Original Article

Stability of Asthma Symptom Control in a Longitudinal Study of Mild-Moderate Asthmatics

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What is already known about this topic? The level of asthma symptom control can change within an individual over time because of intrinsic factors, such as change in asthma activity, or extrinsic factors, such as treatment.

What does this article add to our knowledge? This article examines the degree of stability of asthma symptom control within individuals and the variation in stability across individuals. The stability of symptom control has not previously been investigated as an independent clinical trait.

How does this study impact current management guidelines? This study may help practitioners identify patients who are likely to experience instability in symptom control based on their previous history of control; these patients may require closer monitoring.

BACKGROUND: Achieving and maintaining symptom control is a primary goal of asthma management. Although factors associated with the likelihood of achieving symptom control have been studied, there are unanswered questions on the stability of symptom control, that is, the tendency of individuals to remain at a given symptom control level over time.
OBJECTIVE: The objective of this study was to evaluate the stability of symptom control using a longitudinal cohort of mild-moderate asthmatics.
METHODS: Participants reported symptom control using the Global Initiative for Asthma criteria at 5 assessments during the 1-year follow-up period. We described variability in the stability of symptom control between individuals, and used a random-effects logistic regression model to evaluate the impact of a suite of factors on the stability of symptom control.
RESULTS: A total of 429 individuals (67% female, mean age 51.6) contributed 2141 study visits. Individuals varied from completely stable in symptom control (18% remained at the same control level in all 5 visits) to completely unstable (12% changed the control level between all subsequent visits). Only 4% of between-individual variation in the stability of symptom control was explained by the included exposures, and a secondary analysis indicated that the history of symptom control stability was the best predictor of current stability.
CONCLUSIONS: The tendency to remain at a given control level varies significantly among patients with asthma. Only a small fraction of this variability is explained by observable characteristics. In the absence of predictors, a previous history of symptom control stability is the best indicator of future stability and should be considered when monitoring symptom control. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;■:■-■)

Key words: *Asthma; Asthma control; Symptom control; Variability; Heterogeneity; Observational studies*

Asthma is an inflammatory disease of the airways that affects more than 300 million people worldwide.[1] It is associated with variable airflow obstruction that results in respiratory symptoms such as wheezing, coughing, breathlessness, and chest tightness.[2] These symptoms are typically intermittent and reversible but often vary in their intensity over time.[2]

A major target of asthma management is to achieve and maintain asthma control. The Global INitiative for Asthma (GINA) defines asthma control as the degree to which the manifestations of asthma are reduced or removed by treatment.[2] The GINA divides asthma control into 2 components: symptom control and the future risk of adverse outcomes such as exacerbations or lung function decline.[2] Asthma symptoms can be controlled in most cases with pharmacological interventions and by reducing exposure to triggers. However, despite the availability of treatments, asthma remains uncontrolled in a substantial fraction of the population.[3] Patients with uncontrolled asthma tend to have higher medical costs,[4] greater productivity loss,[5] and decreased quality of life.[6]

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Abbreviations used
CI- Confidence interval
FEV_1- Forced expiratory volume in 1 second
FVC- Forced vital capacity
GINA- Global initiative for asthma
MPR- Medication possession ratio
OR- Odds ratio
PEF- Peak expiratory flow
R^2- Coefficient of determination
SCQ- Self-administered Comorbidity Questionnaire

Previous studies have examined factors associated with the likelihood of achieving symptom control.[7-10] However, the concept of "stability" in symptom control has received less attention. The stability of a disease marker is fundamentally different from the nominal value of that marker, and different factors are expected to affect each construct. For example, variations in blood pressure and heart rate are well-recognized clinical characteristics with associated predictors and prognostic implications independent of their nominal values.[11,12]

To the best of our knowledge, the stability of asthma symptom control as a clinical characteristic has not yet been studied. Here, we define stability as the likelihood of a change in symptom control over time. We consider symptom control as stable in a period of time when the level of symptom control remains constant within that period, and unstable when the level of symptom control changes. Documenting heterogeneity and identifying factors associated with the stability of symptom control is of pathophysiological and clinical importance. High variability in symptom control could reflect differences in asthma treatments and environmental exposures, or it could be an innate feature of asthma. Identifying factors that affect the stability of symptom control may therefore improve our understanding of the disease mechanisms. It can also help identify subgroups of patients that might need closer monitoring of their symptom control over time.

The purpose of this study was to document between-individual variability in the stability of symptom control (objective 1) and to determine whether sociodemographic factors and clinical characteristics explain variation in the stability of control status (objective 2). We hypothesized that the stability of control varies between individuals, and that there are clinical, demographic, and environmental factors that are associated with the stability of symptom control.

METHODS

Study design and sample

We used data from the Economic Burden of Asthma study, a prospective, longitudinal cohort study (University of British Columbia Human Ethics #H10-01542) of patients with asthma. The details of this study have been described elsewhere.[13,14] Study inclusion criteria are explained in Text E1, available in this article's Online Repository at www.jaci-inpractice.org. A total of 618 individuals were recruited and followed for 12 months with visits scheduled at 3-month intervals, resulting in 5 visits for individuals who completed the study (data from additional medical visits outside of the study visits were not included in this analysis). We considered all participants who were not hospitalized or admitted to the intensive care unit for an asthma-related event during or in the year before the start of the study as having mild-moderate asthma. Severe asthma cases were excluded because there were very few of them in the original sample and also because we believe different mechanisms might affect the stability of symptom control in these individuals. The subsample for this analysis included adult ($\geq$19 years) participants with mild-moderate asthma, having observations of control status from at least 2 consecutive visits, and having complete information for all studied exposures with the exception of income on those visits. Missing observations of income were included in the subsample as a separate category.

Outcome and exposure variables

Outcome: stability of symptom control. The GINA criteria were used to classify participants as uncontrolled, partially controlled, or controlled at each visit based on whether they had experienced daytime asthma symptoms more than twice per week, limited activity, nocturnal symptoms, or the need for rescue treatment more than once per week during the previous 4 weeks.[2] GINA-defined symptom control is shown to be well correlated with patient-reported outcomes.[6]

The observation unit for this analysis was the change of symptom control status between consecutive visits (1: change [unstable transition], 0: no change [stable transition]). This resulted in a maximum of 4 observations of the stability of symptom control for participants with complete follow-up. Our sample included 4 individuals with 3 observations of stability (4 visits); these participants were included in all analyses unless otherwise noted. The definition of stability was agnostic to the direction of change in control status to enable inference on stability independent of the likelihood of improvement in the level of control (as opposed to previous studies of symptom control[9,15]). Therefore, observations of stable asthma control included individuals who maintained uncontrolled, partially controlled, or controlled asthma between consecutive visits. In the main analysis, the definition of stability was also agnostic to the magnitude of change (eg, transition from controlled to uncontrolled and from controlled to partially controlled were both coded as unstable [value of 1]). However, stability was redefined as a 3-level ordinal variable in a sensitivity analysis to capture the magnitude of change (a value of 2 represented a change from uncontrolled to controlled, or vice versa).

Exposure variables. We evaluated the association between the stability of symptom control and multiple variables representing the sociodemographic status of participants and their clinical characteristics. At baseline, participants reported their age, sex, ethnicity, education, annual household income, and when they were first diagnosed with asthma. We also recorded their smoking status and history (measured in pack-years), the duration of time they worked in a "dusty job," and the number of allergens that triggered their asthma symptoms. We used the meteorological seasons to categorize the date of each of the visit transitions as winter, spring, summer, or fall (according to the date of the later visit). Participants reported the number of months and the number of days per week they took medications for their asthma during the 3 months before each follow-up visit (questionnaire in Figure E1, available in this article's Online Repository at www.jaci-inpractice.org). These data were converted to the medication possession ratio (MPR), which indicates the proportion of total days in which controller medications were available to the participant.[16] A list of the medications used to assess MPR is included in Table E1 (available in this article's Online Repository at www.jaci-inpractice.org). Treatment intensity was classified as low if MPR was less than 80% and high if MPR was