
Asthma control and activity limitations: insights from the Real-world Evaluation of Asthma Control and Treatment (REACT) Study

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Background: Uncontrolled asthma remains prevalent in the United States and confers a substantial burden on the health care system.

Objectives: To evaluate the association between uncontrolled asthma and activity limitations in a nationally representative sample of patients with moderate-to-severe-treated asthma and to assess the degree to which demographics and comorbidities were associated with activity limitations.

Methods: Patients who participated in the Real-world Evaluation of Asthma Control and Treatment study were surveyed regarding type and degree of activity limitations in 4 categories: outdoor activity, physical activity, daily activity, and environmental triggers. Information about asthma control, demographics, and comorbidities was collected. Multivariable regression was used to assess the association between uncontrolled asthma and activity limitations while adjusting for demographic characteristics and comorbid conditions.

Results: Uncontrolled asthma was associated with a greater than 2-fold risk of outdoor (odds ratio [OR], 2.58; 95% confidence interval [CI], 1.90–3.51) or physical (OR, 2.62; 95% CI, 1.90–3.61) activity limitations and a 66% increased risk of daily activity limitations (OR, 1.66; 95% CI, 1.09–2.51). Comorbidities associated with activity limitation included hives, chronic sinusitis, arthritis, gastroesophageal reflux disease, hypercholesterolemia, and depression. The observed associations between uncontrolled asthma and activity limitation remained significant after controlling for demographic characteristics and comorbid conditions.

Conclusions: Compared with patients with controlled asthma, those with uncontrolled asthma are at higher risk for limitations in outdoor activity, physical activity, and daily activity. To help patients achieve optimal health, asthma management should include routine assessment of activity limitations and assessment and coordinated care for comorbid conditions.

Ann Allergy Asthma Immunol. 2010;104:471–477.

INTRODUCTION

Poorly controlled asthma can be a debilitating chronic disease that incurs significant costs in terms of morbidity, quality of life, and health care utilization. Asthma costs have been shown to be directly related to patient level of asthma control, with the highest costs incurred by patients with severe uncontrolled asthma.^{1–4} Indeed, patients with moderate-to-severe asthma have significantly more uncontrolled events,

leading to hospitalizations, emergency department visits, clinic visits, and, consequently, higher total treatment costs than do those with mild asthma.^{5–7} The concept of disease control as a principal outcome measure has only recently become the focus of asthma management strategies, clinical trials, and evidence-based consensus guidelines.⁸ Although asthma control is the central focus of therapy, many patients do not achieve partial or full control with available medications.^{9–12} These patients remain at risk for asthma-related morbidity, increased health care costs, and diminished quality of life.

Few studies have examined the impact of uncontrolled asthma on daily function and physical activities. Most of these studies examined activity limitations in asthmatic populations using subscales of quality of life instruments¹³ or as part of general surveys conducted in Europe.¹⁴ Large-scale studies examining the relationship between uncontrolled asthma and activity limitations in asthmatic patients in the United States have focused predominantly on work impairment.

The Real-world Evaluation of Asthma Control and Treatment (REACT) study is a nationally representative sample of patients with moderate-to-severe asthma who are taking standard asthma medications.¹¹ The primary objective of this analysis was to evaluate the association between uncontrolled

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Disclosures: Drs Haselkorn and Peters are paid consultants to Genentech, Inc. Mr Miller is employed by ICON Clinical Research, an organization that receives research funding from Genentech and other industry sponsors.

Funding Sources: This study was supported by Genentech, Inc. and Novartis Pharmaceuticals Corp.

Received for publication November 6, 2009; Received in revised form March 17, 2010; Accepted for publication April 8, 2010.

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doi:10.1016/j.anai.2010.04.006

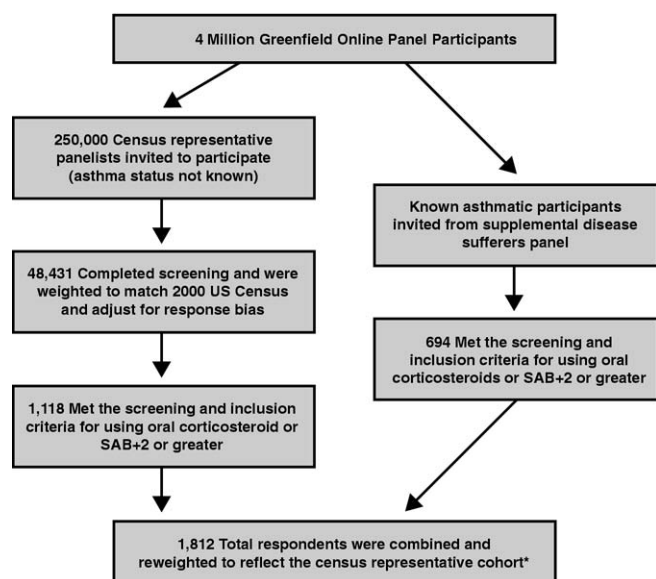


Figure 1. Study design. *Weights applied were adjusted for age, sex, race/ethnicity, region, and household income. SAB+2 indicates short-acting β -agonists plus 2 or more controller medications.

asthma and activity limitations in this real-world setting of treated asthmatic patients. The secondary objective was to evaluate the degree to which demographics and comorbidities were predictive of activity limitations in asthmatic patients. We hypothesized that patients with uncontrolled asthma would be at higher risk for activity limitations than patients with controlled asthma and that the association cannot be explained by other factors, such as demographics or comorbidities.

METHODS

Study Design

The methods and baseline population characteristics of the REACT study have been described previously.¹¹ Briefly, the REACT study surveyed a nationally representative sample of patients with asthma in the United States who were receiving a short-acting β -agonist and at least 2 asthma controller medications. Survey participants were members of the Greenfield Online Panel (GOL), a diverse Web-based cohort of approximately 4 million individuals.^{15,16} Members voluntarily opt into the GOL and are recruited from a diverse pool of sources, including Internet portals, special interest Web sites, and age- and ethnicity-focused Web sites primarily using text links, banner ads, and affiliate programs. Respondents were weighted to match the 2000 US Census to adjust for lower numbers of economically disadvantaged respondents that were not captured owing to lower rates of computer ownership (response bias). This approach also removes the effects of differences in age or other confounding variables, such as sex, race, and socioeconomic status. Thus, the proportions of minorities in the REACT study were, by design, representa-

tive of the distribution of minorities in the United States, as were age, sex, and socioeconomic measures.

Each respondent was assigned a unique respondent ID, and information provided to the GOL was kept confidential. This study was exempt from institutional review board approval. A total of 1,812 adults met the enrollment criteria and were included in the analysis: (1) diagnosed as having asthma at least 1 year ago by a physician and (2) currently using oral corticosteroids (a minimum of 2 courses in the past 12 months) or short-acting β -agonists and at least 2 additional long-term controllers, suggesting moderate-to-severe persistent asthma (as defined by the 2004 Global Initiative for Asthma guidelines, steps 3 and 4, respectively) (Fig 1).

Assessments

Respondents completed the 5-item Asthma Control Test (ACT)¹⁷ and an observational, cross-sectional questionnaire on demographics, comorbidities, health care use, and attitudes and behaviors toward asthma. Comorbidities were self-reported by answering the question, "Which of the following conditions do you have?" and checking all relevant conditions from a list. The REACT survey included 14 questions about type and degree of activity limitations (Table 1), to which respondents chose from 4 responses: (1) I do this

Table 1. Activity Limitation Categories

1. Outdoor activity
 - To what extent do you limit outdoor winter activities because of your asthma?
 - To what extent do you limit going outside in the cold because of your asthma?
 - To what extent do you limit going outside during allergy season because of your asthma?
 - To what extent do you limit going outside when damp, humid, or windy because of your asthma?
2. Physical activity
 - To what extent do you limit exercising because of your asthma?
 - To what extent do you limit lifting or otherwise exerting yourself because of your asthma?
 - To what extent do you limit playing sports because of your asthma?
 - To what extent do you limit climbing stairs because of your asthma?
3. Environmental triggers
 - To what extent do you limit interacting with pets because of your asthma?
 - To what extent do you limit visiting people with pets because of your asthma?
 - To what extent do you limit going places where there might be dust, mold, or other allergens because of your asthma?
 - To what extent do you limit going places where there might be cigarette smoke because of your asthma?
4. Daily activity
 - To what extent do you limit housework/cleaning the house because of your asthma?
 - To what extent do you limit going outside for gardening or shopping because of your asthma?

whenever I want, (2) I do this less often because of asthma, (3) I rarely do this because of asthma, and (4) does not apply.

Statistical Analysis

Respondents were stratified by asthma control status, determined by the ACT score. Scores of 5 to 19 indicated uncontrolled asthma, and scores of 20 to 25 indicated controlled asthma. The 14 activity limitations questions were grouped into 4 activity limitation categories (ie, outdoor activity, physical activity, daily activity, and environmental triggers) based on item content. For each category, we identified respondents who answered “I rarely do this because of my asthma” to at least 1 of the questions in that category.

Candidate predictor variables for activity limitation were asthma control, age, race/ethnicity, sex, education, region, income, smoking status, health insurance, and comorbidities, which included hay fever, hives, chronic sinusitis, atopic dermatitis, arthritis, high blood pressure, high cholesterol, diabetes mellitus, gastroesophageal reflux disease (GERD), obesity, and depression.

Multivariable backward stepwise logistic regression was used to determine which of the demographic variables and comorbidities were associated with activity limitations in each of the 4 categories. Asthma control was forced into the model, and the remaining demographic and comorbidity variables were removed from the model 1 at a time if they did not meet the inclusion threshold of $\alpha = .05$. Odds ratios (ORs), 95% confidence intervals (95% CIs), and *P* values derived from the Wald χ^2 test were computed using SAS PROC SURVEYLOGISTIC (SAS Institute Inc, Cary, North Carolina). All the analyses were performed using SAS version 9.1.

RESULTS

A total of 1,812 asthmatic patients who met the inclusion criteria and completed the ACT and the REACT survey were included. According to ACT scores, 809 participants (45%) had controlled asthma and 1,003 (55%) had uncontrolled asthma. The REACT study patient demographics have been previously described in detail.¹¹ Most participants in this analysis were white (66%), female (59%), and aged 25 to 54 years (62%). Most participants had less than a college education (57%) and were working full-time (46%); and most participants earned less than \$75,000 annually (74%), had health insurance (87%), and were currently nonsmokers (83%) (Table 2). The most common comorbidity in the cohort was hay fever/allergic rhinitis (51%) (Table 3). Approximately 30% of patients reported arthritis (31%), chronic sinusitis (27%), depression (25%), GERD (27%), high blood pressure (30%), high cholesterol (25%), and obesity (27%).

Outdoor Activity Limitations

In multivariable analyses, patients with uncontrolled asthma had a greater than 2-fold increased risk of outdoor activity limitations compared with patients with controlled asthma (OR, 2.58; 95% CI, 1.90–3.51) (Fig 2). Nonsmokers were twice as likely to have outdoor activity limitations compared with smokers. Hives, chronic sinusitis, GERD, and depres-

Table 2. Baseline Characteristics of the 1,812 Study Participants

Characteristic	Participants, % ^a
Age, y	
18–24	15.0
25–34	19.8
35–44	22.0
45–54	20.3
55–64	10.3
≥65	12.6
Sex	
Male	40.5
Female	59.5
Race/ethnicity	
White	66.3
Black	10.0
Hispanic	16.5
Asian	3.9
Native American	1.0
Prefer not to state	0.4
Education ^b	
Less than college	56.9
College or more	43.1
Employment status	
Full-time	46.3
Part-time	14.2
Not employed	15.6
Retired	13.7
Disabled	10.2
Region	
Urban	26.9
Suburban	50.8
Rural	22.3
Annual income	
<\$75,000	74.1
≥\$75,000	25.9
Health insurance	
Yes	86.7
No	13.3
Cigarette smoking status	
Current smoker	17.1
Current nonsmoker	82.9

^a Percentages are weighted.

^b The college or more category includes completed university or college and postgraduate studies. The less than college category includes high school or less, some university or college, and vocational/technical studies.

sion were each independently associated with a 50% to 90% increased risk of outdoor activity limitations. Having no health insurance and a lower income were also associated with outdoor activity limitations.

Physical Activity Limitations

Uncontrolled asthma was associated with a greater than 2-fold increased risk of physical activity limitations (OR, 2.62; 95% CI, 1.90–3.61) (Fig 3). Having arthritis or not having insurance was associated with a nearly 2-fold increased risk of physical activity limitations. Depression and

Table 3. Comorbid Conditions in the 1,812 Study Participants

Comorbid Condition	Participants, %
Arthritis	
No	69.4
Yes	30.6
Eczema/atopic dermatitis	
No	84.6
Yes	15.4
Chronic sinusitis	
No	73.2
Yes	26.8
Depression	
No	74.8
Yes	25.2
Diabetes mellitus	
No	88.3
Yes	11.7
Gastroesophageal reflux disease	
No	73.0
Yes	27.0
Hay fever/allergic rhinitis	
No	48.9
Yes	51.1
High blood pressure	
No	70.2
Yes	29.8
High cholesterol	
No	74.7
Yes	25.3
Hives	
No	87.7
Yes	12.3
Obesity	
No	72.7
Yes	27.3

hives were associated with 75% and 52% increased risks, respectively, of physical activity limitations. Females were more likely than males to have physical activity limitations.

Daily Activity Limitations

Uncontrolled asthma was associated with a 66% increased risk of daily activity limitations (OR, 1.66; 95% CI, 1.09–2.51) (Fig 4). Being nonwhite was associated with a nearly 2-fold increased risk of daily activity limitations (OR, 1.92; 95% CI, 1.20–3.03). Hives, high cholesterol, and depression were also associated with increased risk of daily activity limitations.

Environmental Trigger Activity Limitations

The risk of environmental trigger activity limitations in patients with uncontrolled asthma was 30% higher than in patients with controlled asthma. Although this association did not reach statistical significance, a nonstatistically significant trend was observed ($P = .08$) (Fig 5). Nonsmokers had a greater than 2-fold increased risk of environmental trigger activity limitations (OR, 2.44; 95% CI, 1.61–3.70). Being nonwhite or having chronic sinusitis, arthritis, or GERD was

also associated with an increased risk of environmental trigger activity limitations.

To assess the extent to which avoidance of secondhand smoke by nonsmokers may have affected the results, we performed a sensitivity analysis in which the smoking-related item was removed from the environmental trigger category. When environmental trigger activity limitation was redefined in this manner, uncontrolled asthma became a significant predictor of activity limitation, and smoking status was dropped from the final model by the process of backward stepwise selection.

DISCUSSION

In this study, we assessed the relationship between asthma control and a broad range of specific types of activity limitation in a nationally representative sample of 1,812 American patients with moderate-to-severe asthma. Despite evidence of receiving care in accordance with asthma guidelines (short-acting β -agonists and ≥ 2 asthma controller medications), the degree of activity limitations and the extent of activity limitations, particularly in uncontrolled asthmatic patients in this cohort, was noteworthy. Patients with uncontrolled asthma were at higher risk for limitations in 3 of 4 activity categories (outdoor activity, physical activity, and daily activity) compared with patients with controlled

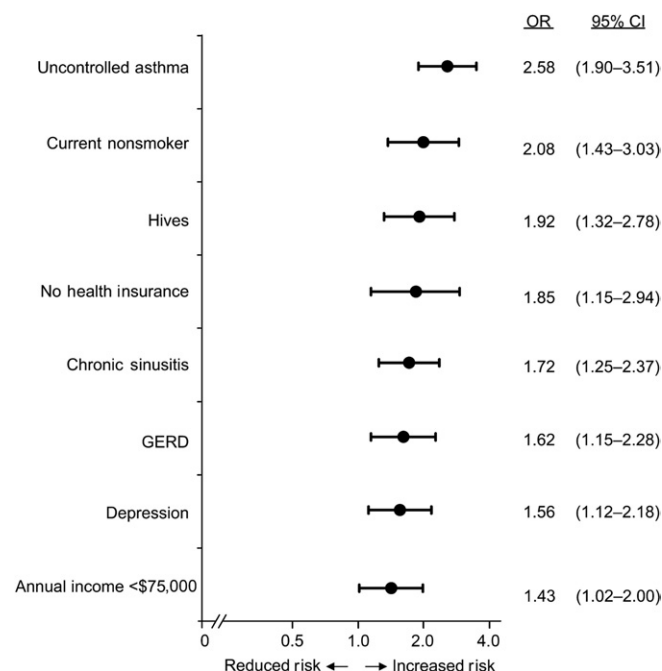


Figure 2. Outdoor activity limitations. Multivariable backward stepwise logistic regression was used to identify factors independently associated with outdoor activity limitations. The variables considered were asthma control (as measured using the Asthma Control Test), age, race/ethnicity, sex, educational level, type of residence, income, smoking status, health insurance status, and all comorbidities. CI indicates confidence interval; GERD, gastroesophageal reflux disease; and OR, odds ratio.

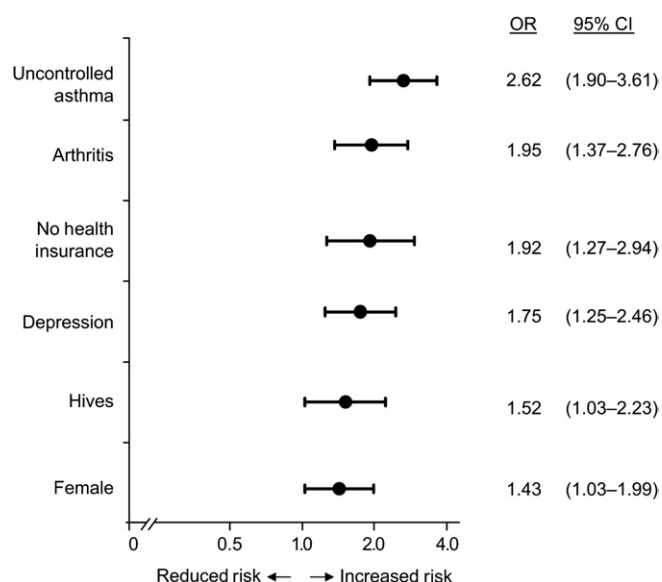


Figure 3. Physical activity limitations. Multivariable backward stepwise logistic regression was used to identify factors independently associated with physical activity limitations. The variables considered were asthma control (as measured using the Asthma Control Test), age, race/ethnicity, sex, educational level, type of residence, income, smoking status, health insurance status, and all comorbidities. CI indicates confidence interval; and OR, odds ratio.

asthma. Uncontrolled asthma was most strongly associated with outdoor activity limitations and physical activity limitations, with a greater than 2-fold risk of limitations in each of these categories. In addition, patients with uncontrolled asthma were more likely to experience limitations in daily activity than were patients with controlled asthma. These

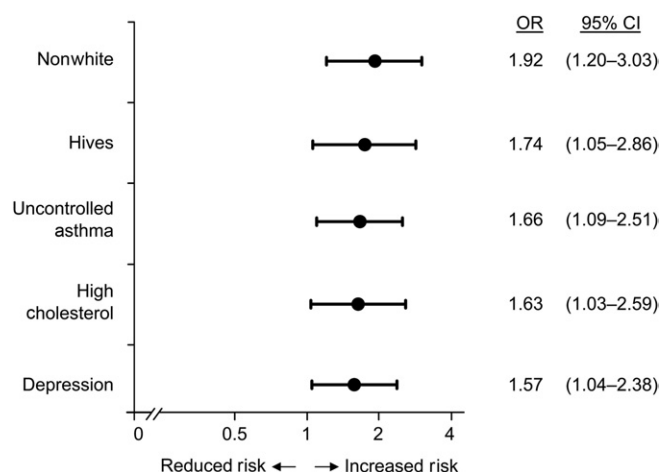


Figure 4. Daily activity limitations. Multivariable backward stepwise logistic regression was used to identify factors independently associated with daily activity limitations. The variables considered were asthma control (as measured using the Asthma Control Test), age, race/ethnicity, sex, educational level, type of residence, income, smoking status, health insurance status, and all comorbidities. CI indicates confidence interval; and OR, odds ratio.

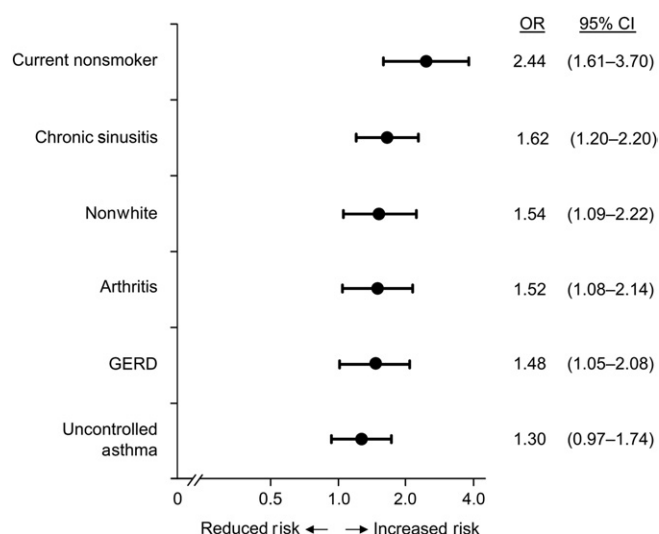


Figure 5. Environmental trigger activity limitations. Multivariable backward stepwise logistic regression was used to identify factors independently associated with allergic trigger activity limitations. The variables considered were asthma control (as measured using the Asthma Control Test), age, race/ethnicity, sex, educational level, type of residence, income, smoking status, health insurance status, and all comorbidities. CI indicates confidence interval; GERD, gastroesophageal reflux disease; and OR, odds ratio.

relationships persisted despite controlling for demographic characteristics and a spectrum of comorbid conditions.

Few studies have directly assessed the impact of asthma control across a detailed and wide range of activities. A recent cross-sectional survey of asthmatic patients from the US National Health and Wellness Survey determined that patients with controlled asthma (as defined by the ACT) experienced significantly less activity impairment, as measured using the Work Productivity and Activity Impairment questionnaire,¹⁸ than did patients with uncontrolled asthma (29% vs 51%; $P < .001$).⁷ After adjusting for demographics and comorbidity, patients with controlled asthma experienced 16.4% overall lower activity impairment than did patients with uncontrolled asthma. One limitation of the Work Productivity and Activity Impairment instrument, however, is that activity impairment is measured using only a single item and, therefore, provides little insight into different types of activity impairment outside of the workplace.

These findings, along with those of others,^{8,19,20} continue to build a growing body of evidence supporting the use of self-reported outcome measures in the assessment of asthma. The recently updated 2007 guidelines for the diagnosis and management of asthma from the National Heart, Lung, and Blood Institute⁸ place greater emphasis on the assessment of asthma control than on asthma severity and promote the use of a combination of measures, rather than any single measure, for a more complete evaluation of asthma control. This relatively new paradigm delineates components of an impairment domain, which includes symptoms and their interference with normal activity, nighttime awakenings, use of

short-acting β -agonists, and lung function. As demonstrated in this analysis, interference with normal activities was substantial for patients with moderate-to-severe asthma despite receiving standard asthma medications when assessed across a broad range of activities.

Recognizing that asthma often coexists with other disease states, we also assessed the impact of comorbidities on activity limitation in each of the models. In multivariable analyses, chronic sinusitis, depression, arthritis, hives, and GERD were each independently associated with several types of activity limitation examined and in some cases represented greater risks of activity limitation than demographic measures or uncontrolled asthma. For example, hives conferred a higher risk of outdoor activity limitation (OR, 1.92; 95% CI, 1.32–2.78) than did having no health insurance (OR, 1.85; 95% CI, 1.15–2.94), or, having an annual income of less than \$75,000 (OR, 1.43; 95% CI, 1.02–2.00); chronic sinusitis (OR, 1.62; 95% CI, 1.20–2.20), arthritis (OR, 1.52; 95% CI, 1.08–2.14), and GERD (OR, 1.48; 95% CI, 1.05–2.08) each conferred a higher risk of environmental trigger activity limitation than did uncontrolled asthma (OR, 1.30; 95% CI, 0.97–1.74).

Depression was particularly prevalent in the study cohort, with more than 25% of patients reporting depression. Asthmatic patients are known to be at greater risk for depression compared with the general population.^{21–23} Furthermore, asthmatic patients who report a history of depressive symptoms have significantly worse functional status than do those without symptoms of depression.²⁴ The relationship between asthma and depression is complex, and it remains unclear whether those conditions share physiologic etiologies or whether depression develops in response to asthma. Currently, the US Preventive Services Task Force recommends screening for depression for all adults as part of routine health maintenance. The present results suggest that for patients with asthma, screening and treatment for uncontrolled asthma and depression are particularly important to alleviate activity limitations and to guide a comprehensive approach to health and wellness.

The presence of hives has also been associated with significantly lower scores on physical functioning domains of standard quality of life assessments.²⁵ Thus, hives may contribute significantly to activity limitations reported by asthmatic patients who have both conditions. Arthritis, sinusitis, and GERD are also frequently reported comorbidities in asthma.^{26–30} We found that patients in the REACT study with any of these conditions were likely to report limitations in 1 or more of the activity limitation categories. Whether activity limitations associated with these coexisting conditions are mediated by lack of asthma control remains controversial.³¹

It is possible that some of the activity limitations that patients in the REACT study perceived to be due to asthma were, in fact, due to or confounded by the presence of these comorbid conditions. Although we attempted to adjust for common comorbidities in each of the models, the possibility of residual confounding remains.

We also considered the relationship between demographic characteristics and activity limitations in asthma. The associations observed between female sex, nonwhite race, lack of health insurance, and annual income less than \$75,000 and increased risk of activity limitations are consistent with results reported in other studies.^{24,32–36} Patients in the REACT study who were nonsmokers were more than twice as likely to limit their outdoor activity and activities involving environmental triggers. One potential explanation for this finding is that nonsmokers are more likely to limit activities that could expose them to environmental triggers, such as tobacco smoke, to which they may be more sensitive. In the case of environmental triggers, we found that nonsmoking status was associated with activity limitation, but that uncontrolled asthma was not. When we performed sensitivity analyses excluding the item “going places with cigarette smoke,” we found that uncontrolled asthma became a significant predictor of activity limitation, while the association between nonsmoking status and activity limitation was lost. Thus, the inability to demonstrate a relationship between uncontrolled asthma and environmental trigger activity limitation in the primary analyses may be due to the fact that nonsmokers with controlled asthma are more likely to limit their participation in activities that may involve exposure to secondhand smoke.

Other limitations inherent in the study design must also be considered. The REACT study was designed as a national survey, and, therefore, assessments of activity limitation were based on self-report, which could be compromised by patients’ ability to accurately recall or communicate medical information. Furthermore, the REACT study population was selected from a Web-based cohort and, therefore, could be biased toward persons who had computer access and were willing to take the time to complete the survey. However, an estimated 70% of the US population was using the Internet in 2005, and 1 in 4 people currently have Internet access in the world.³⁷ The sheer size of the online panel (4 million participants in the United States) helps ensure a demographically diverse sample of Internet users, which can be additionally balanced and weighted to ensure the representativeness of the target population of interest. In addition, similar types of bias are common in most studies using random-digit dialing and other survey methods.¹¹ Finally, the ACT was used as the primary questionnaire to assess asthma control and implements a 4-week recall period. It may have been more appropriate to use the modified Asthma Control Questionnaire, which is reflective across the past week and may be a more accurate indicator of asthma control.

In summary, we found that uncontrolled asthma was associated with a range of different types of activity limitation in moderate-to-severe asthmatic patients receiving standard asthma medications. These results indicate that the goal of asthma therapy (ie, the maintenance of normal activity levels) is not being achieved in many patients³² and highlight the importance of assessing activity limitations as part of the routine clinical management of asthma. Moreover, these findings suggest that comorbidities contribute significantly to

activity limitations in asthma. Consequently, physicians who treat asthmatic patients may also need to evaluate and treat comorbid conditions to effectively minimize activity limitations.

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