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Sources and Characteristics of Utility Weights for Economic Evaluation of Pediatric Vaccines: A Systematic Review

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ABSTRACT

Background: Cost-effectiveness analysis of pediatric vaccines for infectious diseases often requires quality-of-life (utility) weights. **Objective:** To investigate how utility weights have been elicited and used in this context. **Methods:** A systematic review was conducted of studies published between January 1990 and July 2013 that elicited or used utility weights in cost-effectiveness analyses of vaccines for pediatric populations. The review focused on vaccines for 17 infectious diseases and is presented following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology. **Results:** A total of 6410 titles and abstracts and 225 full-text articles were reviewed. Of those selected for inclusion (n = 101), 15 articles described the elicitation of utility weights and 86 described economic modeling studies using utilities. Various methods were used to generate utilities, including time trade-off, contingent valuation, and willingness to pay, as well as a preference-based measure with associated value sets, such as the EuroQol five-dimensional questionnaire or the Health Utilities Index. In modeling studies, the source of utilities used was often unclear, poorly reported, or based on weak underlying evidence. We found no articles that reported on the elicitation or use of utilities in diphtheria, polio, or tetanus. **Conclusions:** The scarcity of appropriate utility weights for vaccine-preventable infectious diseases in children and a lack of standardization in their use in economic assessments limit the ability to accurately assess the benefits associated with interventions to prevent infectious diseases. This is an issue that should be of concern to those making decisions regarding the prevention and treatment of infectious childhood illnesses.

Keywords: infectious diseases, literature review, pediatric, utilities, vaccine-preventable.

Introduction

The cost-effectiveness of health care interventions is an important element in making decisions regarding access to and reimbursement of health care technologies. The quality-adjusted life-year (QALY), a measure of quantity and quality of life (QOL), is widely used as a measure of incremental effect in economic evaluations of medical interventions and is a stipulated outcome in the National Institute for Health and Care Excellence's (NICE's) reference case [1]. In the case of vaccines, UK's Joint Committee on Vaccination and Immunisation (JCVI) also specifies that evaluation of new vaccines should take into account "cost effectiveness based on costs per QALY and as a function of vaccine price at different cost per QALY thresholds" [2].

Estimating QALYs requires that values (*utilities* or *weights*) be assigned to health states (HSs) that are relevant to the condition of interest. In some cases, values are elicited directly by using techniques such as time trade-off (TTO) and standard gamble (SG). Alternatively, values can be obtained indirectly by using a generic HS classification system, such as the EuroQol five-dimensional questionnaire (EQ-5D) [3] or the Health Utilities Index (HUI) [4,5], which is accompanied by value sets. In practice, various approaches have been used to elicit utility weights [6–8], although a recent review of how QALYs are estimated for pediatric patients in cost-utility analyses performed in the United Kingdom [9] found that QALYs were generated most frequently using existing preference-based instruments, particularly the EQ-5D and the HUI.

The methods used to obtain values for HSs can affect the conclusions drawn about the cost-effectiveness of health care interventions, including vaccines, because several studies have shown that different methods lead to different utility weights [10–12]. Although measuring and valuing health is a complex task in adults, it is perhaps even more conceptually and

Conflict of interest: M. Herdman, A. Cole, C. K. Hoyle, and N. Devlin are or were all employees of the Office of Health Economics at the time this study was performed. V. Coles and S. Carroll are or were employees of Sanofi-Pasteur MSD at the time this study was performed.

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methodologically demanding in children [13–15], and the appraisal of vaccines in pediatric populations is particularly challenging, as highlighted recently by Bruggenjurgen et al. [16]. Although previous reviews have examined the generation and use of utility weights in pediatric populations in general [6,9], none has focused specifically on the use of utility weights for HSs associated with infectious diseases and their use in economic evaluations of vaccines to prevent those diseases.

The Patient Reported Outcomes in Children with Infectious Diseases (PROCHID) study was a project to systematically review the development and use of patient- reported outcome (PRO) measures in pediatric populations with vaccine-preventable infectious diseases. As part of that project, we reviewed the use of utility measures and utility weights in that population, which is reported in this article. The methods and results of the PRO element of the PROCHID project are reported elsewhere [17].

Methods

Search Strategy, Data Sources, and Eligibility Criteria

The overall review for the PROCHID study, of which the review of utility generation and use formed a part, was conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18]. The search period was from January 1, 1990, to July 31, 2013, and included MEDLINE and EMBASE using the SCOPUS search engine. Published studies that reported the generation and/or use of utility weights for the pediatric population with vaccine-preventable infectious diseases of interest were identified using the general study algorithm and the utility-specific algorithm presented in Appendix 1.

The aim was to identify studies that had generated or used utility weights for the economic evaluation of vaccines used in pediatric populations (defined for the purpose of this study as populations aged <18 years) to prevent any of the following 17 infectious diseases: anogenital warts (AGWs), diphtheria, hepatitis B, *Haemophilus influenzae* type B (HiB), influenza, measles, mumps, rubella, meningococcal B meningitis, meningococcal C meningitis, norovirus, pertussis, polio, pneumococcal disease, rotavirus, tetanus, or varicella.

The search focused on publications in English and Spanish, which were the languages spoken by members of the study team, and on studies performed in Europe, North America, Australia, and New Zealand, because we were primarily interested in the economic evaluation of vaccines in developed countries.

Study Selection

Two independent reviewers screened the titles and abstracts of all the studies identified by the search algorithms to determine whether they met selection criteria. Discrepancies in the selection of publications were resolved through discussions between reviewers and recourse to a third reviewer where necessary. Studies were included for full-text review if they

1. described the elicitation or generation of utility weights for HSs associated with any of the infectious diseases of interest;
2. described the use of utility weights in cost-effectiveness or cost-utility analysis of vaccines to prevent any of the infectious diseases of interest;
3. referred to pediatric populations (age <18 years);
4. were performed in the countries of interest;
5. were published in English or Spanish; and
6. were available as full-text publications.

The reference lists of all full-text articles retrieved were reviewed to further identify potentially relevant studies. We excluded gray literature, such as unpublished manuscripts, government reports, or conference proceedings, and studies that were performed only in adult populations.

Data Extraction and Synthesis

A predesigned data extraction form was used to extract information on the following: year(s) of research, country, study type (HS valuation, cost-effectiveness, cost–utility, burden of disease, modeling, others), study objectives, intervention evaluated, study population (particularly any information on age groups), strategy used to estimate utility decrements (including source of utility weights and method of elicitation), and utility weights generated or used in any modeling. We also recorded any study limitations noted by the authors in relation to the utilities derived or used. Data extraction was performed for each full-text article by two reviewers. If doubts arose, for example, about the methods or sources used to obtain utilities or about the values themselves, these were resolved through discussions between the two reviewers and, if need be, through recourse to a third reviewer. A thematic approach to data synthesis was adopted on the basis of the information retrieved. From an early stage in the review of the full-text articles, they were organized and analyzed according to whether they were primarily concerned with generating HS utilities or with applying utilities in economic models.

Results

The searches performed for the PROCHID project as a whole yielded 6410 journal article references covering both PRO and utility-based studies. Of these, 6301 were excluded because of duplication or a failure to meet inclusion criteria after title or abstract review (Fig. 1). Full-text articles were retrieved and reviewed for the remaining 107 references (two articles could not be obtained). The review of reference lists identified a further 118 journal articles for full-text review, giving a total of 225 articles. Of these, 101 were retained for data extraction—15 articles reported on the elicitation of utility weights and 86 referred to the application of utility weights in economic models involving pediatric populations. A summary of results from the two types of study is provided in Tables 1 and 2, respectively (for further information, see Appendix Tables 1 and 2 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2015.11.003). No full-text articles referring to either utility generation or modeling involving utilities were identified for diphtheria, polio, or tetanus.

Utility Generation Studies

Table 1 presents the key features of 15 studies reporting on the generation of utility weights. *Utility generation studies* were defined as those in which utility weights were elicited from the general population and/or patient samples either directly (using valuation methods such as the TTO or the SG) or indirectly (after collecting data from relevant patient and/or caregiver samples using a preference-based measure, such as the EQ-5D or the HUI, which has accompanying value sets). Modeling studies that used utility estimations based on author or expert opinion were not considered elicitation studies and are described later in the article. No studies were found that reported utility generation for children with diphtheria, hepatitis B, HiB, measles, mumps, rubella, norovirus, or tetanus. The main findings for each condition are summarized hereafter. Further information on these studies can be found in Appendix Table 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2015.11.003.