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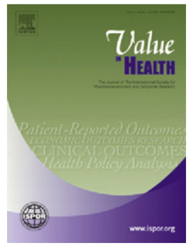

Quality of Life and Asthma Symptom Control: Room for Improvement in Care and Measurement

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ABSTRACT

Background: The recent Global Initiative for Asthma management strategy recommends achieving symptom control and minimizing the future risk of poor outcomes as priorities for asthma management. **Objective:** The objective was to quantify the association between symptom control and health-related quality of life in asthma. **Methods:** In a prospectively recruited random sample of adults with asthma, we ascertained symptom control and measured health-related quality of life using a generic (EuroQol five-dimensional questionnaire [EQ-5D]) and a disease-specific (Asthma Quality of Life Questionnaire) instrument, to estimate EQ-5D and five-dimensional Asthma Quality of Life Questionnaire (AQL-5D) utilities, respectively. We measured the adjusted difference in utilities across symptom control levels and calculated the loss of predictive efficiency due to aggregating multiple symptoms into one symptom control variable. **Results:** The final sample included 958 observations from 494 individuals (mean age at baseline 52.2 ± 14.5 years; 67.0% women). Asthma was symptomatically controlled, partially controlled, and uncontrolled in 269 (28.1%), 367 (38.3%), and 322 (33.6%) observations, respectively. A person with symptomatically uncontrolled asthma would gain 0.0512 (95% CI 0.0339–0.0686) in EQ-5D or 0.0802 (95% CI 0.0693–0.0910) in AQL-5D utilities by achieving symptom control. The loss of predictive efficiency was 55.4% and 27.6% for EQ-5D and AQL-5D utilities, respectively. **Conclusions:** Asthma symptom control status corresponds well with both generic and disease-specific quality-of-life measures. The trade-off, however, between ease of use and predictive power should be reconsidered in developing simplified measures of control. Our results have direct relevance in informing decision-analytic models of asthma and deducing the effect of interventions on quality of life through their impact on asthma control.

Keywords: asthma, observational studies, quality of life, regression analysis.

Introduction

Impairment due to asthma can have a substantial impact on quality of life [1]. Because there are no realistic options to completely prevent or cure asthma, the emphasis of current asthma management guidelines is to control the manifestations of the disease [2,3]. One of the most widely used measures of asthma control is the definition developed by the Global Initiative for Asthma (GINA). In the most recent version of the GINA management strategy, assessment of asthma control is divided into assessing *symptom control* and risk factors for future poor asthma outcomes [4]. This is a departure from the previous GINA strategy, which included both symptoms and lung function metrics in the definition of *clinical* control [5].

Given the central role of asthma control as a framework for the management of asthma, guidelines have emphasized the use of asthma control as a relevant outcome both in clinical practice and in research [3]. From a policy perspective, however,

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measuring the merits of asthma interventions will require mapping the causal relationships between asthma control and policy-relevant outcomes such as costs and quality of life. Estimating the impact of interventions on health-state utility values (utilities) enables quantification of their health impact in terms of quality-adjusted life-year (QALY) as the metric of choice for cost-effectiveness studies [6]. As such, estimates of change in utility as a result of change in asthma control can be of value in informing decision-analytic models of asthma.

Developing simple and easy-to-use measures of asthma control involves aggregating different metrics to calculate one or more global scores. In the case of GINA symptom control, the four domains with binary (yes/no) responses create 16 permutations, which are then reduced to a three-level symptom control variable. Such an aggregation inevitably results in loss of information. Evaluating the impact of information loss in terms of the efficiency of the GINA definition of symptom control in predicting policy-relevant outcomes will help researchers refine such measures. In the present study, we investigated such issues using the 2014 GINA definition of asthma symptom control as it relates to quality of life. The primary objective of this study was to quantify the gain in quality of life that can be achieved by achieving GINA symptom control in patients with symptomatically uncontrolled or partially controlled asthma. We pursued several secondary objectives: to estimate the loss of predictive efficiency by aggregating four symptom domains into a single symptom control variable, to evaluate the relative influence of individual symptom domains on quality of life, and to evaluate the impact of the removal of lung function measurement in the recent GINA definition on its association with quality of life.

Methods

Study Population

This study was based on data from the Economic Burden of Asthma, a prospective observational study aimed at measuring the economic and humanistic burden of asthma at the population level (University of British Columbia Human Ethics no. H10-01542). Details about the study have been described elsewhere [7,8]. Through random digit dialing in two census areas in British Columbia, Canada, the study recruited 618 individuals with self-reported, physician-diagnosed asthma. The census areas consisted of the Metro Vancouver and Okanagan regions (2011 populations of 603,502 and 179,830, respectively [9]); these areas were chosen to represent both urban and rural populations. Eligibility criteria also included having had at least one asthma-related encounter with the health care system in the past 5 years, not being pregnant or planning to become pregnant in the next 12 months, and planning to reside in the study area for the next 12 months. The follow-up time was 12 months, with visits scheduled every 3 months. At baseline and final visits, individuals underwent spirometry and responded to an asthma symptoms questionnaire, permitting the evaluation of asthma control according to both 2012 and 2014 GINA guidelines [2]. The final visit was generally around 1 year after entry; however, for participants who notified the investigators of their withdrawal, spirometry was performed in their last visit before withdrawal. The subsample for the present study included adults in whom both asthma control and quality of life had been measured at first and/or last visits.

Exposure

The main exposure was symptom control as defined by the 2014 GINA management strategy [4]. This definition is based on four domains, which focus on outcomes from the past 4 weeks, each taking a binary value (no = 0, yes = 1): daily symptoms (two or less vs. more), limitations of activities (none vs. any), nocturnal symptoms/awakening (none vs. any), and need for reliever or rescue treatment (two or fewer vs. more). The previous (2012) GINA management strategy defined clinical control (as opposed to symptom control) on the basis of the same symptom domains plus a fifth domain that is the ratio of forced expiratory volume in 1 second (FEV_1) to its predicted value (cutoff 80%) [5]. For the sake of brevity, we use the term *control* to refer to clinical control or symptom control, respectively, whenever the 2012 or 2014 versions of GINA management strategies are considered. In both versions, asthma is defined as uncontrolled if three or more of the domain values are positive, partially controlled if one or two values are positive, and controlled otherwise.

Outcomes

Individuals at baseline and all follow-up visits filled out a generic preference-based instrument (EuroQol five-dimensional questionnaire [EQ-5D], three-level version [10]), as well as the short version of the Asthma-related Quality of Life Questionnaire (mini-AQLQ [11]). We used the National Health and Nutrition Examination Survey reference standards for estimating predicted FEV_1 values [12]. Both EQ-5D and AQLQ responses were converted to health-state utility values (utilities). To derive EQ-5D utilities, we used the algorithm as described by Dolan et al. [13]. For AQLQ, we followed the two-step approach as described by Yang et al. [14]: first, the response levels were reduced from seven to five as proposed in Young et al. [15] and then the algorithm proposed by Yang et al. [14] was used to calculate five-dimensional Asthma Quality of Life Questionnaire (AQL-5D) utilities. Given that the latter weight is based on a UK sample, we also used UK tariffs for the EQ-5D to ensure comparability [13].

Statistical Analysis

All statistical analyses were performed in SAS (version 9.3, Carey, NC). Two-tailed *P* values at the 0.05 level were evaluated for statistical significance. The unit of observation in this study was a study visit resulting in concomitant assessment of both utilities and asthma control. Chi-square test for categorical variables and analysis of variance for continuous variables were used to examine the distribution of variables across control levels.

Adjusted analyses were based on fitting regression models that would associate utilities with asthma control, adjusting for potential confounding variables. Given that a proportion of individuals would report a utility value of 1, the assumptions of normally distributed regression residuals, required for inference in the conventional ordinary least squares (OLS) regression, would not be satisfied. We therefore used a two-part regression model, with logistic and OLS components [16]. The logistic component was fitted to model the impact of independent variables on the probability of having a utility of 1, and an OLS regression was fitted in the subset of individuals with a utility of less than 1 to model the linear effect of independent variables on utility values. We used generalized linear models with generalized estimating equations for both components to account for the clustering of observations (visits) within individuals [17]. The three-level GINA control variable entered the model as two dummy variables representing partially controlled and uncontrolled asthma with the reference being controlled asthma. Inference was made using parametric bootstrapping with 100 replications. For both components, we chose the following covariates as potential confounders: age at baseline visit, sex, income (high vs. low at the cutoff of Can $60,000 per year), education level (high [postsecondary education or higher] vs. low),