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BRIEF REPORTS

A Pilot Study of Multicriteria Decision Analysis for Valuing Orphan Medicines

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ABSTRACT

Objective: To pilot the use of multicriteria decision analysis to establish and apply a framework of weighted attributes to value orphan medicinal products. **Methods:** Literature searches on the natural history and burden of 40 rare diseases and of how payers assess treatment value and three workshops with, respectively, GlaxoSmithKline managers working on orphan medicinal products, European Union clinical and health economics experts, and representatives of rare diseases patient groups in the European Union. **Results:** Eight nonmonetary attributes were identified and weights agreed: four concern the disease being treated and four the treatment itself. About half of the weight went to attributes of the disease treated and half to attributes of the treatment. Patient group representatives gave greater weight than did the experts to patients' and carers' quality of daily life. **Conclusions:** The multicriteria decision analysis approach piloted works and could be developed for use by payers and health technology assessment bodies.

Keywords: HTA bodies, methods, orphan drugs, payers, rare diseases.

Introduction

This article presents an experimental pilot study that tests a multicriteria decision analysis (MCDA) approach [1] to establish a framework for valuing orphan medicinal products (OMPs) and providing an explicit understanding of trade-offs for decisions on their eligibility for funding.

All health care systems' health technology assessment (HTA) and reimbursement decisions depend on an implicit, if not explicit, assessment of value as the first step. Efforts by policymakers and payers to better determine the value of medicines are widespread internationally. The 2011 AMNOG (Arzneimittelmarktneuordnungsgesetz, or medicines market restructuring law) reforms in Germany and the development of "value-based pricing" in the United Kingdom are two high-profile examples [2,3] among many others [4,5]. No HTA agency yet uses MCDA, but the European Medicines Agency is developing an MCDA approach to balancing the benefits and risks of new medicines considered for licensing [6] and National Health Service England has proposed what is in effect an MCDA process for deciding which oncology medicines will be funded by the national Cancer Drugs Fund for National Health Service patients in England [7]. The literature on MCDA in health care is growing [1,8].

MCDA is a set of methods to aid decision making where more than one criterion is relevant, which make explicit the impact on the decision of all the criteria and the relative importance attached to them. The main steps are (see [1] for more detail) as follows:

- establish the decision context—what is to be decided, by whom;
- identify attributes for assessing the value of each medicine;
- assign weights to the attributes to indicate their relative importance to the decision;
- score the expected performance of each medicine against the attributes;
- combine weights and scores to indicate overall value; and
- consider the implications of the results and test their sensitivity to reasonable variations in weights and scores.

Variants of MCDA range from those using sophisticated algorithms to identify the total (dis-)benefits of an option to more basic approaches limited to providing and recording a structured and explicit deliberative process. All forms of MCDA aim to achieve replicability and transparency, and hence accountability, in decision making. MCDA has been extensively used in health care and other sectors (transport, social services, immigration policy, etc.). MCDA aids and structures the exercise of judgment by decision makers but does not do away with the need for that judgment [8].

OMPs are treatments for patients with rare diseases, defined in Europe as conditions affecting fewer than 1 in 2000 people. Rare diseases are often chronic, progressive, and life threatening;

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many of them affect children; and there is often a lack of effective treatments for these diseases. Small populations, substantial heterogeneity, lack of knowledge about natural history, and difficulty in defining practical clinical end points create greater uncertainty around evidence in rare diseases than in common ones. The development of OMPs is often accompanied by partial knowledge of diseases and scarce medical expertise. Legislation has accordingly been introduced in the United States and the European Union (EU), establishing special incentives for the development of treatments for rare diseases, and increased numbers of orphan drug designations have followed [4].

Payers commonly treat OMPs distinctly from other medicines. A number of HTA systems have special arrangements for the assessment or reimbursement of OMPs. In England and Wales, treatments for very rare conditions are assessed and commissioned in a separate process from other treatments (until April 2013 by the Advisory Group for National Specialised Services [9] and since then by the National Institute for Health and Care Excellence [NICE] whose Highly Specialised Technologies Evaluation Committee is building on the work done by the Advisory Group for National Specialised Services [10]). The process uses criteria in addition to health gains, including attributes related to societal value and impact on clinical practice. In Scotland, a special fund specifically for OMPs was set up in early 2013 [11]. At the European level, policy initiatives are aimed at improving the approach to assessing the value of new OMPs. For example, the EUCERD (European Union Committee of Experts on Rare Diseases) [12] is developing processes to inform decision makers about the clinical added value of OMPs and facilitate timely reimbursement.

Winquist et al. [13] have proposed a process for reviewing OMPs by payers that works around problems with demonstrating clinical effectiveness. But we have not been able to find in the literature a value framework for assessing OMPs that sets clinical effectiveness alongside other attributes of value.

Launching a treatment for a hitherto untreated rare disease puts that disease on the clinical map. Clinicians are then more likely to be aware of the disease, to recognize cases that present to them, and to have the necessary skills to help [14]. This suggests that the existence of an unmet need for treatment might be more important when determining the value of an OMP than when evaluating treatments of more prevalent conditions.

For all these reasons, it is important to relate the "significant benefit" value criterion required for OMP designation with a framework that, as pointed out by Hughes-Wilson et al. [15], would permit consistent value assessments of OMPs across different jurisdictions and across diverse rare diseases. To that end, we piloted the identification of benefit attributes to include in an OMP value framework and the determination of their relative importance via an MCDA process.

We did not attempt to assign monetary values to different levels of the benefit attributes. Few HTA or pricing and reimbursement (P&R) bodies do so explicitly, and NICE offers only a range of values and only for one dimension of value, namely, the incremental quality-adjusted life-years (QALYs) produced [16]. We focus on the benefits of OMPs, which can then be compared with net costs, including the price of the OMP itself.

Methods

We identified an initial list of value attributes from a literature review of rare diseases, a review of HTA for OMPs, and interviews with clinical experts, economists, and representatives from rare disease patient groups. A literature search was undertaken on the natural history and burden of 40 rare diseases (see Appendix A in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2013.10.002. There are more than 7000 rare diseases, and so a comprehensive literature review was impractical. A subset of 40 diseases was selected on the basis of availability of literature on morbidity, mortality, broader patient and carer burden, disease frequency, severity, degree of scientific understanding, and prog ress in developing effective treatments. Searches were conducted in MEDLINE, EMBASE, the Cochrane database, Orphanet, and the EURORDIS patient association Web site. For each condition, disease impact was broken down by individual or group affected (patients, family, society), nature of the effect (pathological, clinical, symptomatic, outcomes, economic), and the proximity of the effect to the primary manifestation of the disease.

A second search looked for how existing payer frameworks estimate treatment value in 10 OECD (Organisation for Economic Co-operation and Development) countries with OMP regulatory pathways and well-established pharmaceutical reimbursement processes (Australia, France, Germany, Italy, Japan, The Netherlands, Spain, Sweden, the United Kingdom, and the United States). A related search focused on rationales given in reimbursement decisions for OMPs in those EU countries where the reports were available in English: the United Kingdom (NICE and SMC [the Scottish Medicines Consortium]), France (Transparency Commission), and Germany (GBA [Gemeinsame Bundesausschuss, or the Joint Federal Committee]—IQWiG [Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, or the Institute for Quality and Efficiency in the Health Service]). These searches were supplemented through 10 interviews with clinical experts, academics specialized in health economics and policy, and rare diseases patient group representatives in the EU and the United States.

This process yielded 14 attributes. Practical guides to MCDA recommend using fewer than 10 attributes. We excluded the net monetary cost impacts of the disease and the treatment, as to include them would require monetary values for all the nonmonetary attributes. We sought instead to establish the value of an OMP to set against its net cost impact. We discussed the attributes at a workshop in March 2012 with GSK managers working on the development and commercialization of OMPs, and aggregated them into the following eight attributes:

- impact of the rare disease and associated unmet need:
  1. availability of effective treatment options/best supportive care in the absence of the new medicine;
  2. disease survival prognosis with current standard of care;
  3. disease morbidity and patient clinical disability with current standard of care;
  4. social Impact of the disease on patients' and carers' daily lives with current standard of care;
- impact of the new medicine:
  5. treatment innovation, defined as the scientific advance of the new treatment together with contribution to patient outcome;
  6. evidence of treatment clinical efficacy and patient clinical outcome;
  7. treatment safety; and
  8. social impact of the treatment on patients' and carers' daily lives.

The rationales for these attributes and their particular relevance in rare diseases, with references to the literature from which they are drawn, are detailed in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2013.10.002. The inclusion of attributes of the disease, as well as of the treatment itself, is recognized as relevant by various authorities (e.g., [3] and [17]).

To provide a combined value assessment based on these attributes, we used an MCDA approach. We selected a "value measurement model" [8] as being of most value to HTA and