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Investigating the Generalizability of Economic Evaluations Conducted in Italy: A Critical Review

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ABSTRACT

Objectives: To assess the methodological quality of Italian health economic evaluations and their generalizability or transferability to different settings. **Methods:** A literature search was performed on the PubMed search engine to identify trial-based, nonexperimental prospective studies or model-based full economic evaluations carried out in Italy from 1995 to 2013. The studies were randomly assigned to four reviewers who applied a detailed checklist to assess the generalizability and quality of reporting. The review process followed a three-step blinded procedure. The reviewers who carried out the data extraction were blind as to the name of the author(s) of each study. Second, after the first review, articles were reassigned through a second blind randomization to a second reviewer. Finally, any disagreement between the first two reviewers was solved by a senior researcher. **Results:** One hundred fifty-one economic evaluations eventually met the inclusion criteria. Over time, we observed an increasing transparency in methods and a greater generalizability of results, along with a wider and more representative sample in trials and a larger adoption of transition-Markov models. However, often context-specific economic evaluations are carried out and not enough effort is made to ensure the transferability of their results to other contexts. In recent studies, cost-effectiveness analyses and the use of incremental cost-effectiveness ratio were preferred. **Conclusions:** Despite a quite positive temporal trend, generalizability of results still appears as an unsolved question, even if some indication of improvement within Italian studies has been observed.

Keywords: economic evaluation, model-based economic evaluation, review, trial-based economic evaluation.

Introduction

Health care systems worldwide are under increasing financial pressure. Policymakers are constantly interested in finding measures to support them in achieving the balance between the increasing demand for health technologies and the strict budget constraints. Health technology assessment (HTA) represents a rigorous approach aimed at informing efficient allocation of health care resources, through the provision of information on efficacy, efficiency, appropriateness, and costs of health technologies, as well as on their organizational, societal, and ethical impact.

Nowadays, HTA is a deep-rooted culture in many (local and national) policymaking settings, and current collaborations among national HTA bodies play a key role in avoiding unnecessary overlapping of research efforts. To this extent, the ability to produce research findings that are transferable across jurisdictions becomes an important objective. Unfortunately, resource use and costs documented in health economic evaluation (HEE) studies carried out in a given jurisdiction are hardly directly applicable to another [1]. Problems such as variation in the underlying morbidity/mortality patterns or in clinical practice among different countries and the absolute and relative differences in price weights could potentially threaten the generalizability of economic results from one country to another. Several studies attempted to assess the extent to which results and reporting of HEE studies allow the generalization of their results from one context to another [2–4]. Augustovski et al. [3] recent looked at this in the Latin-American and the Caribbean region. They found a large number of issues associated with the reporting and the transparency of the methodology used in multinational and local HEE studies, which precluded the assessment of their generalizability within the region. Urdahl et al. [4] reviewed model-based HEEs in the field of osteoporosis to assess whether the quality of reporting could allow for generalizing study results across clinical settings and jurisdictions. They found that the variability in

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cost-effectiveness across different settings prevents decision makers from using the evidence produced in a different context [4].

As noted by the ISPOR task force, in the review of national guidelines on economic evaluations, there are several important methodological and practical issues surrounding the transferability of economic data. The work of the task force also confirmed that many international guidelines for economic evaluation make reference to problems concerning economic data transferability and include requirements for jurisdiction-specific data or methods. Such guidelines, however, entail different recommendations and requirements concerning economic data transferability; thus, this issue would need to be assessed more in depth [5].

Nonetheless, this type of assessment is expected to be increasingly necessary for the internationalization of clinical trials and HEEs and the rapid diffusion of new health technologies. Decision makers operating in countries with limited financial and human resources are in constant struggle when assessing the transferability of results of HEEs conducted elsewhere [1].

In Italy, the existence of a regionally based health care system in which 21 regional decision makers are supposed to decide about the uptake of technologies within a nationally defined normative framework has made the issue of generalizability even more crucial in the last few years, representing a hot topic for discussion among scientific societies and the research community. To this end, a recent study provided an overview of the state of regional and central HTA initiatives in Italy with the aim of investigating the consequences of a multilevel structure of HTA agencies or initiatives in regionalized health care systems. Using document analysis and semi-structured interviews with relevant actors of the HTA process in different regional settings, Ciani et al. [6] found that although the National Agency for Regional Healthcare Services (Age.Na.S) has certainly contributed to HTA diffusion through supporting and training activities, the multilevel structure of HTA in Italy still lacks coordination and harmonization of practices and outcomes, which ultimately contributes to exacerbating inequality of access to innovative technologies across Italian regions [6].

In this context, the need of methodological harmonization and the creation of networks to support the process of HTA are becoming an urgent policy objective, especially in those regions where they are still poor [7]. One effort to move things in this direction is represented by the publication of the Guidelines for Economic Evaluation of Healthcare Programs (2009) by the Italian Health Economics Association.

Economic evaluations can be considered generalizable when their results hold true in a multiplicity of jurisdictions without needing any adjustment for interpretation. When some adaptations are needed for their results to be applicable in other settings, studies can be considered transferable [8]. Sometimes, however, transferability is not possible for a number of reasons, for example, because the study is meant to inform decisions on a context-specific issue, or just because the reporting is not detailed enough to appraise the applicability of results in other contexts.

The present study aims to assess the methodological quality and the generalizability of results of HEEs performed in Italy through a methodological systematic review of both trial and model-based analyses.

Methods

Data Search Strategy

The studies included in the review were identified by searching the PubMed database through the following search strategy:

("Ita*") AND ("Markov model" OR "economic model" OR "economic evaluation" OR "cost studies" OR "cost effectiveness" OR "utility cost" OR "cost benefit" "OR" costs "OR" pharmacoeconomic "OR" decision model "OR" QALY).

Publication date and language restrictions were applied to the search to select studies only in English and Italian language published between 1995 and 2013.

Inclusion and Exclusion Criteria

Eligible studies needed to fulfill the following criteria jointly:

1. Trial-based, nonexperimental prospective studies or model-based economic evaluation;
2. Study carried out in Italy;
3. Full economic evaluation comparing costs and benefits of two or more alternative technologies (i.e., screening/prevention programs, drugs, devices, equipment, clinical procedures, organizational arrangements). Thus, cost-benefit analyses, cost-utility analyses (CUAs), cost-effectiveness analyses, and cost-minimization analyses were considered eligible for the current review.

Review Process and Data Extraction

The studies identified were randomly assigned to four reviewers (V.I., S.C., P.C., and F.R.) who applied the checklist developed by Augustovski et al. [3]. The review process followed a three-step blinded process. The reviewers who carried out the data extraction were blind as to the name of the author(s) of each study. Second, after the first review, articles were reassigned through a second blind randomization to a second reviewer. Finally, any disagreement between the first two reviewers was solved by a senior researcher.

The checklist was structured in three sections. The first section focused on a set of general characteristics for each study and comprised 25 items, which evaluated the presence or absence of useful contextual information. The second section, specific to trial-based HEEs and HEEs conducted alongside nonexperimental studies, included 10 items and focused on quality assessment, including methods used in data analysis and reporting of results. The third section, specific for model-based HEE, included 27 items investigating the type of model used to estimate the health benefits, the clarity of model assumptions, and the presence of an adequate justification of model assumptions, together with the presence/absence of a stochastic analysis performed to assess the robustness of results.

Data extracted through the checklist were recorded into an Excel spreadsheet, and summarized in graphical and tabular format.

To better distinguish generalizable from transferable studies, we focused on some items of the checklist specifically relevant to ascertaining the generalizability of HEEs. These were identified on the basis of recommendations for the generalizability of economic evaluations previously published by Drummond et al. [9].

Overall, 12 items were selected for HEEs performed alongside clinical studies, 6 concerning the study design and analysis and 6 concerning the quality of reporting. The first subset of items included the multicentric study design, the clinical and cost data referring to the whole study population, the preference data relevant to the study population, the presence of quantitative/qualitative analysis performed to appraise the variability of results from setting to setting, the adoption of a wide study perspective (National Health Service or societal); the second subset of items included the full reporting of baseline characteristics of the study sample, the clear description of the study