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Do Model-Based Studies in Chronic Obstructive Pulmonary Disease Measure Correct Values of Utility? A Meta-Analysis

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a progressive chronic disease that has considerable impact on utility-based health-related quality of life. Utility is a key input of many decision analytic models used for economic evaluations. **Objective:** To systematically review COPD-related utilities and to compare these with alternative values used in decision models. **Methods:** The literature review comprised studies that generated utilities for COPD-related stages based on EuroQol five-dimensional questionnaire surveys of patients and of decision models of COPD progression that have been used for economic evaluations. The utility values used in modeling studies and those from the meta-analysis of actual patient-level studies were compared and differences quantified. **Results:** Twenty decision modeling studies that used utility value as an input parameter were found. Within the same span of publication period, 13 studies involving patient-level utility data were identified and included in the meta-analysis. The estimated mean utility values ranged from 0.806 (95% confidence interval [CI] 0.747–0.866) for stage I to 0.616 (95% CI 0.556–0.676) for stage IV. The utility scores for comparable stages in modeling studies were different (significant difference 0.045 [95% CI 0.041–0.052] for stage III). Modeling studies consistently used higher utility values than the average reported patient-level data. **Conclusions:** COPD decision analytic models are based on a limited range of utility values that are systematically different from average values estimated using a meta-analysis. A more systematic approach in the application of utility measures in economic evaluation is required to appropriately reflect current literature.

Keywords: chronic obstructive pulmonary disease (COPD), EQ-5D, health state utility value, Markov model, meta-analysis, modeling, utility.

Introduction

Economic models of chronic obstructive pulmonary disease (COPD) are intended to simulate disease progression and quantify the impact of interventions on outcomes primarily in terms of quality-adjusted life-years (QALYs). An important aspect of these models is health state utility value (HSUV) (commonly referred to as utility), which, associated with the major stages of COPD, and disutility related to major events such as exacerbations form the basis of QALY outcomes. A systematic search of the health economic literature located a large number of studies reporting progression models [1–24] that included utility values for one or more stages of COPD.

The utility values used to estimate the base case in each model were dependent on information from a single study, which has been standard practice in the health economic literature. Utilities used in COPD models to date have come from summary measures derived from the EuroQol five-dimensional questionnaire (EQ-5D) index, a generic instrument of HSUV, and show variation in utility assumption across models. This variation is likely to have an impact on the generalizability of model outputs and raises the question as to whether the model would have produced outcomes that were sufficiently different to have an impact on cost-effectiveness decisions.

In recent years, meta-analysis has emerged as a strategy to generate overall utility values for common health states. This has included studies of utility values for HIV/AIDS [25], chronic kidney disease [26], diabetes [27], and various types of cancer [28,29]. To date, there has been only one meta-analysis of utility values of COPD stages [30], which is surprising given the large number of evaluations of COPD therapies that have been routinely undertaken. These results have not been used as inputs to COPD modeling studies.

The aim of this study was to conduct a systematic review of utilities assigned to the different stages of COPD used in modeling studies and to compare these with summary measures from meta-analyses of available utility studies within the publication period of modeling studies derived from patients with COPD. We also examined the implications of differences between utility used in past models and estimates of the average utility for health states that are derived from a meta-analysis of the available literature of patient-derived values for utility associated with COPD states.

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Methods

Study Selection

Two systematic literature reviews were conducted.

Patient-Reported Outcome Studies

The first literature review covered HSUV studies in COPD that used the EQ-5D index to estimate utility value for patient-level research in COPD.

Studies matched with the following criteria were included:

1. health utility studies published before 2014 (the publication date of the last COPD model included in this study);
2. utility scores based on UK tariff value set;
3. the sample population had a confirmed COPD according to the standard criteria for COPD diagnosis and spirometric confirmation (should clearly be addressed in the methodology of included studies);
4. English language publications; non-English language studies were included if they accommodated English abstracts.

Exclusion was applied for the following criteria:

1. editorials/opinion pieces, letters, systematic reviews, and meta-analyses;
2. studies that reported utilities from proxies (e.g., reported by family member or doctor);
3. studies that obtained utility estimates from the literature, if there was not enough information on the derivation of utility, or if utility values were not reported;
4. studies that did not distinguish COPD from other types of obstructive pulmonary disease such as asthma or cystic fibrosis;
5. articles using utility values mapped from other reported quality-of-life studies;
6. studies that reported simulation-based utilities.

To minimize within-study correlation, especial effort was made to exclude studies using the same population and report multiple HSUV measures.

This study covers four COPD severity staging classifications: Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) [31], American Thoracic Society [32], European Respiratory Society [33,34], and British Thoracic Society [35,36] staging systems. All are based on the severity of airflow obstruction captured by spirometric examination, but differ according to the cutoff points evolved over time. An attempt was made to match similar levels of severity levels of above-mentioned staging systems with each other.

Modeling Studies

A second literature review captured reported EQ-5D–derived HSUV from COPD Markov modeling studies. The literature review has been conducted for articles that used, developed, or conducted a mathematical simulation model to describe COPD progress as a first outcome.

Studies meeting the following criteria were included:

1. model-based studies of COPD;
2. English-language studies;
3. input values for utility scores of COPD stages reported or the reference articles cited.

To evaluate the reference citations of COPD modeling research studies, all available modeling articles were reviewed. Hand searches and citation tracking were also conducted.

These systematic reviews followed MOOSE guidelines for observational studies [37].

Search Methods

The systematic literature review of utility values for COPD in each stage was part of a wider systematic review of economic evidence on COPD disease, related pharmacological and psychological interventions, and progression modeling for patients with COPD. The following electronic databases were searched for relevant articles: MEDLINE, EMBASE (for the period before 2014), Web of Science, CINAHL, ProQuest (including PsycINFO and 61 other databases), the Cochrane Library Database (which includes NHS Economic Evaluation Database, Health Technology Assessment Database, Cochrane Database of Systematic Reviews, and three other databases), International Society for Pharmacoeconomics and Outcomes Research, and Google Scholar. An attempt was made to find unpublished literature and to decrease the likelihood of publication bias [38], using dissertation abstracts, authors, and Web sites of key academic institutions such as the National Institute of Clinical Excellence, Canadian Cooperating Office for Health Technology Assessment, the Swedish Council on Technology Assessment in Health Care, the Health Economic Evaluations Database, and the Cost Effectiveness Analysis Registry at Tufts-New England Medical Centre.

The same electronic databases were searched for modeling studies.

A search strategy was used for MEDLINE database (Supplementary Material) and was adapted for other databases. Endnote X7.0 was used to download citations and to identify and extract duplicate studies.

Data Extraction and Management

The following variables were obtained from each citation: principal author, year of publication, clinical characteristics and demographic characteristics of patients, number and country of patients, study design, HSUV measure, and its estimate (mean and SD). In intervention studies—for example, randomized control trials—baseline characteristics were used to avoid the potential effect of the intervention on quality-of-life estimates. When a demographic or clinical factor split intervention groups, the entire number of the group was adapted where possible. For the modeling studies, results of sensitivity analysis for utility values were captured.

Assessment of study eligibility and extract of information from each study were carried out by two independent reviewers.

Data Analysis

To estimate a single utility score value for each COPD stage, meta-analysis was conducted. Utility value point estimates and 95% confidence intervals (CIs) were calculated and displayed in forest plots.

The command “metan” [39] was used to conduct meta-analysis and graph the result in a funnel plot, using Stata version 13.1. To account for anticipated study heterogeneity, random-effects models were used [40]. Heterogeneity among the studies was measured using I^2 statistics and 95% CI. If a study did not present enough data to calculate standard error, it was excluded.

Differences between the utility scores used in modeling studies and those in the meta-analysis were evaluated using an unpaired t test. Statistical significance was accepted at a P level of less than 0.05.

To investigate the impact of the estimated utility values derived from meta-analysis on the output of the COPD model, we estimated the relationship between changes in utility values and changes in the incremental cost-effectiveness ratios based