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A Systematic Review of Health Economics Simulation Models of Chronic Obstructive Pulmonary Disease

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ABSTRACT

Background: Many decision-analytic models with varying structures have been developed to inform resource allocation in chronic obstructive pulmonary disease (COPD). **Objectives:** To review COPD models for their adherence to the best practice modeling recommendations and their assumptions regarding important aspects of the natural history of COPD. **Methods:** A systematic search of English articles reporting on the development or application of a decision-analytic model in COPD was performed in MEDLINE, Embase, and citations within reviewed articles. Studies were summarized and evaluated on the basis of their adherence to the Consolidated Health Economic Evaluation Reporting Standards. They were also evaluated for the underlying assumptions about disease progression, heterogeneity, comorbidity, and treatment effects. **Results:** Forty-nine models of COPD were included. Decision trees and Markov models were the most popular techniques (43 studies). Quality of reporting and adherence to the guidelines were generally high, especially in more recent publications. Disease progression was modeled through clinical staging in most studies. Although most studies (n = 43) had incorporated some aspects of COPD heterogeneity, only 8 reported the results across subgroups. Only 2 evaluations explicitly considered the impact of comorbidities. Treatment effect had been mostly modeled (20) as both reduction in exacerbation rate and improvement in lung function. **Conclusions:** Many COPD models have been developed, generally with similar structural elements. COPD is highly heterogeneous, and comorbid conditions play an important role in its burden. These important aspects, however, have not been adequately addressed in most of the published models.

Keywords: chronic obstructive pulmonary disease, cost-effectiveness, discrete-event simulation, Markov models, modeling.

Introduction

Predicting the outcomes of alternative scenarios and policies is a central theme in many disciplines. Epidemiological projections, such as estimating the future prevalence of a given condition, can be used as a guide for policymakers for long-term planning. Predicting costs and health consequences associated with the adoption of competing health technologies informs technology adoption and resource allocation decisions. Challenges involved in such predictions include the availability of evidence from multiple sources, the need for long-term predictions beyond available data, and the requirement for translating evidence on intermediate outcomes to policy-relevant messages. Overcoming such challenges typically requires disease simulation and decision-analytic modeling. Given that such challenges prevail in almost all contexts in health care decision making, the use of decision-analytic modeling in medical decision making is considered inevitable [1].

The development and validation of a disease model is typically a highly complex process requiring several fundamental assumptions related to, for example, natural history, impact of the health technologies on natural history, choice of model structure, relevant time horizon for the analysis, and the outcomes of interest [2].The next step is typically parameterization through evidence synthesis. Although it is unlikely to have a general consensus among the investigators along the process, exploring and understanding the different decisions that investigators have made in the course of developing a disease model

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can inform and make more comprehensive the process of subsequent model development.

The disease of focus for the present study is chronic obstructive pulmonary disease (COPD), a progressive condition of the airways characterized by diminishing lung function and episodes of symptom worsening called exacerbations [3]. At present, COPD is estimated to be the fifth cause of death worldwide, but studies project that it will become the third cause of death globally by 2030 [4]. The significant economic and humanistic burden of COPD has caused many treatments and management strategies to emerge for prevention, diagnosis, and management of the disease [5,6]. Projection of the future burden of COPD and the requirement for economic evaluations of existing and emerging technologies have resulted in multiple COPD models. Understanding the general characteristics of such models, such as the target population, model structure, and type of questions answered, can provide future investigators with a systematic and broad view of the COPD modeling landscape.

In addition to the general features of the models, characterizing the COPD-specific assumptions made in such models can support future model development and decision analysis in terms of comprehensiveness. COPD is a remarkably heterogeneous disease [7], which suggests that the benefits of interventions can differ among different subgroups of individuals. In addition, the devastating impact of comorbid conditions in COPD is well recognized [8]. One other potentially important assumption is how the effect of pharmacological treatments ismodeled, because clinical trials have evaluated the impact of pharmacotherapy in terms of both change in the rate of lung function decline and change in the incidence of exacerbations. Finally, there are alternative choices for modeling COPD progression; some studies model disease progression directly through the continuum of lung function, whereas others model it indirectly by translating lung function decline to discrete clinical states defined by the Global Initiative for Obstructive Lung Disease (GOLD) grades [3].

The aim of this review was to synthesize the state of science in the field by systematically exploring the characteristics of COPD models. Our review considered adherence to the best practice modeling guidelines as well as the assumptions made in COPD models relating to specific aspects of the disease. We were interested in finding the areas of similarity as well as differences across published COPD models in search of opportunities for potential improvement in decision-analytic modeling in the field of COPD.

Methods

A systematic review was undertaken on the basis of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [9]. We performed a search in MEDLINE and Embase (completed on August 24, 2015) limited to articles in English. In addition, we performed manual searches on the reference lists of the included articles and consulted with experts for relevant publications. Details of the literature search are provided in Appendix I in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.08.003.

Studies that met the inclusion criteria were those that used a formal decision-analytic modeling approach to project the future burden of COPD or were studies that undertook a cost-effectiveness analysis of alternative interventions. Only studies with a primary focus on COPD were considered; therefore, publications considering COPD as an event or a complication of another condition were excluded.

Study selection was carried out in two phases. First, title and abstract screening was performed, independently and in duplicate, by the primary reviewer (Z.Z.) and then a secondary reviewer (T.C. or M.S.). Discrepancies between reviewers' findings were discussed and resolved through consensus. Second, full-text analysis was performed by the primary reviewer, who identified the final set of studies to be included in the analysis. A customized checklist was created to summarize key parameters of all simulation models. A second reviewer (A.K.) independently extracted data from a random selection (10%) of studies to ensure consistency in data extraction. Key information from the reviewed articles was extracted and categorized according to the following three groups: adherence to guidelines, model lineage (i.e., further development of a previously published model), and COPD assumptions.

General Characteristics and Adherence to Reporting Guidelines

We summarized the general characteristics of the models using a modified checklist that was initially based on a previously published study [10]. It included the target jurisdiction (country), authors, year of publication, type of model (models were classified according to published taxonomies [11], summarized in Table 1), intervention, type of population (static population, which is the evolution of a fixed cohort, and dynamic[or open] population, which incorporates arrival of new individuals during the study period), time horizon, cycle length (if applicable), perspective of the evaluation (e.g., third-party or societal), discount rate, how effect measure was modeled (if applicable), and whether indirect costs were included.

We also evaluated the adherence of models to the health economic modeling report guidelines: the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) [2].

Model Lineage

Often, disease models, once developed, are used for various purposes over time. This involves rounds of model expansion and revisions, generating various model versions based on the same model structure. Studying the evolution or lineage of such models over time provides another means for mapping the COPD modeling landscape. On the basis of statements made by authors and works cited in the articles, we mapped the lineage or history of the models.

Exploration of COPD-Specific Assumptions

We explored the COPD-specific elements of each model with a focus on the areas of active research in COPD, which were defined by the expert clinician of our team. The first criterion considered was COPD progression. This could be modeled in terms of transition either through severity stages (e.g., GOLD grade) or through continuous changes in lung function metrics (e.g., forced expiratory volume in 1 second [FEV_1]). Although GOLD grades are mainly based on FEV_1 cutoffs, a fixed transition rate across GOLD grades does not necessarily correspond to a fixed rate of FEV_1 decline. The second criterion was the impact of pharmacotherapy in terms of assumptions about the impact of treatment on lung function or exacerbation rate. Given that exacerbation is a function of COPD severity (lung function), modeling treatment effect on lung function indirectly affects exacerbation rates. Many studies, however, have reported the direct impact of pharmacotherapy on exacerbation rates, which might not necessarily be mediated through lung function. Furthermore, the assumptions regarding heterogeneity in the natural history of COPD were investigated. Studies were assessed in terms of whether they incorporated heterogeneity in model calculations and whether they reported results across subgroups. Finally, we determined whether COPD comorbidities were considered explicitly in the model.