Ann Allergy Asthma Immunol 117 (2016) 251–257

Contents lists available at ScienceDirect

Exploring asthma control cutoffs and economic outcomes using the Asthma Control Questionnaire

Patrick W. Sullivan, PhD [*]; Gary Globe, PhD [†]; Vahram H. Ghushchyan, PhD [‡,§]; Jonathan D. Campbell, PhD [‡]; Bruce Bender, PhD [¶]; David J. Magid, MD, MPH [‖]

[*] Regis University School of Pharmacy, Denver, Colorado
[†] Amgen Inc, Thousand Oaks, California
[‡] Center for Pharmaceutical Outcomes Research, Department of Clinical Pharmacy, University of Colorado, Aurora, Colorado
[§] American University of Armenia, Yerevan, Armenia
[¶] Department of Pediatrics, National Jewish Health, Denver, Colorado
[‖] Institute for Health Research, Kaiser Permanente Colorado, Denver, Colorado

ARTICLE INFO

Article history:
Received for publication April 18, 2016.
Received in revised form June 1, 2016.
Accepted for publication July 15, 2016.

ABSTRACT

Background: Understanding the effect of worsening asthma control on expenditures and health resource utilization (HRU) is important.
Objective: To explore the association of economic outcomes with asthma control cutoffs and longitudinal changes on the Asthma Control Questionnaire 5 (ACQ-5).
Methods: The Observational Study of Asthma Control and Outcomes was a survey of patients with persistent asthma who were patients of Kaiser Colorado, including claims-based HRU. Patients completed the ACQ-5 three times during 1 year between April 2011 and June 2012. The ACQ-5 cutoffs that indicated control were assessed in cross-sectional analyses. Longitudinal changes in control were explored: controlled (ACQ-5 score <0.75), indeterminate (ACQ-5 score 0.75 to <1.5), not well controlled (ACQ-5 score 1.5 to <3.0), and very poorly controlled (ACQ-5 score ≥3.0). Analyses used generalized linear models with log link (expenditures) and negative binomial regression (HRU).
Results: There were 6,666 completed surveys (1,799 individuals completed all 3 survey waves). In the cross-sectional analyses, compared with an ACQ-5 score less than 0.5, individuals with ACQ-5 scores of 4 to 4.5 incurred 7.2 times the number of oral corticosteroid prescriptions, 4.3 times the number of emergency department visits, 6 times the number of inpatient visits, 10.4 times the number of asthma-specific emergency department visits, 4.58 times the number of asthma-specific inpatient visits, and $2,892 more in all-cause and $1,877 in asthma-specific expenditures during 4 months. In the longitudinal change analyses, individuals who improved from an ACQ-5 of 3.0 or greater to less than 0.75 incurred $6,023 less in asthma-specific expenditures during 4 months than those remaining at an ACQ-5 score of 3.0 or higher.
Conclusion: Results provide preliminary economic data on possible control cutoffs for the ACQ-5. Improving asthma control over time may result in significant savings that may justify financial investments designed to improve control.

Introduction

Asthma guidelines have focused on maintaining and improving asthma control as the goal of therapy and have categorized control into 3 levels: controlled or well controlled, partially controlled or not well controlled, and uncontrolled or very poorly controlled.[1,2] Several instruments have been developed to measure asthma control. One example, the Asthma Control Questionnaire (ACQ) has been used extensively as a standardized measure[3] and has been designated as a core measure for research supported by the National Institutes of Health in adults.[4] Developers have conducted investigations to determine the cutoff points of the ACQ that correspond to different levels of control. Established cutoffs include controlled asthma (ACQ score ≤0.75) and uncontrolled asthma (ACQ score ≥1.5).[5] There is no clear evidence for the ACQ score cutoff to distinguish between not well controlled and very poorly controlled corresponding to the guideline-based levels above.[6]

Reprints: Patrick W. Sullivan, PhD, Regis University School of Pharmacy, 3333 Regis Blvd, Building H28, Denver, CO 80221; E-mail: psulliva@regis.edu.
Disclosures: Dr Sullivan reported receiving research grants from Amgen Inc. Dr Globe reported being an employee of Amgen Inc. No other disclosures were reported.
Funding Sources: This study was funded by a research grant from Amgen Inc.

http://dx.doi.org/10.1016/j.anai.2016.07.020
1081-1206/

Economic outcomes are an important part of optimizing asthma treatment given the reality of limited financial resources. According to the Global Initiative for Asthma, the main goal of asthma treatment is to achieve control and reduce risk of future exacerbations with regard to the cost of treatment.[2] To understand the true effect of treatment, it is imperative to comprehensively understand the economic effect of changes in asthma control. A promising new asthma management program or intervention may result in improved control, but is it financially viable? Knowledge of the economic effect of improving asthma control is essential to answering this question.

Asthma results in increased health resource utilization (HRU) and expenditures.[7,8] In particular, poorly controlled asthma has a significant negative effect on HRU and expenditures compared with adequately controlled asthma, and patients with the most severe disease account for most of the cost.[9–12] Increasing scores (worsening asthma control) on the ACQ-5 (a 5-item patient-reported questionnaire about asthma symptoms) are strongly associated with increased HRU, expenditures, and risk of exacerbations in cross-sectional analyses of a general population of individuals with persistent asthma.[13] However, little is understood about the association between clinical cutoff points of asthma control and economic outcomes. In addition, previous research on the economic effect of asthma control has been based on cross-sectional associations not longitudinal changes over time. Cross-sectional associations do not incorporate within-person improvement or deterioration over time. Given limited longitudinal estimates, most cost-effectiveness studies are forced to assume that cross-sectional associations are good proxies of actual longitudinal changes. Because all asthma interventions aim to improve control over time, longitudinal analyses are the most accurate means of estimating their effect. The purposes of this research are to explore the association of economic outcomes with cutoff points in asthma control via the ACQ-5 and to quantify the economic effect of changes in control level over time (ie, from very poorly controlled to controlled).

Methods

Data Source

The Observational Study of Asthma Control and Outcomes (OSACO) was a prospective survey and retrospective claims-based analysis of patients with persistent asthma 12 years or older who where patients of Kaiser Permanente of Colorado (KPCO).[13] Eligible patients were sent surveys during 3 waves during 1 year between April 2011 and June 2012. The survey included questions on asthma control (ACQ-5), smoking status, sex, family income level, race, educational attainment, and ethnicity.

HRU and expenditures from the KPCO administrative and claims data were combined into 4-month panels (2 months before and 2 months after survey completion) with 3 waves of surveys, resulting in three 4-month panels in 1 year. For example, total expenditures for wave 1 were calculated as the sum of all expenditures incurred during the 2 months before and the 2 months after completion of the first survey. Although actual HRU was obtained directly from the KPCO administrative and claims data, expenditures associated with each utilization event were imported from an exogenous data source, which is more representative of the cost of typical care in the United States. KPCO offers prepaid health insurance and owns its own clinics and thus uses proprietary internal billing and costing methods atypical of other health insurance organizations. Expenditure data were derived from an exogenous commercial claims database. Each KPCO utilization event (eg, office visit or intravenous medication administered in the emergency department [ED]) was matched in by the respective billing code (*Current Procedural Terminology* code) and place of service; then the mean amount paid was used to represent expenditures per event in the KPCO data. Expenditure data included the cost to the health plan and copayments.

Asthma Control

Asthma control was assessed in the survey by the inclusion of the ACQ-5, a 5-item patient-reported questionnaire about asthma symptoms. The questions are equally weighted, and the ACQ score is the mean of all questions, with the final score between 0 (totally controlled) and 6 (severely uncontrolled). The minimum clinically important difference of the ACQ has been suggested to be a change or difference in score of 0.5.[14] The ACQ developers have estimated that the optimal cutoff to be confident that a patient has well-controlled asthma is 0.75.[5] The authors also recommend using a cutoff of 1.5 to be confident that the patient has poorly controlled asthma. Other authors have estimated the cutoff between controlled and poorly controlled asthma to be 0.83 for the ACQ without lung function testing.[15] These authors also suggest that an ACQ score between 0.83 and 1.5 indicates some level of control and recommend 1.5 as a hard cutoff for poorly controlled asthma.

Statistical Analysis

Cross-sectional analyses

On the basis of previously published information, the following ACQ-5 cutoffs were explored in the cross-sectional analyses: (1) ACQ-5 categories cut by 0.5 (0–0.5, 0.5–1, 1–1.5, …, 4.5–5, >5); and (2) single cutoff to differentiate controlled and poorly controlled asthma (0.75, 0.83, and 1.5). Unadjusted means (SDs) were calculated across ACQ-5 levels cut by 0.5. For adjusted analyses, HRU measures were regressed on ACQ-5 score categories using negative binomial models that controlled for wave and group fixed effects, age, sex, family income level, race, educational attainment, ethnicity, and smoking status. To address the skewed and censored characteristics of expenditure data, adjusted analyses of expenditures used generalized linear models with log link controlling for wave and group fixed effects, age, sex, family income level, race, educational attainment, ethnicity, and smoking status. The logarithm of expected medical expenditures was regressed on ACQ-5 score categories with a gamma distribution assumed for the error term. The monthly health care inflation index was used to express all expenditures in 2013 dollars. Results of adjusted regression analysis of asthma-specific health care expenditures and ACQ-5 scores were visually presented to explore potential cutoff points for the ACQ-5.

Longitudinal change analyses

Analyses were also conducted to examine the effect of changes in asthma control over time on HRU and expenditures. Asthma control was separated into controlled (ACQ-5 score <0.75), indeterminate (ACQ-5 score 0.75 to <1.5), not well controlled (ACQ-5 score 1.5 to <3.0), and very poorly controlled (ACQ-5 score ≥3.0). All possible changes from one wave to the next were categorized and included as independent variables in the regressions (please see Table 4 for an example of all possible change categories). The dependent variable was the change in HRU or expenditures, regressed on the aforementioned categorical independent variables, controlling for wave change (1 to 2 or 2 to 3) and group, age, sex, family income level, race, educational attainment, ethnicity, and smoking status. Ordinary least squares regression analysis was used for the change in expenditures and HRU because the characteristics of the change in expenditure and HRU data does not exhibit the same statistical properties that require the use of generalized linear models or negative binomial regression (as was used in the cross-sectional analysis of expenditure and HRU data).

Results

Cross-sectional Analyses

Unadjusted HRU and expenditures by ACQ-5 scores cut by 0.5 are presented in Table 1. All measures of HRU and expenditures increased with increasing ACQ-5 scores. There were few individuals with ACQ-5 scores greater than 4.5, and estimates are much less consistent for these categories. Individuals with ACQ-5 scores between 4 and 4.5 filled 1.4 prescriptions for short-acting β-agonists (SABAs), had 3 outpatient visits (1.1 with asthma diagnosis), and incurred $7,298 (all-cause) and $4,108 asthma-specific expenditures in 4 months.

Table 2 gives the adjusted results for different cut points that indicate poorly controlled asthma, controlling for sociodemographic characteristics and smoking status. All 3 cut points were statistically significantly associated with higher measures of HRU and expenditures except for inpatient visits. Individuals with ACQ-5 scores of 1.5 or higher had 2.3 times the expected number of oral corticosteroid prescriptions, 1.86 times the expected number of SABA prescriptions, and 2.3 times the expected number of asthma-specific ED visits in 4 months than individuals with ACQ-5 scores less than 1.5. They also incurred $795 more in all-cause health care expenditures during 4 months ($463 asthma specific).

Adjusted results across more granular categories of ACQ-5 scores are presented in Table 3. Individuals with ACQ-5 scores of 4 to 4.5 incurred 7.2 times the expected number of oral corticosteroid prescriptions than those with ACQ-5 scores less than 0.5. Likewise, they incurred 4.3 times the expected number of ED visits, 6 times the expected number of inpatient visits, 10.4 times the expected number of asthma-specific ED visits, and 4.58 times the expected number of asthma-specific inpatient visits. Individuals with ACQ-5 scores of 4 to 4.5 incurred $2,892 more in all-cause and $1,877 in asthma-specific health care expenditures during 4 months compared with those with ACQ-5 scores less than 0.5.

Figure 1 presents the results of the regression analysis of asthma-specific health care expenditures by ACQ-5 category (cut by 0.5). There seems to be a natural break for ACQ-5 scores above the 1.5 to 2 category and another break above ACQ-5 scores of greater than 3 to 3.5. This information was used in combination with previous publications to inform the categorizations of uncontrolled asthma in the longitudinal change analysis.

Longitudinal Change Analyses

Unadjusted mean and median changes in asthma-specific expenditures and corresponding numbers of individuals are presented in Table 4. In adjusted longitudinal regressions, changes in asthma control over time were statistically significantly associated with changes in asthma-specific health care expenditures (Table 5). The reference group is individuals whose asthma remained very poorly controlled over time (eg, from ACQ-5 score $\geq$3.0 in wave 1 to ACQ-5 score $\geq$3.0 in wave 2). Individuals who improved from ACQ-5 $\geq$ 3.0 to ACQ-5 $<$ 0.75 incurred $6,023 less in asthma-specific health care expenditures during 4 months than individuals who remained at ACQ-5 $\geq$ 3.0. Similarly, individuals who improved from an ACQ-5 $\geq$ 3.0 to ACQ-5 1.5-3.0 incurred $3,323 less in asthma-specific health care expenditures during 4 months than individuals who remained at ACQ-5 $\geq$ 3.0. In addition, individuals who started with better control than the reference group and whose asthma control remained stable or improved over time incurred lower asthma-specific health care expenditures. For example, individuals whose asthma remained controlled (eg, ACQ-5 <0.75 in both wave 1 and wave 2) incurred $2,244 less in asthma-specific health care expenditures than those who continued to have very poorly controlled asthma (ACQ-5 $\geq$3.0) over time. Individuals whose asthma remained not well controlled

Table 1
Unadjusted Health Care Resource Utilization and Expenditures by ACQ-5 Score (per 4 Months, Cross-Sectional)

Variable	ACQ-5 score										
	0–0.5 (n = 2,371)	0.5–1 (n = 1,283)	1–1.5 (n = 1,345)	1.5–2 (n = 639)	2–2.5 (n = 535)	2.5–3 (n = 224)	3–3.5 (n = 153)	3.5–4 (n = 38)	4–4.5 (n = 23)	4.5–5 (n = 6)	>5 (n = 5)
No. of prescriptions, mean (SD)											
Oral prednisone	0.11 (0.43)	0.1 (0.39)	0.15 (0.48)	0.21 (0.57)	0.22 (0.57)	0.33 (0.76)	0.54 (0.92)	0.47 (0.8)	0.74 (1.01)	0.5 (0.84)	0.4 (0.55)
SABA	0.31 (0.59)	0.48 (0.75)	0.61 (0.94)	0.77 (0.96)	0.78 (0.96)	0.92 (1.28)	1.2 (1.31)	1.53 (1.18)	1.39 (1.31)	0.83 (0.75)	1.8 (0.84)
No. of visits, mean (SD)											
All cause											
ED	0.04 (0.23)	0.06 (0.3)	0.07 (0.39)	0.12 (0.51)	0.12 (0.41)	0.12 (0.45)	0.12 (0.37)	0.11 (0.31)	0.26 (0.62)	NR	NR
Inpatient	0.02 (0.14)	0.02 (0.16)	0.02 (0.15)	0.03 (0.19)	0.03 (0.2)	0.04 (0.25)	0.07 (0.34)	0.08 (0.36)	0.13 (0.34)	NR	NR
Outpatient	2.06 (2.73)	2.04 (2.81)	2.1 (3.14)	2.43 (3.71)	2.69 (4.5)	2.35 (3.07)	2.97 (5.5)	2.5 (2.72)	2.96 (3.59)	2.83 (3.25)	4.8 (2.59)
Asthma specific											
ED	0.02 (0.15)	0.03 (0.19)	0.04 (0.3)	0.07 (0.39)	0.07 (0.32)	0.08 (0.34)	0.08 (0.29)	0.08 (0.27)	0.22 (0.6)	NR	NR
Inpatient	0.02 (0.13)	0.02 (0.15)	0.02 (0.14)	0.02 (0.16)	0.03 (0.2)	0.04 (0.25)	0.06 (0.33)	0.08 (0.36)	0.09 (0.29)	NR	NR
Outpatient	0.34 (0.64)	0.37 (0.66)	0.4 (0.72)	0.48 (0.83)	0.53 (0.9)	0.54 (0.85)	0.82 (1.18)	0.63 (0.85)	1.09 (1.24)	0.67 (1.63)	0.6 (0.55)
Expenditures											
All cause											
Mean (SD)	3,083 (6,996)	3,305 (6,961)	3,400 (7,183)	3,864 (8,519)	4,158 (8,609)	4,377 (9,731)	5,394 (12,344)	4,725 (6,130)	7,298 (12,834)	3,959 (3,333)	4,682 (2,494)
Median	1,213	1,249	1,345	1,521	1,692	1,618	1,809	2,841	2,748	3,551	5,359
Asthma specific											
Mean (SD)	1,223 (4,258)	1,320 (4,398)	1,551 (4,862)	1,433 (4,068)	2,004 (6,847)	2,424 (8,417)	2,907 (10,758)	2,707 (5,613)	4,108 (9,243)	1,227 (955)	1,244 (1,062)
Median	496	513	496	557	569	575	693	870	1216	951	1,117

Abbreviations: ACQ-5, Asthma Control Questionnaire 5; ED, emergency department; NR, insufficient sample size or no events reported; SABA, short-acting β-agonist.

Table 2
Adjusted Mean Health Care Resource Utilization and Expenditures by ACQ-5 Score Cut Points (per 4 Months, Cross-sectional)[a]

Variable	ACQ-5 score					
	≥0.75		≥0.83		≥1.5	
	IRR or mean (95% CI)	*P* value	IRR or mean (95% CI)	*P* value	IRR or mean (95% CI)	*P* value
No. of prescriptions						
Oral prednisone	1.90 (1.58–2.28)	<.01	2.07 (1.74–2.48)	<.01	2.31 (1.95v2.73)	<.01
SABA	1.92 (1.76–2.10)	<.01	1.87 (1.71–2.04)	<.01	1.86 (1.71–2.03)	<.01
No. of visits						
All cause						
ED	1.68 (1.26–2.24)	<.01	1.75 (1.31–2.35)	<.01	1.81 (1.46–2.26)	<.01
Inpatient	1.22 (0.88–1.69)	.23	1.20 (0.87–1.66)	.26	1.35 (0.93–1.97)	.11
Outpatient	1.11 (1.02–1.21)	.02	1.17 (1.07–1.28)	<.01	1.24 (1.12–1.38)	<.01
Asthma specific						
ED	2.41 (1.63–3.57)	<.01	2.40 (1.63–3.53)	<.01	2.31 (1.74–3.06)	<.01
Inpatient	1.28 (0.90–1.82)	.17	1.23 (0.87–1.74)	.24	1.33 (0.89–2.00)	.16
Outpatient	1.36 (1.24–1.49)	<.01	1.39 (1.27–1.53)	<.01	1.51 (1.36–1.67)	<.01
Expenditures						
All cause	562 (163–961)	.01	597 (191–1,004)	<.01	795 (356–1,234)	<.01
Asthma specific	433 (189–677)	<.01	419 (173–666)	<.01	463 (197–729)	<.01

Abbreviations: ACQ-5, Asthma Control Questionnaire 5; CI, confidence interval; ED, emergency department; IRR, incident rate ratio.
[a]Regression of outcome on ACQ-5 category controlling for wave and group fixed effects, age, sex, family income level, race, educational attainment, ethnicity, and smoking status (reference is ACQ-5 score less than cutoff).

(eg, 1.5≤ACQ-5≤3.0 in wave 1 and wave 2) incurred $2,530 less than those whose asthma remained very poorly controlled.

The remaining results of the longitudinal analysis of HRU and expenditures are presented in the eAppendix and discussed in the Discussion section below. Changes in all-cause expenditures did not reveal statistically significant association with the asthma control change categories. Measures of asthma-specific HRU were statistically significantly associated with some longitudinal changes in asthma control (eAppendix), but all-cause HRU was not statistically significant across most categories of change.

Discussion

This research suggests that there is an economic benefit to improving asthma control over time in a general population. For example, improving patients progressing from very poorly controlled to controlled asthma resulted in a savings of $6,000 (4-month cost). In addition, this research reveals a strong association between greater HRU and expenditures and common cutoff points for poor control on the ACQ-5. It also provides preliminary information about which ACQ-5 points may be relevant cutoffs for economic outcomes.

Strengths of this research include the use of observational, real-world data in a general population of patients with persistent asthma, which results in more representative costs, patterns of use, and asthma control than specialty or clinical trial populations. Inclusion of a standardized measure of asthma control (ACQ-5) with real-world data in a longitudinal study design provides a unique opportunity to examine changes in asthma control and economic outcomes over time. Asthma is a chronic but sporadic disease. Inclusion of multiple survey points across 1 year enabled longitudinal analyses of asthma control, use, and costs.

Previous cross-sectional research found that poor asthma control is associated with greater HRU and expenditures in general populations using proxy measures of control[9,10,12] and in clinical trial populations of those with severe asthma using validated measures of control.[16,17] The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study indicated that asthma costs increased in direct proportion to the number of asthma control problems on the multilevel ATAQ control

Table 3
Adjusted Mean Health Care Resource Utilization and Expenditures by ACQ-5 Score (per 4 Months, Cross-sectional)[a]

Variable	ACQ-5 score									
	0.5–1	1–1.5	1.5–2	2–2.5	2.5–3	3–3.5	3.5–4	4–4.5	4.5–5	>5
No. of prescriptions										
Oral prednisone	0.99[b] (0.13)	1.46 (0.18)	2.02 (0.28)	2.09 (0.31)	3.22 (0.58)	5.26 (1.02)	3.87 (0.96)	7.19 (1.91)	5.22 (3.38)	3.38 (1.46)
SABA	1.52 (0.09)	1.84 (0.11)	2.36 (0.16)	2.37 (0.17)	2.64 (0.28)	3.33 (0.32)	4.51 (0.65)	4.17 (0.84)	2.46 (0.81)	4.68 (0.9)
No. of visits										
All cause										
ED	1.4[b] (0.24)	1.62 (0.35)	2.39 (0.52)	2.35 (0.44)	2.27 (0.67)	2.04 (0.6)	1.73[b] (0.83)	4.31 (1.86)	NR	NR
Inpatient	1.27[b] (0.31)	1.12[b] (0.26)	1.2[b] (0.37)	1.18[b] (0.38)	1.63[b] (0.8)	2.63 (1.14)	3.88[b] (2.78)	5.96 (3.08)	NR	NR
Outpatient	1.02[b] (0.05)	1.06[b] (0.06)	1.18 (0.08)	1.34 (0.12)	1.18[b] (0.11)	1.48 (0.2)	1.21[b] (0.23)	1.61[b] (0.45)	1.61[b] (0.73)	NR
Asthma specific										
ED	1.44[b] (0.34)	2.15 (0.59)	3.03 (0.89)	3.36 (0.85)	4.05 (1.39)	3 (1.1)	2.89 (1.51)	10.38 (5.61)	NR	NR
Inpatient	1.32[b] (0.35)	1.2[b] (0.3)	1.08[b] (0.37)	1.34[b] (0.44)	1.85[b] (0.93)	2.6 (1.24)	4.38 (3.09)	4.48 (2.96)	NR	NR
Outpatient	1.09[b] (0.07)	1.21 (0.07)	1.39 (0.11)	1.58 (0.12)	1.68 (0.19)	2.65 (0.31)	1.85 (0.45)	3.13 (0.8)	2.21[b] (1.28)	2.23[b] (1.48)
Expenditures										
All cause	384[b] (267)	401[b] (271)	634[b] (342)	996 (334)	1,288 (550)	1,583 (617)	1,990 (896)	2,892 (1,059)	NR	NR
Asthma specific	175 (169)	344 (167)	202 (175)	646 (226)	962 (357)	1,068 (391)	1,468 (632)	1,877 (612)	NR	NR

Abbreviations: ACQ-5, Asthma Control Questionnaire 5; ED, emergency department; NR, insufficient sample size or no events reported; SABA, short-acting β-agonist.
[a]Data are presented as incident rate ratios or mean (SD). Regression of outcomes on ACQ-5 categories controlling for wave and group fixed effects, age, sex, family income level, race, educational attainment, ethnicity, and smoking status (reference is ACQ-5 scores of 0–0.5).
[b]$P > .05$ (not statistically significant).

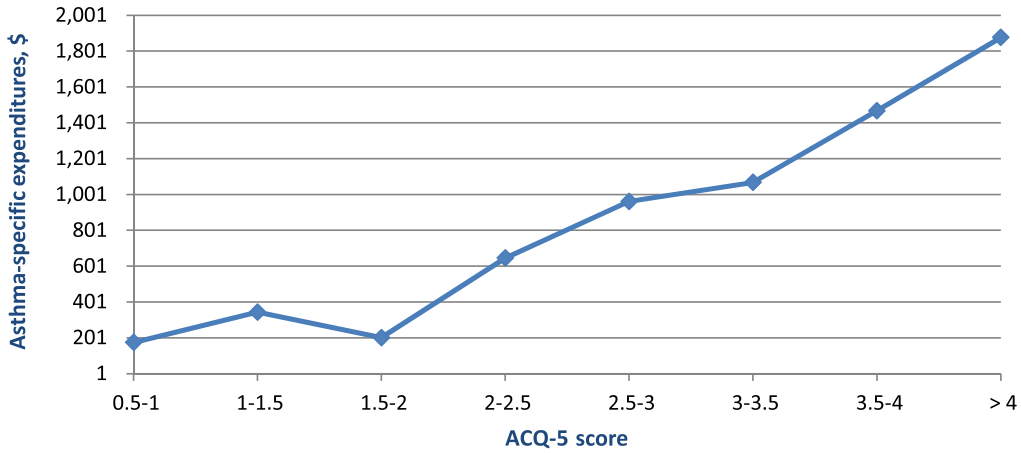

Figure 1. Adjusted asthma-specific health care expenditures by Asthma Control Questionnaire 5 (ACQ-5) score (cut by 0.5, cross-sectional). Results from regression analysis of expenditures on ACQ-5 score categories controlling for wave and group fixed effects, age, sex, family income level, race, educational attainment, ethnicity, and smoking status (reference category is ACQ-5 score of 0–0.5).

instrument in patients with severe asthma.[16] Previous OSACO research found that greater HRU and expenditures are associated with worse control using the validated ACQ-5 in cross-sectional analyses in a general population.[13] However, there are 2 developments driven by recent guidelines related to asthma control where evidence of economic outcomes has been lacking. The current study provides novel insight into how economic outcomes correlate with recommended asthma control levels (controlled, not well controlled, and very poorly controlled) over time. In particular, the results of this research explore economic outcomes associated with cutoffs in a validated asthma control measure (ACQ-5) corresponding to these levels. In addition, the principal goal of treatment is improvement of control over time. Our results provide quantification of changes in expenditures associated with changes in control levels over time.

Evidence from these economic outcomes is consistent with the accepted clinical cutoff for controlled asthma. Juniper et al[5] published evidence to suggest that an ACQ-5 score lower than 0.75 corresponds to controlled asthma, with ACQ-5 scores of 0.75 to less than 1.5 indeterminate. In adjusted analyses using a single crude separation between controlled and uncontrolled asthma, Table 2 reveals that all 3 previously published cutoffs (0.75, 0.83, and 1.5) were statistically significant in distinguishing HRU and expenditure outcomes except for inpatient visits. However, this combines all uncontrolled asthma into 1 category.

The more granular analyses provide more insight into the cutoff for controlled asthma. Results suggest that an ACQ-5 scores less than 0.5 would not be a better cutoff of controlled asthma for economic outcomes. The coefficient for ACQ-5 scores of 0.5 to 1 was not statistically significantly different than for ACQ-5 scores of 0 to 0.5 for any HRU or expenditure outcomes except SABA use (Table 3). In contrast, when comparing ACQ-5 scores of 0.75 to 1.5 and ACQ-5 scores of 0 to 0.75 in similar regressions, the coefficients were statistically significant for most HRU and expenditure outcomes compared (data not shown). Taken together, these results support 0.75 as a cutoff for controlled asthma with respect to economic outcomes.

There were several economic trends consistent with previously accepted clinical cutoffs in ACQ-5 scores in the results of the cross-sectional analyses. For example, Figure 1 presents results of adjusted regression analyses of asthma-specific health care expenditures by ACQ-5 category (cut by 0.5). (Adjusted analyses are likely more appropriate because they better isolate the effect

Table 4
Unadjusted Mean Change in Asthma-Specific Health Care Expenditures (per 4 Months, Longitudinal)

ACQ-5 change category[a]	No. of patients	Median change	Mean change	SD
ACQ < 0.75 to ACQ < 0.75	1,398	0	195	5,185
ACQ < 0.75 to 0.75 ≤ ACQ < 1.5	361	0	97	5,652
ACQ < 0.75 to 1.5 ≤ ACQ < 3.0	100	296	1,322	4,213
ACQ < 0.75 to ACQ ≥ 3.0	12	30	232	13,308
0.75 ≤ ACQ < 1.5 to ACQ < 0.75	378	0	111	7,227
0.75 ≤ ACQ < 1.5 to 0.75 ≤ ACQ < 1.5	493	0	198	6,272
0.75 ≤ ACQ < 1.5 to 1.5 ≤ ACQ < 3.0	262	79	482	5,341
0.75 ≤ ACQ < 1.5 to ACQ ≥ 3.0	26	310	528	2,828
1.5 ≤ ACQ < 3.0 to ACQ < 0.75	88	−226	−603	3,520
1.5 ≤ ACQ < 3.0 to 0.75 ≤ ACQ < 1.5	248	0	1,096	8,107
1.5 ≤ ACQ < 3.0 to 1.5 ≤ ACQ < 3.0	410	0	62	8,233
1.5 ≤ ACQ < 3.0 to ACQ ≥ 3.0	61	61	1,444	6,463
ACQ ≥ 3.0 to ACQ < 0.75	7	−693	−3,667	6,130
ACQ ≥ 3.0 to 0.75 ≤ ACQ < 1.5	12	−239	867	8,259
ACQ ≥ 3.0 to 1.5 ≤ ACQ < 3.0	48	0	−693	10,106
ACQ ≥ 3.0 to ACQ ≥ 3.0	35	0	2,580	13,122

Abbreviation: ACQ-5, Asthma Control Questionnaire 5.
[a]Wave 1 to wave 2 or wave 2 to wave 3. Each wave is 4 months.

Table 5
Adjusted Analysis: Change in Asthma-Specific Health Care Expenditures (per 4 Months, Longitudinal)[a]

ACQ-5 change category[b]	Coefficient	SE	*P* value	95% CI
ACQ < 0.75 to ACQ < 0.75	−2,244	1,105	.04	−4,410 to −77
ACQ < 0.75 to 0.75 ≤ ACQ < 1.5	−2,376	1,140	.04	−4,610 to −142
ACQ < 0.75 to 1.5 ≤ ACQ < 3.0	−1,096	1,262	.39	−3,570 to 1,378
ACQ < 0.75 to ACQ ≥ 3.0	−2,220	2,144	.30	−6,423 to 1,982
0.75 ≤ ACQ < 1.5 to ACQ < 0.75	−2,337	1,139	.04	−4,570 to −104
0.75 ≤ ACQ < 1.5 to 0.75 ≤ ACQ < 1.5	−2,251	1,127	.05	−4,460 to −42
0.75 ≤ ACQ < 1.5 to 1.5 ≤ ACQ < 3.0	−2,010	1,159	.08	−4,281 to 262
0.75 ≤ ACQ < 1.5 to ACQ ≥ 3.0	−2,226	1,661	.18	−5,483 to 1,031
1.5 ≤ ACQ < 3.0 to ACQ < 0.75	−3,045	1,285	.02	−5,563 to −526
1.5 ≤ ACQ < 3.0 to 0.75 ≤ ACQ < 1.5	−1,419	1,161	.22	−3,696 to 858
1.5 ≤ ACQ < 3.0 to 1.5 ≤ ACQ < 3.0	−2,530	1,133	.03	−4,752 to −309
1.5 ≤ ACQ < 3.0 to ACQ ≥ 3.0	−1,145	1,358	.40	−3,807 to 1,517
ACQ ≥ 3.0 to ACQ < 0.75	−6,023	2,671	.02	−11,259 to −786
ACQ ≥ 3.0 to 0.75 ≤ ACQ < 1.5	−1,625	2,143	.45	−5,826 to 2,577
ACQ ≥ 3.0 to 1.5 ≤ ACQ < 3.0	−3,323	1,424	.02	−6,115 to −531

Abbreviation: ACQ-5, Asthma Control Questionnaire 5; SE, standard error.
[a]Wave 1 to wave 2 or wave 2 to wave 3. Each wave is 4 months. Regression of asthma-specific health care expenditures on ACQ-5 change categories controlling for wave change (1 to 2 or 2 to 3) and group, age, sex, family income level, race, educational attainment, ethnicity, and smoking status.
[b]Reference category is ACQ ≥3.0 to ACQ ≥3.0.

of asthma control on outcomes controlling for sociodemographic characteristics and smoking status.) The results suggest the potential for 3 separate groupings of asthma cost. There seemed to be a natural break for ACQ-5 scores above the 1.5 to 2 category and another break above the greater than 3 to 3.5 category. This information was used in combination with previous publications to inform the categorizations of uncontrolled asthma in the longitudinal change analysis. Taken with the results of the longitudinal change analysis (Table 5), this may suggest the potential for a cutoff of ACQ-5 score greater than 1.5 for not well-controlled asthma and ACQ-5 score greater than 3 for very poorly controlled asthma.

The longitudinal change analysis by asthma control levels provides important insight into the cost of asthma control improvements or decrements. Improving patients with very poorly controlled to controlled asthma was associated with $6,023 in savings compared with those whose asthma remained very poorly controlled (Table 5). This finding reflects the change in 4-month cost and is quite substantial. Cost savings of this magnitude could substantiate financial investment into asthma control interventions or treatments. Likewise, improving patients from very poorly controlled to not well controlled asthma was associated with a $3,323 reduction in cost during 4 months. Improving patients from very poorly controlled to indeterminate asthma status with ACQ-5 score of 0.75 to less than 1.5 was not associated with a statistically significant change in cost. This lack of significance likely reflects the small sample ($n = 12$) combined with the large SD in mean change in cost ($8,259) (Table 4). Many other changes were statistically significantly lower than the reference group (those whose asthma remained very poorly controlled: ACQ-5 score of $\geq$3.0 to $\geq$3.0). This finding is not surprising given that the most expensive group is patients whose asthma remains very poorly controlled. In addition to quantifying the cost of changes in asthma control, the longitudinal analysis provides preliminary support for categorizing control levels by ACQ-5 score with respect to economic outcomes: controlled asthma, ACQ-5 score less than 0.75; not well-controlled asthma, ACQ-5 score of 1.5 to less than 3.0; and very poorly controlled asthma, ACQ-5 score of 3.0 or greater. It also may provide indirect support for these as clinical cutoffs.

The $6,023 savings compared with those whose asthma remained very poorly controlled (Table 5) may be largely attributable to reductions in asthma inpatient and ED expenditures. This can be implied from the results of the specific elements of HRU and expenditures in the eAppendix. Asthma-specific medical expenditures appear to be driving much of the magnitude in total costs. In contrast, asthma-specific outpatient costs were not statistically significant for many of the comparisons.

It is unclear how the results of this research would be different for other asthma control questionnaires. For example, the Asthma Control Test uses 5 questions with many similar domains to the ACQ-5, suggesting that results may be similar. Similar research using the Asthma Control Test would be useful.

There are limitations associated with analyzing cost data in general and in our study approach specifically. We limited the presentation of the main results of the longitudinal analyses to asthma-specific health care costs. Similar regression specifications were conducted on all-cause health care expenditures and the delineated HRU measures; results of these analyses are presented in the eAppendix. Cost data are challenging because they are highly variable, with some patients incurring no cost and others incurring exorbitantly high cost. This is particularly true of all-cause expenditures because individuals vary more in their non–asthma-related health and outcomes. Although our analyses controlled for sociodemographic characteristics and smoking status, the variability in all-cause expenditures was not significantly explained by longitudinal changes in asthma control outcomes. There were also few individuals in some of the clinically important longitudinal change categories, making statistical significance more challenging. However, all-cause expenditures were statistically significantly associated with ACQ-5 scores in all of the cross-sectional analyses, highlighting the importance of analyzing longitudinal changes rather than assuming cross-sectional associations can be used in their place. Asthma-specific inpatient and outpatient expenditures were not consistent: a few categories were significant, but overall the relationship was not clear. In contrast, asthma-specific medical expenditures were robust and significant. This also likely reflects the fact that medical expenditures include all outpatient and inpatient expenditures combined, making for a more robust association. Results of the longitudinal analysis of HRU outcomes are also presented in the eAppendix. Many of the change categories were statistically significant across longitudinal changes (in particular asthma-specific prescriptions, oral corticosteroids, SABAs, and asthma-specific outpatient visits). Longitudinal results of all-cause HRU were largely insignificant and inconsistent likely because of many of the reasons listed above.

The small sample sizes for some of the longitudinal change categories highlight the difficulty of conducting longitudinal analyses that use validated measures of control, such as the ACQ-5. The sample size in this study is large, considering that it includes the ACQ-5 and actual pharmacy and medical claims for all individuals and was conducted in a general sample of patients with persistent asthma. Clinical trial data including the ACQ-5 with similar sample sizes exists but does not incorporate HRU and expenditures that reflect real-world use, which is likely why expenditure data on longitudinal changes in asthma control using a validated instrument is scarce. Additional future research incorporating a validating asthma control instrument with real-world economic data would be valuable. In addition, our research only compared longitudinal changes from wave 1 to wave 2 and wave 2 to wave 3. It is unclear how the results may have been different if wave 1 was compared to wave 3.

This study provides important quantification of the cost and HRU associated with asthma control levels. The results may help public health authorities or large health organizations to quantify the economic effect of asthma interventions and treatments via changes in the ACQ-5. These estimates can be incorporated into cost-effectiveness models to estimate the potential cost effect of treatments or interventions that improve asthma control. These results also support financial investment in interventions aimed at improving asthma control.

In addition to those discussed above, there are other limitations of this study. Our analysis explored possible cutoffs in the ACQ-5 for uncontrolled asthma. The results are preliminary, apply to economic outcomes, and may not reflect clinically derived cutoffs. Future research on identifying clinically relevant cutoffs for uncontrolled asthma is needed. As discussed in previous publications,[13] the design of the OSACO study also presents some potential limitations. Individuals who consented to participate may differ from those who declined. The generalizability of the findings may also be limited to the KPCO population, which is representative of the Colorado population, but may not be generalizable to other regions.

In conclusion, this study provides preliminary economic evidence of possible cutoffs in the ACQ-5 associated with levels of control consistent with asthma guidelines using a validated measure of asthma control. The quantification of cost savings associated with improving asthma control over time may justify financial investment in interventions or treatments aimed at improving control.

Acknowledgment

We thank Denise Globe, PhD, for her valuable contribution to the conception and design of the study.

Supplementary Data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.anai.2016.07.020.

References

[1] National Asthma Education and Prevention Program. Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma Update on Selected Topics–2002. *J Allergy Clin Immunol*. 2002;110(5 suppl):S141–S219.
[2] From the Global Strategy for Asthma Management and Prevention. Global Initiative for Asthma (GINA) 2014. http://www.ginasthma.org/. Accessed May 31, 2016.
[3] Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J*. 1999;14:902–907.
[4] Cloutier MM, Schatz M, Castro M, et al. Asthma outcomes: composite scores of asthma control. *J Allergy Clin Immunol*. 2012;129(3 suppl):S24–S33.
[5] Juniper EF, Bousquet J, Abetz L, Bateman ED. Identifying 'well-controlled' and 'not well-controlled' asthma using the Asthma Control Questionnaire. *Respir Med*. 2006;100:616–621.
[6] Jia CE, Zhang HP, Lv Y, et al. The Asthma Control Test and Asthma Control Questionnaire for assessing asthma control: Systematic review and meta-analysis. *J Allergy Clin Immunol*. 2013;131:695–703.
[7] Bahadori K, Doyle-Waters MM, Marra C, et al. Economic burden of asthma: a systematic review. *BMC Pulm Med*. 2009;9:24.
[8] Sullivan PW, Ghushchyan VH, Slejko JF, Belozeroff V, Globe DR, Lin S-L. The burden of adult asthma in the United States: Evidence from the Medical Expenditure Panel Survey. *J Allergy Clin Immunol*. 2011;127:363–369.e363.
[9] Vollmer WM, Markson LE, O'Connor E, Frazier EA, Berger M, Buist AS. Association of asthma control with health care utilization: a prospective evaluation. *Am J Respir Crit Care Med*. 2002;165:195–199.
[10] Stempel DA, McLaughin TP, Stanford RH, Fuhlbrigge AL. Patterns of asthma control: a 3-year analysis of patient claims. *J Allergy Clin Immunol*. 2005;115:935–939.
[11] Campbell JD, Blough DK, Sullivan SD. Comparison of guideline-based control definitions and associations with outcomes in severe or difficult-to-treat asthma. *Ann Allergy Asthma Immunol*. 2008;101:474–481.
[12] Sullivan PW, Slejko JF, Ghushchyan VH, et al. The relationship between asthma, asthma control and economic outcomes in the United States. *J Asthma*. 2014;51:769–778.
[13] Sullivan PW, Campbell JD, Globe G, et al. Measuring the effect of asthma control on exacerbations and health resource use. *J Allergy Clin Immunol*. 2015;136:1409–1411.e1–6.
[14] Juniper EF, Svensson K, Mork AC, Stahl E. Measurement properties and interpretation of three shortened versions of the asthma control questionnaire. *Respir Med*. 2005;99:553–558.
[15] Sastre J, Olaguibel J, Vega JM, Del Pozo V, Picado C, Lopez Vina A. Cut-off points for defining asthma control in three versions of the Asthma Control Questionnaire. *J Asthma*. 2010;47:865–870.
[16] Sullivan SD, Rasouliyan L, Russo PA, Kamath T, Chipps BE; for the TSG. Extent, patterns, and burden of uncontrolled disease in severe or difficult-to-treat asthma. *Allergy*. 2007;62:126–133.
[17] Meltzer EO, Busse WW, Wenzel SE, et al. Use of the Asthma Control Questionnaire to predict future risk of asthma exacerbation. *J Allergy Clin Immunol*. 2011;127:167–172.

eAppendix

Additional Results of Longitudinal Change Regression Analyses of Health Resource Utilization and Expenditures[a]

	Coefficient	SE	*t*	$P > \|t\|$	95% CI
No. of oral corticosteroid prescriptions					
Wave 2	0.014933	0.01816	0.82	.411	−0.02067 to 0.050537
ACQ < 0.75 to ACQ < 0.75	0.06506	0.097406	0.67	.504	−0.12591 to 0.256032
ACQ < 0.75 to 0.75 ≤ ACQ < 1.5	0.094954	0.100453	0.95	.345	−0.10199 to 0.2919
ACQ < 0.75 to 1.5 ≤ ACQ < 3.0	0.220534	0.111236	1.98	.047	0.002447 to 0.438621
ACQ < 0.75 to ACQ ≥ 3.0	0.7205	0.18896	3.81	<.001	0.35003 to 1.09097
0.75 ≤ ACQ < 1.5 to ACQ < 0.75	0.045452	0.100393	0.45	.651	−0.15138 to 0.24228
0.75 ≤ ACQ < 1.5 to 0.75 ≤ ACQ < 1.5	0.103524	0.099318	1.04	.297	−0.0912 to 0.298245
0.75 ≤ ACQ < 1.5 to 1.5 ≤ ACQ < 3.0	0.074105	0.102131	0.73	.468	−0.12613 to 0.27434
0.75 ≤ ACQ < 1.5 to ACQ ≥ 3.0	0.53761	0.146436	3.67	<.001	0.250511 to 0.824709
1.5 ≤ ACQ < 3.0 to ACQ < 0.75	−0.00986	0.113245	−0.09	.931	−0.23189 to 0.212162
1.5 ≤ ACQ < 3.0 to 0.75 ≤ ACQ < 1.5	−0.02965	0.102372	−0.29	.772	−0.23036 to 0.171058
1.5 ≤ ACQ < 3.0 to 1.5 ≤ ACQ < 3.0	0.066727	0.099869	0.67	.504	−0.12907 to 0.262527
1.5 ≤ ACQ < 3.0 to ACQ ≥ 3.0	0.126934	0.1197	1.06	.289	−0.10775 to 0.361616
ACQ ≥ 3.0 to ACQ < 0.75	−0.54331	0.235441	−2.31	.021	−1.00491 to −0.0817
ACQ ≥ 3.0 to 0.75 ≤ ACQ < 1.5	−0.02127	0.18891	−0.11	.91	−0.39164 to 0.349105
ACQ ≥ 3.0 to 1.5 ≤ ACQ < 3.0	−0.1445	0.125522	−1.15	.25	−0.39059 to 0.101596
No. of SABA prescriptions					
Wave 2	−0.08232	0.027972	−2.94	.003	−0.13716 to −0.02748
ACQ < 0.75 to ACQ < 0.75	−0.00838	0.150036	−0.06	.955	−0.30254 to 0.285775
ACQ < 0.75 to 0.75 ≤ ACQ < 1.5	0.123793	0.154729	0.8	.424	−0.17957 to 0.427151
ACQ < 0.75 to 1.5 ≤ ACQ < 3.0	0.332306	0.171339	1.94	.053	−0.00362 to 0.668229
ACQ < 0.75 to ACQ ≥ 3.0	0.237282	0.291058	0.82	.415	−0.33336 to 0.807923
0.75 ≤ ACQ < 1.5 to ACQ < 0.75	−0.06528	0.154637	−0.42	.673	−0.36846 to 0.237898
0.75 ≤ ACQ < 1.5 to 0.75 ≤ ACQ < 1.5	0.031754	0.152981	0.21	.836	−0.26818 to 0.331685
0.75 ≤ ACQ < 1.5 to 1.5 ≤ ACQ < 3.0	0.212472	0.157313	1.35	.177	−0.09595 to 0.520896
0.75 ≤ ACQ < 1.5 to ACQ ≥ 3.0	0.607225	0.225558	2.69	.007	0.165002 to 1.049448
1.5 ≤ ACQ < 3.0 to ACQ < 0.75	−0.15682	0.174433	−0.9	.369	−0.49881 to 0.185168
1.5 ≤ ACQ < 3.0 to 0.75 ≤ ACQ < 1.5	−0.16068	0.157685	−1.02	.308	−0.46983 to 0.148477
1.5 ≤ ACQ < 3.0 to 1.5 ≤ ACQ < 3.0	0.054038	0.153829	0.35	.725	−0.24756 to 0.355632
1.5 ≤ ACQ < 3.0 to ACQ ≥ 3.0	0.128374	0.184376	0.7	.486	−0.23311 to 0.489857
ACQ ≥ 3.0 to ACQ < 0.75	−0.27234	0.362654	−0.75	.453	−0.98335 to 0.438671
ACQ ≥ 3.0 to 0.75 ≤ ACQ < 1.5	−0.76221	0.29098	−2.62	.009	−1.3327 to −0.19172
ACQ ≥ 3.0 to 1.5 ≤ ACQ < 3.0	0.027637	0.193343	0.14	.886	−0.35143 to 0.406701
No. of all-cause outpatient visits					
Wave 2	−0.05678	0.10028	−0.57	.571	−0.25339 to 0.139827
ACQ < 0.75 to ACQ < 0.75	0.17691	0.537883	0.33	.742	−0.87765 to 1.23147
ACQ < 0.75 to 0.75 ≤ ACQ < 1.5	−0.08951	0.554707	−0.16	.872	−1.17705 to 0.998038
ACQ < 0.75 to 1.5 ≤ ACQ < 3.0	0.992013	0.614253	1.61	.106	−0.21228 to 2.196302
ACQ < 0.75 to ACQ ≥ 3.0	0.995438	1.043446	0.95	.34	−1.05032 to 3.041194
0.75 ≤ ACQ < 1.5 to ACQ < 0.75	0.421857	0.554375	0.76	.447	−0.66504 to 1.508751
0.75 ≤ ACQ < 1.5 to 0.75 ≤ ACQ < 1.5	0.261134	0.548441	0.48	.634	−0.81413 to 1.336394
0.75 ≤ ACQ < 1.5 to 1.5 ≤ ACQ < 3.0	0.326719	0.56397	0.58	.562	−0.77899 to 1.432425
0.75 ≤ ACQ < 1.5 to ACQ ≥ 3.0	1.431284	0.808628	1.77	.077	−0.15409 to 3.01666
1.5 ≤ ACQ < 3.0 to ACQ < 0.75	0.144975	0.625344	0.23	.817	−1.08106 to 1.37101
1.5 ≤ ACQ < 3.0 to 0.75 ≤ ACQ < 1.5	0.06175	0.565302	0.11	.913	−1.04657 to 1.170068
1.5 ≤ ACQ < 3.0 to 1.5 ≤ ACQ < 3.0	0.148582	0.55148	0.27	.788	−0.93264 to 1.229801
1.5 ≤ ACQ < 3.0 to ACQ ≥ 3.0	0.961851	0.660991	1.46	.146	−0.33407 to 2.257775
ACQ ≥ 3.0 to ACQ < 0.75	0.123329	1.30012	0.09	.924	−2.42566 to 2.672314
ACQ ≥ 3.0 to 0.75 ≤ ACQ < 1.5	0.985419	1.043169	0.94	.345	−1.05979 to 3.030631
ACQ ≥ 3.0 to 1.5 ≤ ACQ < 3.0	0.304632	0.693139	0.44	.66	−1.05432 to 1.663583
All-cause health care expenditures					
Wave 2	−130.415	301.2357	−0.43	.665	−721.011 to 460.1801
ACQ < 0.75 to ACQ < 0.75	−2,150.09	1,615.769	−1.33	.183	−5,317.93 to 1,017.75
ACQ < 0.75 to 0.75 ≤ ACQ < 1.5	−2,659.42	1,666.307	−1.6	.111	−5,926.34 to 607.5035
ACQ < 0.75 to 1.5 ≤ ACQ < 3.0	−489.34	1,845.179	−0.27	.791	−4,106.96 to 3,128.274
ACQ < 0.75 to ACQ ≥ 3.0	−4,821.97	3,134.452	−1.54	.124	−10,967.3 to 1,323.361
0.75 ≤ ACQ < 1.5 to ACQ < 0.75	−2,236.7	1,665.31	−1.34	.179	−5,501.66 to 1,028.272
0.75 ≤ ACQ < 1.5 to 0.75 ≤ ACQ < 1.5	−2,396.88	1,647.485	−1.45	.146	−5,626.9 to 833.1392
0.75 ≤ ACQ < 1.5 to 1.5 ≤ ACQ < 3.0	−1,653.76	1,694.134	−0.98	.329	−4,975.24 to 1,667.715
0.75 ≤ ACQ < 1.5 to ACQ ≥ 3.0	−1,359.09	2,429.071	−0.56	.576	−6,121.47 to 3,403.291
1.5 ≤ ACQ < 3.0 to ACQ < 0.75	−2,982.68	1,878.498	−1.59	.112	−6,665.62 to 700.2599
1.5 ≤ ACQ < 3.0 to 0.75 ≤ ACQ < 1.5	−1,352.72	1,698.135	−0.8	.426	−4,682.04 to 1,976.604
1.5 ≤ ACQ < 3.0 to 1.5 ≤ ACQ < 3.0	−2,436.29	1,656.615	−1.47	.141	−5,684.21 to 811.6269
1.5 ≤ ACQ < 3.0 to ACQ ≥ 3.0	−940.2	1,985.58	−0.47	.636	−4,833.08 to 2,952.681
ACQ ≥ 3.0 to ACQ < 0.75	−6,100.57	3,905.486	−1.56	.118	−13,757.6 to 1,556.434
ACQ ≥ 3.0 to 0.75 ≤ ACQ < 1.5	330.8747	3,133.619	0.11	.916	−5,812.83 to 6,474.574
ACQ ≥ 3.0 to 1.5 ≤ ACQ < 3.0	−3,117.63	2,082.149	−1.5	.134	−7,199.84 to 964.5865
Asthma-specific outpatient expenditures					
Wave 2	179.1021	81.20728	2.21	.027	19.88907 to 338.3152
ACQ < 0.75 to ACQ < 0.75	276.2217	435.5798	0.63	.526	−577.766 to 1,130.209
ACQ < 0.75 to 0.75 ≤ ACQ < 1.5	162.8811	449.204	0.36	.717	−717.818 to 1,043.58
ACQ < 0.75 to 1.5 ≤ ACQ < 3.0	607.86	497.4244	1.22	.222	−367.378 to 1,583.098
ACQ < 0.75 to ACQ ≥ 3.0	1,785.568	844.9871	2.11	.035	128.9068 to 3,442.23
0.75 ≤ ACQ < 1.5 to ACQ < 0.75	205.2221	448.9351	0.46	.648	−674.949 to 1,085.394

(*continued on next page*)

eAppendix (*continued*)

	Coefficient	SE	*t*	$P > \|t\|$	95% CI
$0.75 \leq$ ACQ < 1.5 to $0.75 \leq$ ACQ < 1.5	297.5198	444.1299	0.67	.503	−573.231 to 1,168.27
$0.75 \leq$ ACQ < 1.5 to $1.5 \leq$ ACQ < 3.0	387.3053	456.7054	0.85	.396	−508.101 to 1,282.711
$0.75 \leq$ ACQ < 1.5 to ACQ ≥ 3.0	469.0702	654.8303	0.72	.474	−814.775 to 1,752.915
$1.5 \leq$ ACQ < 3.0 to ACQ < 0.75	−305.025	506.4065	−0.6	.547	−1,297.87 to 687.824
$1.5 \leq$ ACQ < 3.0 to $0.75 \leq$ ACQ < 1.5	298.9576	457.7841	0.65	.514	−598.563 to 1,196.478
$1.5 \leq$ ACQ < 3.0 to $1.5 \leq$ ACQ < 3.0	45.88182	446.591	0.1	.918	−829.694 to 921.4576
$1.5 \leq$ ACQ < 3.0 to ACQ ≥ 3.0	301.8664	535.2737	0.56	.573	−747.579 to 1,351.311
ACQ ≥ 3.0 to ACQ < 0.75	−417.789	1,052.843	−0.4	.692	−2,481.97 to 1,646.39
ACQ ≥ 3.0 to $0.75 \leq$ ACQ < 1.5	1,194.88	844.7628	1.41	.157	−461.342 to 2,851.101
ACQ ≥ 3.0 to $1.5 \leq$ ACQ < 3.0	−156.114	561.3069	−0.28	.781	−1,256.6 to 944.3711
Asthma-specific medical expenditures					
Wave 2	52.47146	205.0073	0.26	.798	−349.461 to 454.404
ACQ $<$ .075 to ACQ < 0.75	−2,235.05	1,099.619	−2.03	.042	−4,390.94 to −79.1635
ACQ < 0.75 to $0.75 \leq$ ACQ < 1.5	−2,418.68	1,134.013	−2.13	.033	−4,642 to −195.357
ACQ < 0.75 to $1.5 \leq$ ACQ < 3.0	−1,191.1	1,255.745	−0.95	.343	−3,653.08 to 1,270.884
ACQ < 0.75 to ACQ ≥ 3.0	−2,316.02	2,133.165	−1.09	.278	−6,498.25 to 1,866.215
$0.75 \leq$ ACQ < 1.5 to ACQ < 0.75	−2,286.95	1,133.334	−2.02	.044	−4,508.94 to −64.9645
$0.75 \leq$ ACQ < 1.5 to $0.75 \leq$ ACQ < 1.5	−2,271.17	1,121.204	−2.03	.043	−4,469.38 to −72.9678
$0.75 \leq$ ACQ < 1.5 to $1.5 \leq$ ACQ < 3.0	−2,054.56	1,152.95	−1.78	.075	−4,315 to 205.8913
$0.75 \leq$ ACQ < 1.5 to ACQ ≥ 3.0	−2,344.43	1,653.115	−1.42	.156	−5,585.49 to 896.628
$1.5 \leq$ ACQ < 3.0 to ACQ < 0.75	−2,940.25	1,278.421	−2.3	.022	−5,446.69 to −433.804
$1.5 \leq$ ACQ < 3.0 to $0.75 \leq$ ACQ < 1.5	−1,412.49	1,155.673	−1.22	.222	−3,678.28 to 853.2953
$1.5 \leq$ ACQ < 3.0 to $1.5 \leq$ ACQ < 3.0	−2,530.91	1,127.417	−2.24	.025	−4,741.3 to −320.524
$1.5 \leq$ ACQ < 3.0 to ACQ ≥ 3.0	−1,229.9	1,351.296	−0.91	.363	−3,879.22 to 1,419.419
ACQ ≥ 3.0 to ACQ < 0.75	−5,713.45	2,657.897	−2.15	.032	−10,924.5 to −502.438
ACQ ≥ 3.0 to $0.75 \leq$ ACQ < 1.5	−1,465.76	2,132.599	−0.69	.492	−5,646.88 to 2,715.366
ACQ ≥ 3.0 to $1.5 \leq$ ACQ < 3.0	−3,259.36	1,417.016	−2.3	.021	−6,037.52 to −481.188

Abbreviations: CI, confidence interval; SABA, short-acting β-agonist.

[a]Controlling for wave change (wave 2 equals wave 2 to wave 3) and group, age, sex, family income level, race, educational attainment, ethnicity, and smoking status.