

*Original article***Real-world Evaluation of Asthma Control and Treatment (REACT): Findings from a national Web-based survey**

Stephen P. Peters, MD, PhD,^a Craig A. Jones, MD,^b Tmirah Haselkorn, PhD,^c
David R. Mink, MS,^d David J. Valacer, MD,^c and Scott T. Weiss, MD^e *Winston-Salem, NC,
Los Angeles, South San Francisco, and San Francisco, Calif, and Boston, Mass*

Background: Despite health initiatives for advancing the management of asthma, evidence suggests that many asthmatic subjects have uncontrolled disease. However, the prevalence of uncontrolled asthma in the United States is not known and has not been fully characterized.

Objective: We sought to assess the prevalence, morbidity, and factors associated with uncontrolled asthma in a nationally representative sample of patients with moderate-to-severe asthma using standard asthma medications.

Methods: A Web-based survey was administered to patients with diagnoses of asthma for at least 1 year who were receiving multiple controller medications. The Asthma Control Test score was used to stratify respondents into controlled and uncontrolled cohorts.

Results: A total of 1812 patients were assessed; 809 (45%) had controlled asthma, and 1003 (55%) had uncontrolled asthma. Most patients had health care coverage and received care from a general practitioner; a large proportion of patients with

controlled asthma (74%) and patients with uncontrolled asthma (65%) reported never receiving an asthma action plan. Inhaled corticosteroid plus long-acting β -agonist was the most common medication regimen in patients with controlled asthma (60%) and patients with uncontrolled asthma (48%) patients. Patients with uncontrolled asthma reported significantly higher rates of health care use. Several comorbidities were predictive of uncontrolled asthma.

Conclusion: Uncontrolled asthma is highly prevalent (55%) in patients using standard asthma medications. There is need for improved asthma care in patients with moderate-to-severe asthma, including a global evaluation of asthma control, implementation of treatment plans and asthma control tests, and addressing comorbid conditions.

Clinical implications: Improved asthma care requires broader assessments of asthma control, including asthma-related health care and medication use, comorbidities, and the implementation of treatment plans and formal asthma control tests. (*J Allergy Clin Immunol* ■■■■;■■■:■■■-■■■.)

Key words: Asthma control, asthma action plan, health survey, epidemiology, comorbidity

From ^athe Center for Human Genomics and the Department of Internal Medicine, Section on Pulmonary, Critical Care, Allergy and Immunologic Diseases, Wake Forest University School of Medicine, Winston-Salem; ^bthe Division of Allergy and Immunology, Department of Pediatrics, Los Angeles County and University of Southern California Medical Center, Los Angeles; ^cGenentech, Inc., South San Francisco; ^dOvation Research Group, San Francisco; and ^ethe Channing Laboratory, Center for Genetics and Genomics, Brigham & Women's Hospital, Harvard Medical School, Boston.

Supported by Genentech, Inc, South San Francisco, Calif.

Disclosure of potential conflict of interest: S. P. Peters has consulting arrangements with and is on the speakers' bureau for Genentech and Novartis. C. A. Jones has consulting arrangements with Genentech, Merck, Sanofi-Aventis, and AstraZeneca; has received grant support from Genentech and Merck; and is on the speakers' bureau for Genentech, Merck, Sanofi-Aventis, and AstraZeneca. T. Haselkorn has consulting arrangements with Genentech. D. R. Mink is employed by Ovation Research Group, which receives grant support from Genentech. D. J. Valacer owns stock in Genentech and General Electric and is employed by Genentech. S. T. Weiss has consulting arrangements with Glaxo-Wellcome, Roche Pharmaceuticals, Millennium Pharmaceuticals, Genentech, Schering-Plough, Variagics, Genome Therapeutics, and Merck Frost and has received grant support from Glaxo-Wellcome, AstraZeneca, and Pfizer.

Received for publication September 1, 2006; revised March 20, 2007; accepted for publication March 22, 2007.

Reprint requests: Stephen P. Peters, MD, PhD, Center for Human Genomics and Department of Internal Medicine, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157. E-mail: sppeters@wfubmc.edu.

0091-6749/\$32.00

© 2007 American Academy of Allergy, Asthma & Immunology

doi:10.1016/j.jaci.2007.03.022

During the last 15 years, important advances in therapies to control asthma symptoms and exacerbations have emerged. Concurrently, the National Asthma Education and Prevention Program has attempted to promote awareness through education and to advance therapeutic standards with an emphasis on daily preventive management as opposed to episodic care.¹

Despite these efforts, asthma-related morbidity remains high, continuing to have a significant effect on patients' quality of life.² In 2003, asthma caused approximately 24.5 million missed work days for adults, 12.7 million physician office visits, and 1.2 million outpatient visits.³ Health care use for severe asthma exacerbations also remains high, with an estimated 1.9 million asthma-related visits to emergency departments in 2002.³

These data suggest that many patients with asthma remain poorly controlled, despite nationally promoted treatment standards and improved therapeutic agents. Results from the Asthma in America survey conducted in 1998 suggested there were significant gaps between treatment goals and current asthma control levels in the United States.⁴ In that landmark survey, 9% had been

Abbreviations used

ACT: Asthma Control Test
 GERD: Gastroesophageal reflux disease
 REACT: Real-World Evaluation of Asthma Control and Treatment

hospitalized, 23% had received emergency care, and 32% had missed school/work in the previous year.⁴

Reasons for this paradox (recurrent serious asthma exacerbations despite an emphasis on preventive care) are not entirely understood. The primary objective of the Real-World Evaluation of Asthma Control and Treatment (REACT) study was to assess the prevalence of uncontrolled asthma in the United States in a nationally representative sample of patients with moderate-to-severe asthma receiving standard asthma medications. The secondary objective was to characterize uncontrolled asthma in a real-world setting of treated patients by assessing morbidity and factors associated with uncontrolled disease. We hypothesized that the populations with uncontrolled and controlled moderate-to-severe asthma would differ with respect to demographics and comorbidities. Additionally, we hypothesized that some of these variables would remain associated with control after multivariable adjustment.

METHODS

Study design

Greenfield Online. Greenfield Online is a primary research company that maintains global research panels for the purpose of executing research studies for nonprofit and for-profit companies, government agencies, and academic organizations. The Greenfield Online panel is among the largest Web-based survey cohorts in the world, containing nearly 4 million participants in the United States.⁵ Members voluntarily opt into Greenfield Online and are recruited from a diverse pool of sources, including Internet portals, special interest Web sites, and age- and ethnicity-focused Web sites. Each respondent is assigned a unique respondent ID, and information provided to Greenfield Online is kept under strict confidentiality. Online research panels, such as Greenfield, have grown dramatically over the past 10 years in response to the growing number of Internet users and the decrease in cooperation rates with more traditional survey methods, such as random-digit dialing.⁶ An estimated 75% of the US population was online in 2004,⁷ and in 2005, the Internet population was estimated at 1 billion.⁷ The sheer size of the online panel 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.

Sampling process overview. In early 2005, Greenfield Online sent invitations to a stratified random sample of 250,000 adult (≥ 18 years) census-representative panelists from the general population to participate in a screening survey. The asthma status of these panelists was not known beforehand. Of the 250,000 invitees, 48,431 respondents completed a screening survey (see Fig E1 in the Online Repository at www.jacionline.org) and were weighted to match the 2000 US Census (and to adjust for response bias) by using a direct standardization approach.^{8,9} This technique, used in epidemiologic

TABLE I. Inclusion and exclusion criteria for the REACT Study

Inclusion criteria

- Diagnosed with asthma at least 1 y ago by a physician
- Currently taking prescription medications for treatment of asthma

In addition, subjects had to meet at least one of the following criteria:

- Currently using oral steroids (minimum of 2 courses in past 12 mo)
- Currently using short-acting β -agonist plus at least 2 long-term controllers

Exclusion criteria

- Emphysema or chronic bronchitis
- Participation in asthma-related research study within previous 3 mo

research, removes the effects of differences in age or other confounding variables, such as sex, race, and socioeconomic status, when comparing 2 populations. Specific rates in a study population are averaged by using the distribution of a specific standard population as weights (in this case the 2000 US Census). This approach effectively adjusts for potential response bias in the event that those responding to the survey differ from those who do not respond.

Of the 48,431 respondents screened, 1118 met the screening and asthma medication inclusion criteria (Table I) and were included for final analysis. Additional patients with asthma ($n = 694$) were recruited from a "condition-sufferer panel" to supplement the initial sample. All respondents were asked to fill out an observational, cross-sectional questionnaire regarding demographics, comorbidities, health care use, and attitudes and behaviors toward asthma. Because additional respondents were added, the final combined sample of 1812 respondents was reweighted using methods for weighting an unequal probability sample¹⁰ to match the demographic profile of the 2000 US Census based on age, sex, race/ethnicity, region, and household income. This weighting approach inherently adjusted for lower numbers of economically disadvantaged respondents that were not captured because of lower rates of computer ownership and Internet access among the underserved. A flowchart depicting the sampling process is provided in Fig E2 (available in the Online Repository at www.jacionline.org).

Respondents

Respondents were eligible for the REACT study if they met the inclusion and exclusion criteria summarized in Table I. For asthma medication use, respondents were included if they were taking (1) an oral steroid (minimum of 2 courses in the past 12 months) or (2) a short-acting β -agonist and at least 2 additional long-term controllers, suggesting moderate-to-severe persistent asthma (as defined by 2004 Global Initiative for Asthma guidelines, steps 3 and 4, respectively). Long-term controller use was based on patient selection from 4 medication categories (inhaled corticosteroids, long-acting β -agonists, leukotriene modifiers, and methylxanthines) and an option indicating oral steroid use. Of the 1812 patients included in the REACT study, only 1.1% were not taking either an inhaled corticosteroid or had 2 courses of oral steroids.

A total of 1909 patients met the inclusion criteria for the study. Respondents who checked the same response value on greater than 70% of the questions were removed ($n = 77$). Additionally, patients who did not complete the 5-item Asthma Control Test (ACT) were excluded ($n = 20$), resulting in a total of 1812 respondents in the final sample.

Statistical analysis

A respondent's level of asthma control was based on the 5-item ACT; a score of 5 to 19 indicated that the respondent's asthma were uncontrolled, and a score of 20 to 25 indicated that the respondent's asthma were controlled.¹¹ Univariable logistic regression was used to assess the association between each individual variable and the binary outcome measure of asthma control; stepwise multiple logistic regression was then used to assess which variables were independently associated with asthma control. Five key demographic variables (age, race, sex, household income, and education) were forced into the model, whereas remaining factors were entered into the model one at a time if they met the model inclusion α level threshold of 0.05. Odds ratios, 95% CIs, and *P* values based on the Wald χ^2 test were computed by using SAS PROC SURVEYLOGISTIC. No adjustments were made for multiple comparisons. All analyses were conducted with SAS version 9.1 software (SAS Institute, Inc, Cary, NC).

RESULTS

Univariate analysis

A total of 1812 patients were included in this study; of these patients, 809 (45%) had controlled asthma, and 1003 (55%) had uncontrolled asthma. Demographics and disease characteristics for these patients are shown in Table II. Patients with controlled and uncontrolled asthma were similar with regard to age, race/ethnicity, and type of residence. A higher proportion of female than male patients was seen in both groups, but among male patients, a higher proportion was in the uncontrolled group. Patients with uncontrolled asthma were less educated and had somewhat lower household incomes. A high percentage of patients in both groups had health care coverage (88% of patients with controlled asthma and 86% of patients with uncontrolled asthma, *P* = not significant). Type of health care plan did not differ between the 2 groups; the majority had private insurance (preferred provider organization and health maintenance organization, *P* = not significant for all comparisons; see Fig E3 in the Online Repository at www.jacionline.org). Patients with uncontrolled asthma were more likely to have full medication coverage, whereas patients with controlled asthma were more likely to have a copayment for their prescription medication.

About 17% of patients in each group were current smokers. More than half of patients with uncontrolled asthma and 38% of patients with controlled asthma reported having had an asthma attack during which they feared for their lives. About one third of patients with uncontrolled asthma and about one fourth of patients with controlled asthma reported ever receiving a personalized asthma action plan from their physician as part of their asthma care.

There were no differences in treating physician specialty between patients with controlled and uncontrolled asthma; the majority in both groups was under the care of a family physician or internist for their asthma (*P* = not significant for all comparisons, Fig 1). Most patients (60.6% of patients with controlled asthma and 84.6% of patients

TABLE II. Patient demographics and disease characteristics for 809 patients with controlled asthma versus 1003 patients with uncontrolled asthma*

Characteristic	Controlled asthma	Uncontrolled asthma	<i>P</i> value
Age (y)			
18-24	14.1	15.7	NS
25-34	17.5	21.8	
35-44	20.5	23.3	
45-54	22.4	18.7	
55-64	11.6	9.2	
≥65	14.0	11.4	
Sex			.04
Male	36.5	43.6	
Female	63.5	56.4	
Race/ethnicity			
White	70.7	62.8	NS
Black/African American	9.1	10.7	
Hispanic	12.3	20.0	
Asian	4.7	3.3	
Native American	1.1	1.0	
Prefer not to say	2.1	2.3	
Education†			
Less than college	51.2	61.5	.003
College or more	48.8	38.5	
Type of residence			NS
Urban	24.3	29.0	
Suburban	53.4	48.7	
Rural	22.3	22.3	
Household income			
before taxes			
<\$75,000	70.2	77.3	.02
≥\$75,000	29.8	22.7	
Health insurance coverage	88.0	85.8	NS
Type of insurance			NS
HMO	27.7	27.2	
PPO	36.0	30.0	
Traditional	12.1	12.2	
Medicare	15.3	17.5	
Medicaid	4.7	7.8	
Other	4.2	5.4	
How health insurance covers:			.001
Cost of prescription drugs			
No coverage	4.6	6.9	
Full coverage	7.1	17.4	
Requires copayment	75.6	62.8	
Depends on medication	12.7	12.9	
Current cigarette smoking	16.8	17.4	NS
Asthma attack that caused fear for life	37.9	54.0	<.0001
Ever received a personalized asthma action plan from physician for asthma management	26.4	34.9	.008

NS, Not significant; HMO, health maintenance organization; PPO, preferred provider organization.

*Data are presented as weighted percentages.

†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.

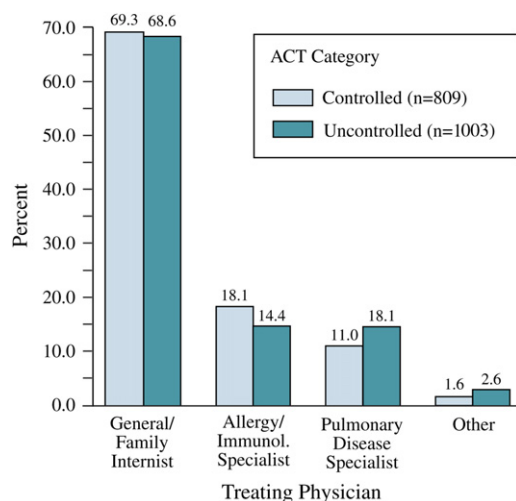


FIG 1. Treating physician for patients with controlled asthma and uncontrolled asthma. There were no statistically significant differences in treating specialty between the controlled and uncontrolled groups.

with uncontrolled asthma, $P < .0001$) visited their primary caregiver 2 or more times in the past year for their asthma, with some patients visiting 7 or more times (4.4% of patients with controlled asthma and 13.3% of patients with uncontrolled asthma, $P < .0001$).

In general, medication regimens most commonly used in patients with controlled asthma and patients with uncontrolled asthma were similar; the majority in each group (60% of patients with controlled asthma and nearly 50% of patients with uncontrolled asthma) were taking an inhaled corticosteroid and long-acting β -agonist (Fig 2). About 20% of patients with controlled asthma and 18% of patients with uncontrolled asthma were taking an inhaled corticosteroid, long-acting β -agonist, and leukotriene modifier. However, about twice as many patients with uncontrolled asthma were taking an oral steroid alone or in combination with another medication compared with patients with controlled asthma (17% vs 8%, respectively; $P < .0001$). More than half (56.6%) of patients with uncontrolled asthma and about a third (29.6%) of patients with controlled asthma reported taking their asthma medications more frequently than prescribed.

Patients with uncontrolled asthma were significantly more likely to have gastroesophageal reflux disease (GERD; 30.7% vs 22.3%, $P = .006$) and chronic sinusitis (29.9% vs 22.9%, $P = .02$); there was borderline significance for high blood pressure (32.6% vs 26.2%, $P = .05$). The proportion of patients with controlled asthma and patients with uncontrolled asthma with each condition who were being treated with a prescription medication for their comorbidity was comparable (data not shown). The full range of comorbidities tested is available in Table E1 (available in the Online Repository at www.jacionline.org).

Patients with uncontrolled asthma reported significantly higher rates of health care use than patients with

controlled asthma for all measures (Table III). The proportion of patients reporting 2 or more emergency department visits or hospitalizations or 3 or more missed days of work/school because of their asthma in the past year was more than 3 times greater in patients with uncontrolled asthma than in patients with controlled asthma ($P < .0001$ for each health care use comparison); patients with uncontrolled asthma also demonstrated significantly higher rates of unscheduled physician's office visits ($P < .0001$).

Multivariable analysis

Multivariable analysis of the demographics and comorbid conditions described above identified several independent factors associated with uncontrolled asthma. Younger age, Hispanic race, male sex, lower income, and lower education level were each individually associated with increased risk of uncontrolled disease (Table IV). Chronic sinusitis, high blood pressure, and GERD were independently associated with uncontrolled asthma. Interactions between race and other socioeconomic variables (ie, education and household income) were tested, and none were detected.

DISCUSSION

To our knowledge, the REACT study is the first to assess the prevalence of uncontrolled asthma in the United States in a nationally representative sample of asthma patients taking standard asthma medications. It is also the first study to use multivariable analyses to examine factors associated with uncontrolled disease in a nationally representative sample of treated American asthma patients. Because patients with more severe asthma confer the highest economic burden in asthma care,^{12,13} we focused on patients in the United States who were using 2 or more controller medications, suggesting moderate persistent asthma or severe persistent asthma according to the 2004 Global Initiative for Asthma guidelines, steps 3 and 4, respectively.¹⁴

We observed a high rate of uncontrolled asthma (55%) and health care use, despite evidence of receiving care in accordance with currently accepted guidelines. We also identified certain demographics and comorbidities independently associated with uncontrolled disease, including GERD, chronic sinusitis, and high blood pressure. Unlike previous studies that focused primarily on burden of disease in patients with low socioeconomic status and limited access to health care, this study assessed asthma-related morbidity patterns in a population with health care coverage who reported regular visits to their physician and who were receiving standard asthma medications. Findings in this study are also generalizable to the US population. According to the US Census Bureau, the estimate of the uninsured population in the United States is 46.6 million.¹⁵ Applying the current US population estimate of 300 million to this figure, 15.5% of Americans are uninsured, or alternatively, 84.5% are insured. Our estimate of 86% to 88% insured in the REACT study is

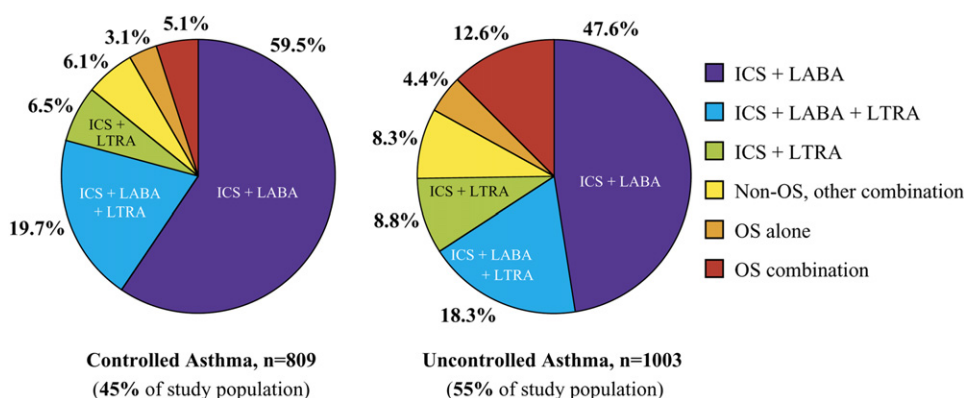


FIG 2. Asthma medication regimens for patients with controlled asthma ($n = 809$) and patients with uncontrolled asthma ($n = 1003$). The medication regimens most commonly used in each group were similar; the majority of patients were taking an inhaled corticosteroid (*ICS*) and long-acting β -agonist (*LABA*). Approximately twice as many patients with uncontrolled asthma were taking an oral steroid (*OS*) alone or in combination with another medication ($P < .0001$). *LTRA*, Leukotriene modifiers.

TABLE III. Health care use and missed work/school in 809 patients with controlled asthma and 1003 patients with uncontrolled asthma

Patients*	Controlled asthma	Uncontrolled asthma	P value
Unscheduled physician office visits due to asthma in past year			
0 (none)	57.0	29.8	<.0001
1-2	31.1	39.0	
≥ 3	11.8	31.2	
ED visits due to asthma in past year			
0 (none)	89.9	64.0	<.0001
1	5.5	18.6	
≥ 2	4.6	17.4	
Hospitalizations due to asthma in past year			
0 (none)	96.7	85.6	<.0001
1	2.4	8.7	
≥ 2	0.9	5.7	
Missed days of work/school in past year			
0 (none)	75.7	47.1	<.0001
1-2	14.4	17.0	
≥ 3	9.9	36.0	

*Data are presented as weighted percentages.

TABLE IV. Multivariable analysis for demographics and comorbid conditions for 809 patients with controlled asthma and 1003 patients with uncontrolled asthma*

Variable	Odds ratio	95% CI	P value
Age (y)			
18-44 vs ≥ 45	1.61	1.20-2.17	.002
Race			
Black/African American vs white	1.34	0.80-2.25	NS
Hispanic vs white	1.82	1.06-3.14	.03
Asian vs white	0.81	0.43-1.52	NS
Native American vs white	0.87	0.30-2.56	NS
Other vs white	1.20	0.55-2.63	NS
Sex			
Male vs female	1.59	1.19-2.13	.002
Household income			
<\$75,000 vs $\geq$ \$75,000	1.42	1.03-1.96	.03
Education†			
Less than college vs college or more	1.59	1.20-2.11	.001
Chronic sinusitis			
Yes vs no	1.45	1.06-1.99	.02
High blood pressure			
Yes vs no	1.54	1.10-2.15	.01
GERD			
Yes vs no	1.51	1.09-2.10	.01

NS, Not significant.

*Higher odds ratio indicates a greater likelihood of having uncontrolled asthma.

†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.

comparable, suggesting results described in this report can be extrapolated to the US population.

Results from recent clinical trials¹⁶⁻¹⁹ suggest that asthma control can be achieved in a subset of a carefully tracked study population. In a 1-year prospective trial (the Gaining Optimal Asthma Control Study), after stepping up treatment, almost 30% of patients who received salmeterol and high-dose fluticasone were unable to

meet the criteria for well-controlled asthma.¹⁶ Another study evaluating patients with moderate asthma demonstrated substantial variability in the proportion of asthma control days achieved with either beclomethasone or montelukast.¹⁹ With either class of medication, approximately

one third of the patients appeared to be unresponsive. In a similar 12-week trial, approximately one third had no improvement in their FEV₁ values when treated with either beclomethasone or montelukast.¹⁷

Although the populations vary, this study provides an ideal reference for assessing whether results of these clinical trials are supported in a real-world setting. Our results indicate that uncontrolled asthma remains highly prevalent (55%). This suggests that clinicians should expect a high rate of uncontrolled disease among patients with asthma, regardless of their economic status, treatment regimen, or frequency of physician visits. Our data also corroborate reports by others who used the ACT score of 19 or less for detecting a high prevalence of patients with uncontrolled asthma^{20,21} and suggest that the ACT might be a useful tool to identify patients with uncontrolled asthma in whom excessive health care use might be expected.

An important finding was the rate of severe asthma attacks despite access to care and recommended therapies. Greater than 50% of subjects with uncontrolled asthma and 38% of subjects with controlled asthma reported having an asthma attack of such severity that they thought their lives were in danger. These results highlight the importance of providing patients with clear information on how to respond to a severe asthma attack. Written asthma action plans have been associated with decreased emergency department visits, fewer hospitalizations, and improved lung function.^{22,23} Notable was the finding that 74% of patients with controlled asthma and 65% of patients with uncontrolled asthma reported never having received an asthma action plan from their physician.

We observed a high frequency of uncontrolled disease, irrespective of the type of treating physician, suggesting that poorly controlled asthma may prevail in both primary care and specialty care settings. Another notable finding was that chronic sinusitis, high blood pressure, and GERD were independently associated with uncontrolled asthma. Previously published information supports these findings in this study, particularly the high rate of sinusitis and GERD associated with asthma.²⁴⁻²⁷ Association between high blood pressure and poorly controlled asthma is not well established and might warrant further investigation. It is possible that treatment for high blood pressure with β -blockers could reduce asthma control. Alternatively, angiotensin-converting enzyme inhibitors could cause cough that could either worsen asthma or increase the perception of uncontrolled asthma.

Multivariable analysis also revealed that younger age, Hispanic race, male sex, lower income, and lower education were independent factors associated with uncontrolled disease. To our knowledge, the REACT study is the first population-based study of a treated cohort of asthmatic patients to assess the relationship between these variables and uncontrolled asthma. Interestingly, despite the REACT cohort representing a population with access to health care, lower income and lower education, consistent factors associated with asthma and more severe disease in other populations,²⁸⁻³¹ were significantly associated with uncontrolled disease in our study. These data

suggest that improved health literacy could increase the proportion of patients with controlled asthma.

Currently, there is no effective or accurate manner in which to measure true asthma medication adherence. Medication regimens for asthma care pose particular adherence problems because of their duration, use of multiple medications, and periods of symptom remission.³² As such, nonadherence in children and adults with asthma is common,^{32,33} and rates have been reported to range from 30% to 70%.³² It is possible that some of the uncontrolled disease seen in the REACT study might be due to poor adherence; however, an accurate and objective measure of adherence was not feasible given the cross-sectional and self-reported nature of data collection.

Although true adherence with medications in this study is not known, several observations can be made. First, most patients had not received a written management plan, a factor that could influence adherence. Our results also indicate that asthmatic patients demonstrate variability in asthma control, even when asthma medications are reported to be easily available and when patients are visiting their asthma-care physician on a regular basis. Furthermore, our study results indicate that uncontrolled asthma does not appear to track with any one pharmacologic treatment approach. The fact that more than half of patients with uncontrolled asthma reported taking their asthma medications more frequently than prescribed might reflect poorly controlled asthma and an effort to relieve symptoms.

Our survey results underscore the need for greater emphasis on the management of patients with uncontrolled asthma. Clinicians should be aware that a significant proportion of patients have uncontrolled disease, despite treatment in accordance with established guidelines. It is well established that pulmonary function testing and current asthma symptoms alone might not accurately reflect the level of asthma severity or control.^{27,34-39} Our findings support the need for a more global ongoing assessment of asthma severity and control, including asthma-related health care use and medication use. Additionally, a formal asthma control assessment (using such instruments as the ACT) should be conducted at each clinical visit, with comparative assessments over time to improve the likelihood of achieving optimal asthma control.

One of the limitations of this study is the accuracy of self-reported data, such as when reporting comorbidities, which might vary with the patient's ability to recall specific information. Different levels of computer expertise among respondents can also be a source of error or nonresponse. Participants willing to take the time to complete the survey might not represent the typical computer user in the general public.⁶ However, it would be expected that such potential response bias would also be intrinsic to random-digit dialing and other survey methodologies. Current research suggests that online users are starting to mirror the US Census.⁵ The ability to obtain representative samples using more traditional sampling methods, such as random-digit dialing, is becoming

increasingly difficult because of low cooperation rates and advances in communications technology (eg, multiple phone lines, call screening, blocking, beepers, and cellular/mobile phones). Only a small percentage of random-digit dialing surveys currently obtain a response of greater than 70%, and surveys that involve household screening have even lower overall response rates.⁴⁰

Data once collected by using other survey methods are now being collected in large-scale Web-based surveys.⁴¹ The Internet allowed us to access a very large number of survey respondents. The growing use of Internet users (47% increase between 2000 and 2003),⁴² with 75% of Americans using the Internet in 2004,¹¹ provides survey researchers with a large population of willing participants. Web-based research offers the ability to ensure the representativeness of Internet users and the US population by using samples from panels that include millions of individuals (≥ 3.4 million US adults, roughly 1.5% of all US adults in our study). In addition, these samples can be balanced and weighted, as was done in the current study, to ensure proper representation of the overall population of interest, as defined by current American population demographics. Web-based surveys also allow higher and faster response rates compared with other types of surveys.⁶

Asthma-related morbidity remains high, despite a concerted effort by the National Asthma Education and Prevention Program and other organizations to promote awareness through education and to advance therapeutic standards with emphasis on daily preventive management. The REACT study shows that even with access to health care, patients prescribed therapy that is recommended for moderate-to-severe asthma still demonstrate high rates of uncontrolled asthma (55%). Our survey results highlight the critical need for improved asthma care, including a more global evaluation of asthma control, implementation of asthma treatment plans, and addressing comorbid conditions (GERD, chronic sinusitis, and high blood pressure) as interventions to improve asthma control in patients with moderate-to-severe asthma.

We thank James E. Fish, MD, of Genentech, Inc, for his contributions to the article and Dave P. Miller, MS, of Ovation Research Group, for his statistical expertise. Writing assistance for this article was provided by Genentech, Inc.

REFERENCES

- National Institutes of Health. Guidelines for the diagnosis and management of asthma: update on selected topics 2002. Bethesda (MD): National Heart Lung and Blood Institutes; 2002. NIH publication no. 02-5075.
- Ehrs P, Nokela M, Stallberg B, Hjendahl P, Wikstrom J. Brief questionnaires for patient-reported outcomes in asthma: validation and usefulness in a primary care setting. *Chest* 2006;129:925-32.
- American Lung Association, Epidemiology and Statistics Unit, Research and Program Services. Trends in asthma morbidity and mortality. Available at: <http://www.lungusa.org>. Accessed November 30, 2006.
- Asthma in America: a landmark survey. Executive summary. Research Triangle Park (NC): GlaxoWellcome. Available at: <http://www.asthmainamerica.com/>. Accessed November 30, 2006.
- Greenfield Online Panel. 2004-2005. Available at: <http://www.greenfield.com/rcpanelbook.htm>. Accessed November 30, 2006.
- Wilson A, Laskey N. Internet based marketing research: a serious alternative to traditional research methods? *Marketing Intell Plann* 2003;21:79-84.
- Nielson Net Ratings. Enumeration study, February 2004. Available at: http://www.nielson-netratings.com/pr_040318.pdf. Accessed November 30, 2006.
- Szklo M, Nieto J. *Epidemiology, beyond the basics*. Gaithersburg (MD): Aspen Publishers, Inc; 2000.
- Last JA. *A dictionary of epidemiology*, 4th ed. New York (NY): Oxford University Press; 2001.
- Lohr SL. *Sampling design and analysis*. Pacific Grove (CA): Duxbury Press; 1999.
- Nathan R, Sorkness C, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test: a survey for assessing asthma control. *J Allergy Clin Immunol* 2004;113:59-65.
- Cisternas MG, Blanc PD, Yen IH, Katz PP, Earnest G, Eisner MD, et al. A comprehensive study of the direct and indirect costs of adult asthma. *J Allergy Clin Immunol* 2003;111:1212-8.
- Sullivan SD, Rasouliyan L, Russo PA, Kamath T, Chipps BE, for the TENOR Study Group. Extent, patterns, and burden of uncontrolled disease in severe or difficult-to-treat asthma. *Allergy* 2007;62:126-33.
- Global Initiative for Asthma (GINA). A pocket guide for physicians and nurses. Updated 2004. Available at: www.ginasthma.com. Accessed November 30, 2006.
- DeNavas-Walt C, Proctor BD, Lee CH. U.S. Census Bureau, current population reports, P26. Income, poverty, and health insurance coverage in the United States: 2005. Washington (DC): US Government Printing Office; 2006.
- Bateman ED, Boushey HA, Bousquet J, Busse WW, Clark TJ, Pauwels RA, et al. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma Control study. *Am J Respir Crit Care Med* 2004;170:836-44.
- Malmstrom K, Rodriguez-Gomez G, Guerra J, Villaran C, Pineiro A, Wei LX, et al. Oral montelukast, inhaled beclomethasone, and placebo for chronic asthma. A randomized, controlled trial. Montelukast/Beclomethasone Study Group. *Ann Intern Med* 1999;130:487-95.
- Szefer SJ, Martin RJ, King TS, Boushey HA, Cherniack RM, Chinchilli VM, et al. Significant variability in response to inhaled corticosteroids for persistent asthma. *J Allergy Clin Immunol* 2002;109:410-8.
- Israel E, Chervinsky PS, Friedman B, Van Bavel J, Skalky CS, Ghannam AF, et al. Effects of montelukast and beclomethasone on airway function and asthma control. *J Allergy Clin Immunol* 2002;110:847-54.
- Lenoir M, Williamson A, Stanford RH, Stempel DA. Assessment of asthma control in a general population of asthmatics. *Curr Med Res Opin* 2006;22:17-22.
- Schatz M, Sorkness CA, Li JT, Marcus P, Murray JJ, Nathan RA, et al. Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. *J Allergy Clin Immunol* 2006;117:549-56.
- Gibson P, Powell H, Coughlan J, Wilson AJ, Abramson M, Haywood P, et al. Self-management education and regular practitioner review for adults with asthma. *Cochrane Database Syst Rev* 2004;(1):CD001117.
- Bunting BA, Cranor CW. The Asheville Project: long-term clinical, humanistic, and economic outcomes of a community-based medication therapy management program for asthma. *J Am Pharm Assoc (Wash)* 2006;46:133-47.
- The ENFUMOSA Study Group. The ENFUMOSA cross-sectional European multicentre study of the clinical phenotype of chronic severe asthma. European Network for Understanding Mechanisms of Severe Asthma. *Eur Respir J* 2003;22:470-7.
- Ben-Noun L. Characteristics of comorbidity in adult asthma. *Public Health Rev* 2001;29:49-61.
- Singh K, Nain CK, Sharma BC, Jindal SK. Silent gastroesophageal reflux in patients with bronchial asthma. *J Assoc Physicians India* 1998;46:179-81.
- Wenzel S, Szefer SJ. Managing severe asthma. *J Allergy Clin Immunol* 2006;117:508-11.
- Eisner MD, Katz PP, Yelin EH, Shibuski SC, Blanc PD. Risk factors for hospitalization among adults with asthma: the influence of sociodemographic factors and asthma severity. *Respir Res* 2001;2:53-60.
- Litonjua AA, Carey VJ, Weiss ST, Gold DR. Race, socioeconomic factors, and area of residence are associated with asthma prevalence. *Pediatr Pulmonol* 1999;28:394-401.

30. Castro M, Schechtman KB, Halstead J, Bloomberg G. Predictors for asthma morbidity and mortality in a large metropolitan city. *J Asthma* 2001;38:625-35.
31. Schatz M, Cook EF, Joshua A, Petitti D. Predictors for asthma hospitalizations in a managed care organization: development of a clinical prediction rule. *Am J Manag Care* 2003;9:538-47.
32. Rand CS, Wise RA. Measuring adherence to asthma medication regimens. *Am J Respir Crit Care Med* 1994;149(suppl):S69-76.
33. Dekker FW, Dieleman FE, Kaptein AA, Mulder JD. Compliance with pulmonary medication in general practice. *Eur Respir J* 1993;6:886-90.
34. Stoloff SW, Boushey HA. Severity, control, and responsiveness in asthma. *J Allergy Clin Immunol* 2006;117:544-8.
35. Attaining optimal asthma control: a practice parameter. *J Allergy Clin Immunol* 2005;116(suppl):S3-11.
36. Calhoun WJ, Sutton LB, Emmett A, Dorinsky PM. Asthma variability in patients previously treated with beta2-agonists alone. *J Allergy Clin Immunol* 2003;112:1088-94.
37. Apter A, Szeffler S. Advances in adult and pediatric asthma. *J Allergy Clin Immunol* 2006;117:512-8.
38. Miller MK, Johnson C, Miller DP, Deniz Y, Bleecker ER, Wenzel SE. Severity assessment in asthma: an evolving concept. *J Allergy Clin Immunol* 2005;116:990-5.
39. Teeter JG, Bleecker ER. Relationship between airway obstruction and respiratory symptoms in adult asthmatics. *Chest* 1998;113:272-7.
40. Massey J, O'Connor D, Krotki K. Response rates in random digit dialing (RDD) telephone surveys. In: 1997 proceedings of the Survey Research Method Section, American Statistical Association. Arlington (VA): American Statistical Association; 1998. p. 707-12.
41. Houston JD, Fiore DC. Online medical surveys: using the Internet as a research tool. *MD Comput* 1998;15:116-20.
42. Madden M. Pew Internet and American Life. America's online pursuits. The changing picture of who's online and what they do, 22 December 2003. Available at: www.pewinternet.org. Accessed November 30, 2006.