: a review and case studies. Health Technology Assessment. 2004;8(49).
3. Drummond M, Barbieri M, Cook J, et al. Transferability of economic evaluations across jurisdictions: ISPOR good research practices task force report. Value in Health (early view 02-2009 doi 10.1111/j.1524-4733.2008.00489.x).
4. O'Sullivan A, Thompson D, Bekker D. Country-to-country adaptation of pharmaco-economic research: methodologic challenges and potential solutions. ISPOR Connections 2009;15(1).
5. <http://www.cochrane.org/resources/glossary.htm> [cited 2009 August 19].
6. De Rijdt T, Willems L, Simoens S. Economic effects of clinical pharmacy interventions: a literature review. Am J Health-Syst Pharm. 2008; 65:1161-72.