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Health Policy Analysis

Assessing the Determinants of the Potential for Cost-Effectiveness Over Time: The Empirical Case of COPD

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ABSTRACT

Objectives: The objective of this study was to assess the potential for cost-effectiveness of new technologies for chronic obstructive pulmonary disease (COPD) over the period from 2001 to 2010. **Methods:** Lung function outcomes and drug prices were observed for a UK COPD population over the period from 2001 to 2010. Cost-effectiveness was assessed at regular intervals on the basis of an established cost-effectiveness model, and the maximum price a technology providing cure could achieve under the current cost-effectiveness rules was estimated. **Results:** The results of this study show that although the scope for clinical improvement in COPD was still considerable, during the 10 years studied, the potential for cost-effectiveness at each point in time was dependent on momentary market characteristics, such as the changing price of comparators and improvements in clinical effectiveness. As a result, the analysis demonstrates that the future cost-effectiveness of a technology in development depends on the manner pricing and clinical effectiveness evolve throughout time. **Conclusions:** Because any predictions will be short-lived and dependent on a number of uncertain factors, we conclude that producing accurate forecasts on the potential for cost-effectiveness of new therapies earlier during the development process is especially difficult under the current static cost-effectiveness framework.

Keywords: chronic obstructive pulmonary disease, cost-effectiveness, dynamic efficiency, pharmaceutical innovation, pharmaceutical policy, research and development.

Introduction

Policy Context

The use of a decision-making framework based on cost-effectiveness is intended to achieve efficiency in drug spending by requiring an acceptable and affordable cost per unit of incremental effect for a new drug compared with existing therapies. However, with price variation over time due to market competition, the launch of new drugs, or the entrance of generic products [1,2], the incremental clinical effectiveness required for any drug to be cost-effective will change. In addition, the minimum price at which a company can launch a drug will be affected by a number of factors, such as the level and cost of regulation, the cost of capital, the size of the target population, the effective patent time before competitors reach the market, or the expected speed of market introduction [3–5].

Throughout the drug development process, candidates for new drugs are traditionally subjected to a rigorous portfolio assessment exercise. The most viable molecules are selected on the basis of a range of factors such as the probability of regulatory success of the compound and clinical unmet need of the disease area and estimated return on investment. Because this process starts many years before the product enters the market, investment decisions in drug development are obviously surrounded by considerable uncertainty. If the expected returns accrued during the approximately 10 to 12 years of market exclusivity do not cover for the cost of development, the candidate drug will not be brought into development and resources will be placed elsewhere.

Contrasting with the dynamic nature of drug development, coverage and reimbursement decisions are increasingly based on a static notion of efficiency. In addition, contrarily to what happens in the drug development process, decisions are made at a single point in time. This has been suggested to cause a clash between the objectives of efficiently allocating available resources and fostering innovation in health care [6,7]. This study attempts to facilitate the discussion on the importance of cost-effectiveness in directing research in health care. It assesses how static cost-effectiveness rules may influence the dynamic environment of drug development, and examines the implications of

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taking static cost-effectiveness into account when developing drugs that will be valued and paid for.

Theoretical Background

This study tests empirically the assumptions underlying the framework proposed by Refoios Camejo et al. [6]. They suggest the existence of a physiologically defined clinical effectiveness ceiling for each disease area (E_D max), that is, a medical optimum from which health would not improve with the use of more health care. The maximum incremental clinical effectiveness (IE_d max) a new drug could attain over the effectiveness of existing standard care (E_c) if research and development resources were infinite is then defined by IE_d max $= E_D$ max $- E_c$. Previous studies [8] have used a similar approach to assess the effect of price reduction over time on the size of the clinical benefit necessary for a new drug to be considered cost-effective.

Funding systems based on cost-effectiveness judge a new technology as cost-effective when the incremental monetary benefit provided is expected to be greater than the incremental costs incurred by adopting a new technology d over the available alternative c. This means that a new technology will be approved to be used in the health system if the net monetary benefit (NMB) achieved by funding is greater than zero; that is, $NMB_d = (E_d - E_c)\times L - (P_d - P_c) > 0$, where L represents a general cost-effectiveness threshold defining the acceptable cost per unit of incremental benefit and which is used to monetize health-related benefits. Because, within the context of a restricted budget, the adoption of a new technology necessarily implies the withdrawal of other (less cost-effective) technologies, this threshold is also said to represent the minimum opportunity cost of funding a new technology, that is, the benefits forgone by disinvesting in displaced technologies. The use of a single cost-effectiveness threshold is also suggested to allow the prioritization across diseases attempting to signal the areas in which research may be socially preferable.

In the case in which all the benefits of innovation accrue to the producer and producer surplus is maximized, NMB is set to equal zero and the price is set so that $(P_d - P_c) = (E_d - E_c)\times L$. In this way, the maximum price premium (P_D max) warranting a positive decision when reaching E_D max can be computed at each time point by taking into consideration the price of the comparator (P_c) and the clinical effectiveness of standard care (E_c). While P_c will greatly depend on the market characteristics and the shape of the innovation curve in that particular disease area, which, in turn, is dependent on the timing of new products entering the market and the magnitude of the clinical effectiveness increment they may bring, IE_d max will tend to decrease over time because of incremental innovation. At an extreme and under the investment rules present in the drug development process, if the minimum possible launch price for a product to be considered a viable investment with a positive net present value (P_d min) is expected to be higher than the maximum price allowed by IE_d max, no more investment will be made in research and development in that particular disease area.

In this context, chronic obstructive pulmonary disease (COPD) was selected to test the proposed framework empirically because the maximum clinical effectiveness possible (E_D max) for the technologies can be adequately defined through diagnostic tests or the nonexistence of exacerbation episodes; the level of clinical effectiveness of standard care (E_c) is expected to have a direct relationship with drug usage; and confounding factors eventually affecting the estimation of E_c are relatively small or can be controlled for.

The Case of COPD

COPD is a lung-related chronic condition lasting over the course of a patient's life that primarily affects people with a history of smoking. Patients with COPD initially complain of breathlessness and may also have cough and increased sputum production, which tend to worsen over time. COPD is a major cause of morbidity and mortality worldwide, and current estimates of COPD prevalence in Europe are between 4% and 10% [9].

Lung function is essential for diagnosis and also an indicator of disease severity. Lung function impairment is measured through spirometry to derive values of forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1). Primary diagnosis criterion is a ratio of FEV_1 to FVC (FEV_1/FVC) smaller than 0.7 [10]. Lung function is often compared with the FEV_1predicted (FEV_1p) for a healthy person of similar age, gender, and body composition. The ratio between FEV_1 and FEV_1p, called forced expiratory volume in 1 second as a percentage of predicted (FEV_1%p), is used to determine COPD severity.

Since the late 1980s, a significant shift in the awareness of COPD has taken place. Previously, there was the widely held opinion that little could be done to treat patients with COPD, and spirometry was performed less frequently. The introduction of new pharmaceuticals together with other system-wide reforms, however, have been shown to bring benefits and contributed to change that view. In the particular case of the United Kingdom, COPD was included in the Quality & Outcomes Framework (QOF) incentive program for general practitioners introduced in 2004. Since then, a consistent move toward the routine collection of spirometry data in primary care became increasingly visible.

The treatment goal for COPD is now to prevent and control symptoms and reduce the frequency and severity of exacerbations [10]. Disease management is generally characterized by a stepwise approach depending on disease severity. More recently, newer treatments for COPD focus on an improved mode of action, for example, combining therapies into one inhaler and reducing the dosage frequency. Despite being a relatively recent area of research in its own right, the development of treatments for COPD has benefited from the knowledge acquired while researching medical technologies for other respiratory conditions. This is significant because innovation in treating respiratory diseases has also been achieved through the development of more efficient delivery systems.

Study Objectives and Scope

The objective of this study was to estimate the potential for cost-effectiveness of new technologies for COPD over time and assess how that is influenced by the evolution of clinical effectiveness, and the pricing pattern of available medical alternatives. The study illustrates how the real-life clinical effectiveness of existing standard care in the population being managed for COPD has changed over time. It subsequently uses the price of pharmaceutical standard care to estimate the maximum cost-effectiveness possible at different points in time and the higher price that a new technology providing cure could achieve under current cost-effectiveness rules when entering the market.

Rather than intending to test the clinical and cost-effectiveness of any particular technology, this study aimed at providing an overall medium-/long-term perspective of the evolving potential for cost-effectiveness in COPD. We then discuss the potential impact of these readings on the development of further technologies.

Methods

Lung function outcomes and prices of available drugs were observed between 2001 and 2010, and cost-effectiveness was estimated at yearly time points to reflect the prevailing prices and gap for clinical improvement. Extensive literature is available on the efficacy of available drugs in managing COPD within