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Internet-Based Monitoring in the Severe Asthma Research Program Identifies a Subgroup of Patients With Labile Asthma Control

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BACKGROUND: We designed an Internet-Based Monitoring Systems (IBS) survey to facilitate monitoring of asthma symptoms and asthma exacerbations in the Severe Asthma Research Program (SARP). Our objective was to evaluate compliance with the IBS survey tool and to explore how data from an IBS tool can inform understanding of asthma phenotypes.

METHODS: We invited adult subjects in the SARP III cohort (N = 528) to complete a monthly IBS asthma control survey. We compared the characteristics of subjects who did and those who did not participate in the IBS survey tool. Among subjects who participated in the IBS (IBS+), we identified participants with low, medium, and high Asthma Control Test (ACT) score variability, and we explored asthma morbidity in these three participant subgroups.

RESULTS: Two hundred fifty-nine subjects participated in the IBS (IBS+) survey. Compared with subjects who did not engage with the IBS (IBS–) survey, IBS+ subjects were older and more likely to be white, college educated, and have an annual household income > $25,000, and have controlled asthma. Among IBS+ participants, the subgroup with the highest ACT score variability was more likely to have severe asthma, with a lower ACT score at baseline and increased asthma-related health-care use (often precipitated by cold and flulike illnesses). Participants with high ACT variability were also characterized by metabolic dysfunction, as evidenced by obesity and hypertension.

CONCLUSIONS: Active participation with an Internet-based symptom survey tool in patients with severe asthma is influenced by race, socioeconomic status, and asthma control. Among survey participants, a group with highly variable (labile) asthma control is identifiable as a specific subgroup with unmet treatment needs. The association of asthma lability, increased susceptibility to adverse asthma effects of cold and flulike illnesses, and metabolic dysfunction provides clues for potentially effective intervention strategies.

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KEY WORDS: asthma control; Internet-based monitoring; labile asthma; metabolic dysfunction; obesity

ABBREVIATIONS: ACT = Asthma Control Test; ATS/ERS = American Thoracic Society/European Respiratory Society; CV = coefficient of variation; IBS = Internet-Based Monitoring Systems; IRR = incident rate ratio; SARP = Severe Asthma Research Program

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Internet-based tools that capture information about symptoms and disease behavior facilitate real-time disease monitoring in chronic diseases.[1] Internet-Based Monitoring Systems (IBS) have the potential to improve understanding of disease behavior, especially in chronic diseases like asthma that have heterogeneous clinical phenotypes. To date, IBS use in asthma has focused largely on special populations such as children,[2] the elderly,[3] and pregnant women,[4] or have used Internet-based surveys to monitor medication compliance.[5] However, few studies have focused on applying IBS to monitor and identify asthma control phenotypes.

Our objective was to evaluate the utility of IBS as a research tool for monitoring asthma control in patients enrolled in the Severe Asthma Research Program-3 (SARP-3), a longitudinal cohort study. We designed an IBS survey tool linked to e-mail reminders, and we collected asthma control data over a 1-year observation period. Our goals were twofold. First, we sought to evaluate participant engagement with the IBS tool and the demographic and clinical characteristics of subgroups who did or did not engage with the tool. Second, we explored the demographic and clinical features of subgroups of patients with asthma with varying degrees of asthma control, with a focus on the subgroup with highly variable (labile) asthma control.

Methods

Study Participants

Data were derived from the SARP III cohort. SARP is an ongoing 3-year longitudinal cohort study consisting of 709 subjects with asthma aged 6-84 years recruited by seven clinical research sites across the United States between November 2012 and February 2015. SARP is focused on severe asthma, and 60% of subjects have American Thoracic Society/European Respiratory Society (ATS/ERS) criteria for severe disease.[6] The SARP protocol involves detailed characterization at enrollment, with biannual telephone follow-up visits and annual in-person follow-up visits for 3 years. Asthma control and asthma exacerbations are monitored prospectively using paper questionnaires during biannual encounters. In addition, shortly after the main study protocol was initiated, an IBS survey was developed and deployed to capture data about asthma control and exacerbations on a monthly basis and during exacerbations. All subjects provided written informed consent to participate in the SARP study; subjects were asked to either opt in or opt out of the IBS survey as part of main study consent (ClinicalTrials.gov: NCT01606826). Details of the baseline characterizations have been described recently,[7,8] with key protocol details relevant to this study provided further on. Only subjects > 18 years of age were included in this study. Study procedures were approved by the institutional review board at each institution and an independent data safety monitoring board.

Baseline Assessment

Baseline questionnaires captured information on demographics, socioeconomic status, medical history, and current medications. Clinical disease characterization was performed for all subjects, including a physician-directed history, asthma characterization questionnaire, Asthma Control Test (ACT) score, spirometry, methacholine challenge, CBC count with cell differential, serum IgE measurements, and fractional exhaled nitric oxide levels.

Prospective Follow-up

Follow-up information about interval health-care use for asthma was collected biannually from subjects at 6 months by telephone and at 12 months in person. Questionnaires were administered by trained clinical research coordinators and included questions about asthma-related health-care visits, including unscheduled office visits, ED visits, overnight hospitalizations, and ICU admissions. Subjects were also asked if they had experienced any exacerbations of asthma that necessitated treatment with systemic steroids. "Severe exacerbations" were defined as an exacerbation requiring an ED visit, an overnight hospitalization, or an ICU admission; and "all exacerbations" were defined as those exacerbations that met the severe criteria and also included exacerbations requiring an unscheduled visit to a physician's office or an oral corticosteroid burst, or both.

Asthma IBS Platform

Self-reported information characterizing exacerbations and periods of worsening symptoms were collected using the asthma IBS tool. The asthma IBS platform was built using online survey software (Qualtrics, Provo, UT) with branching logic that presented the user with more or fewer questions based on previous answers. All subjects who opted in to participate in the IBS survey had their e-mail addresses registered, and a link to the survey was sent at the start of each month. This link was personalized to each participant and could be used multiple times throughout each month to provide real-time updates about worsening asthma control and exacerbations. These instructions were repeated in the e-mail reminder sent each month. The survey contained 26 questions (e-Table 1) about asthma

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control and exacerbation details, including when symptoms began, identifiable triggers (e-Fig 1), and any related changes to therapy. All participants were asked a minimum of eight questions as part of the survey, including the five questions from the ACT.[9] The ACT was reproduced electronically with permission (Quality Metrics Inc.). Participants did not receive additional compensation for participating in the IBS survey. The survey was compatible with desktop computers and smart phones. In addition, one participant elected to complete the survey through monthly telephone interviews. Survey data and SARP questionnaire data captured through December 31, 2015 were included in this analysis.

Statistical Analysis

Statistical analyses were performed using JMP 12 software package (SAS Institute) and Stata, version 12.0 (StataCorp LLC), and P values $< .05$ were considered statistically significant. Two group comparisons between participants who engaged with the IBS platform and those who did not were made using the Student t test for continuous variables meeting the distributional assumption for the t test, the Wilcoxon rank-sum test for continuous variables not meeting those assumptions, and a Fisher exact test for categorical variables. We calculated kappa statistics to quantify agreement between methods to monitor asthma exacerbations between the biannual SARP follow-up asthma exacerbation questionnaire and the IBS tool.

Poisson regression models using robust error variance[10] were constructed to identify the clinical characteristics associated with IBS nonengagement. The binary outcome variable in these models was IBS nonengagement (0 = IBS engagement or IBS+, 1 = IBS nonengagement or IBS–). The predictor variables in these models included all variables that were significantly different between IBS– and IBS+ subjects in an initial unadjusted bivariate analysis ($P < .05$). Results of the final model are presented as incident rate ratios (IRRs) and 95% CIs.

Participants who were enrolled in the platform for at least 12 months and completed at least two surveys in their first year of platform enrollment were included in a secondary analysis to associate variability of asthma control with baseline characteristics and prospective monitoring of exacerbations and periods of worsening asthma control. The coefficient of variation (CV) of the ACT score was calculated for each participant, and the cohort was divided into tertiles based on the CV; tertile 1 was composed of those with the least amount of ACT score variation, and tertile 3 was composed of those with the greatest amount of ACT score variation. Baseline characteristics were then compared across tertiles. Nonparametric tests for trend were used to test differences across ACT score tertiles for discrete variables,[11] and analysis of variance testing was used for continuous variables.

Results

Engagement With the IBS Platform

Monthly monitoring of asthma control: Among SARP subjects, 528 adults (18 years and older) were eligible to participate in IBS-based tracking of asthma symptoms. Of these 528 subjects, 269 (51%) did not log on to the platform at all (IBS–), and 259 (49%) logged on at least once (IBS+). Of these 259 IBS+ participants, 202 (78%) completed surveys in at least two of the first 12 months of platform enrollment, and many (n = 102) of these subjects completed the surveys more than 80% of the time (Fig 1A). Following completion of the first survey, adherence to the platform remained stable during the following year (Fig 1B).

Reporting of asthma exacerbations: Among the 259 IBS+ participants, 104 (40%) reported an exacerbation of asthma using the tool at least once during platform enrollment. Of these, the majority (70 subjects [67%]) reported exacerbations only as part of their monthly reporting, whereas 21 (20%) reported exacerbations using real-time reporting only; 13 subjects (13%) sometimes used monthly reporting and other times used real-time reporting to document exacerbations.

IBS Users vs Nonusers

In comparing the demographic features of IBS+ participants and IBS– participants, we found that IBS+ participants were older and more likely to be white, had received at least some college education, and had an

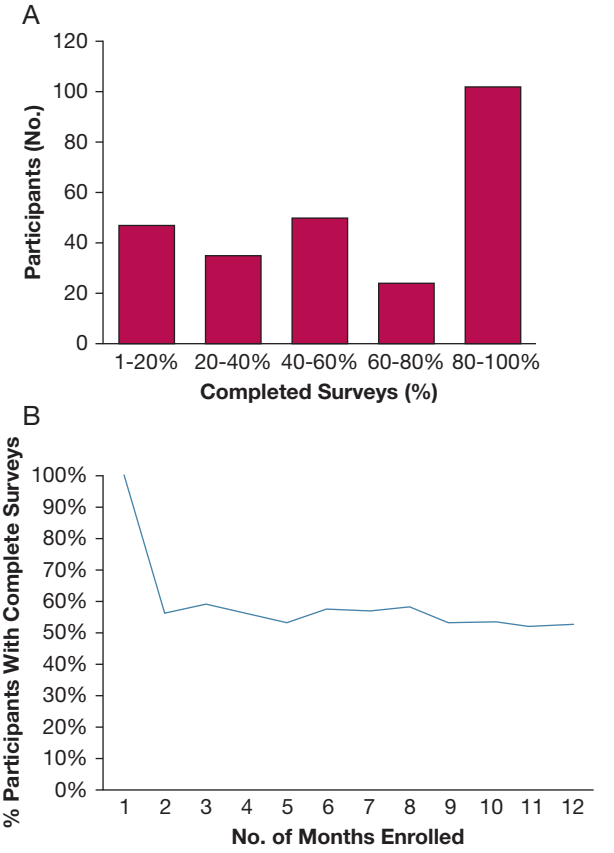

Figure 1 – *Survey adherence among patients who participated in the Internet-based Monitoring Systems (IBS+) survey. A, The percentage of completed surveys (x-axis) among the 259 IBS+ participants. Few subjects completed < 20% of the available surveys, and the majority of subjects completed > 40% of the available surveys. B, Following completion of the first survey, the percentage of participants who completed surveys remained stable over the course of the following year.*

annual household income > $25,000 (Table 1). In comparing the clinical features of IBS+ and IBS– participants, we found that IBS– participants more frequently had uncontrolled asthma, as defined by any of the following criteria: two or more steroid courses in the past year, an asthma-related hospitalization or ICU admission in the past year, need for mechanical ventilation in the past year, an FEV_1 < 80% predicted, or current ACT < 20.[6] Compared with IBS+ participants, IBS– participants demonstrated no difference in FEV_1 % predicted values, no difference in the frequency of subjects with severe asthma, and no difference in the frequency of asthma-associated hospitalizations or ED visits in the previous year (Table 1). IBS– participants did have a higher frequency of missing in-person and telephone visits with SARP study staff compared with IBS+ participants (49 [19%] vs 20 [8%]; $P < .0001$).

Using Poisson regression models, we found that age, race, educational attainment, and asthma control were significant independent predictors of IBS nonuse (Table 2). Attending college and older age were predictive of use, whereas uncontrolled asthma was predictive of nonuse. Subjects identifying as black were more likely than those identifying as white (reference) to not engage with the IBS platform. No other specific racial/ethnic group was significantly more or less likely to engage with the IBS platform compared with the reference group (Table 2).

Comparing Exacerbations Recorded Using IBS and Exacerbations Recorded in the SARP Protocol Using Biannual Questionnaires

IBS defined asthma exacerbations as self-reported periods of worsening symptoms. These self-reported exacerbations could be recorded in real time or at the end of the monthly recording period. The SARP protocol recorded asthma exacerbations at 6-month intervals during telephone calls and in-person visits. The SARP protocol defined an asthma exacerbation as an

TABLE 1] Demographic Features and Asthma Control and Compliance Variables of Participants Who Did or Did Not Engage With the Internet-Based Monitoring Tool (IBS+ and IBS– Subgroups)

Characteristics (as Measured at Baseline)	IBS– (n = 269)	IBS+ (n = 259)	*P* Value
	Mean ± SD or No. (%) or Median (IQR)		
Age, y	45.9 ± 13.5	49.1 ± 14.2	.008
Female sex	178 (66)	176 (68)	.75
Race/ethnicity			< .001
Asian	9 (3)	11 (4)	
Black	94 (35)	39 (15)	
White, non-Hispanic	143 (53)	194 (75)	
American Indian/Alaskan Native	1 (0)	1 (0)	
Other/more than one	22 (8)	14 (5)	
Household annual income < $25,000[a]	54 (20)	34 (14)	.001
BMI, kg/m^2	33.0 ± 8.2	32.0 ± 8.5	.06
Some college education or more	209 (79)	241 (93)	< .0001
Baseline FEV_1 % predicted	72.1 ± 19.5	72.8 ± 19.9	.66
Adult-onset of asthma, ≥ 18 y	174 (65)	153 (59)	.18
Uncontrolled asthma[b]	256 (95)	233 (90)	.02
Severe asthma	158 (59)	157 (61)	.66
Asthma-related ED visit past 12 m	66 (25)	60 (23)	.71
Asthma-related hospitalization past 12 m	26 (10)	30 (12)	.47
ACT score	17 (13-21)	18 (14-21)	.28
MARS score	23 (20-24)	23 (21-24)	.26

ACT = Asthma Control Test; IBS+ = patients who participated in the Internet-based Monitoring Systems survey; IBS– = patients who did not participate in the Internet-based Monitoring Systems survey; MARS = Medication Adherence Report Scale.
[a]Seventy-eight participants did not have information about household income.
[b]Uncontrolled asthma defined as one or more of the following: (1) two or more steroid courses in the past year, (2) an asthma-related hospitalization or ICU admission in the past year, (3) need for mechanical ventilation in the past year, (4) FEV_1 < 80% predicted, or (5) current ACT score < 20.

TABLE 2] Race, Education, and Poor Asthma Control Predict Nonengagement With the IBS Tool

Outcome	IRR	95% CI	*P* Value
Race/ethnicity[a]			
White	Reference		
Black	1.40	1.11-1.76	.004
Asian	1.30	0.76-2.2	.35
More than one	1.40	0.97-2.00	.07
Some college education	0.70	0.55-0.87	.002
Income < $25,000	1.18	0.93-1.48	.17
Uncontrolled asthma	1.62	1.00-2.63	.05
Age, 10-y increase[b]	0.93	0.86-1.00	.05

IRR = incident rate ratio.
[a]Two American Indian/Alaskan Natives omitted due to limited data.
[b]Age reflects the change in IRR for each 10-year increase in age.

increase in the use of systemic corticosteroids lasting 3 days or more. We compared the agreement between exacerbations reported using the IBS tool and exacerbations recorded through the biannual SARP exacerbation questionnaire. We found that agreement between the biannual SARP follow-up and the IBS data regarding reporting of exacerbations was fair (kappa = 0.56). Specifically, 78% of participant reports of asthma exacerbations in the previous year were congruent in the SARP questionnaire data and the IBS data; 12% of participants reported an exacerbation using the IBS tool but did not report an exacerbation using the SARP questionnaire, whereas 9% reported an exacerbation using the SARP questionnaire but did not report one using the IBS tool.

Variability of Asthma Control Over Time

In examining ACT scores over time in different participants, we noted that some participants had ACT scores that varied widely from month to month (Fig 2). To quantify this variability or lability in asthma control, we focused on a subgroup of the 202 IBS users who completed surveys in at least two of the first 12 months of platform enrollment. For this purpose, we excluded 27 participants who did not have the opportunity to complete 12 months of surveys (either because they did not remain enrolled in SARP or because they opted in to receive surveys < 12 months prior to the close of data collection) and an additional 30 participants who completed only one monthly survey during the first year of platform enrollment. Among the remaining 202 participants, the average number of monthly survey completions was eight (range, two to 12), and we set out to analyze the data for variability in asthma control in these patients, with an emphasis on the subgroup with highly variable symptoms. Because the survey data included the five questions from the Asthma Control Test,[9] it allowed an ACT score to be generated from each survey completion. We used multiple ACT scores from each participant in the first year of platform enrollment to calculate the CV for their ACT scores. We found that the IBS captured significantly more ACT variability compared with the SARP biannual ACT questionnaires (e-Fig 2). We then examined the summary ACT CV data for the cohort as tertiles representing low, medium, and high levels of variability in the ACT score.

Patients with asthma in the highest ACT CV tertile did not differ from the lower tertiles regarding age, race/ethnicity, income, or educational attainment, but their baseline questionnaire data showed that they were more likely to be women and reported more ED visits for asthma in the previous 12 months (Table 3). In addition, they reported more hospitalizations (including ICU care) for asthma during their lifetimes (Table 3). Furthermore, patients with asthma in the highest ACT CV tertile had lower baseline ACT scores and several features of metabolic dysfunction, including higher BMI, greater frequency of hypertension, and a trend toward higher numbers of WBC counts (Table 3). Notably, blood and airway measures of type 2 inflammation (eosinophils, exhaled nitric oxide) did not differ among patients with asthma in the three ACT CV tertiles (Table 3) nor did outcomes of atopy (total IgE).

In examining asthma exacerbation data, we found that patients with asthma in the highest ACT CV tertile had a higher cumulative incidence of experiencing an asthma exacerbation at 12-month follow-up. In addition, subjects with asthma and high ACT variability also experienced a higher cumulative incidence of a severe

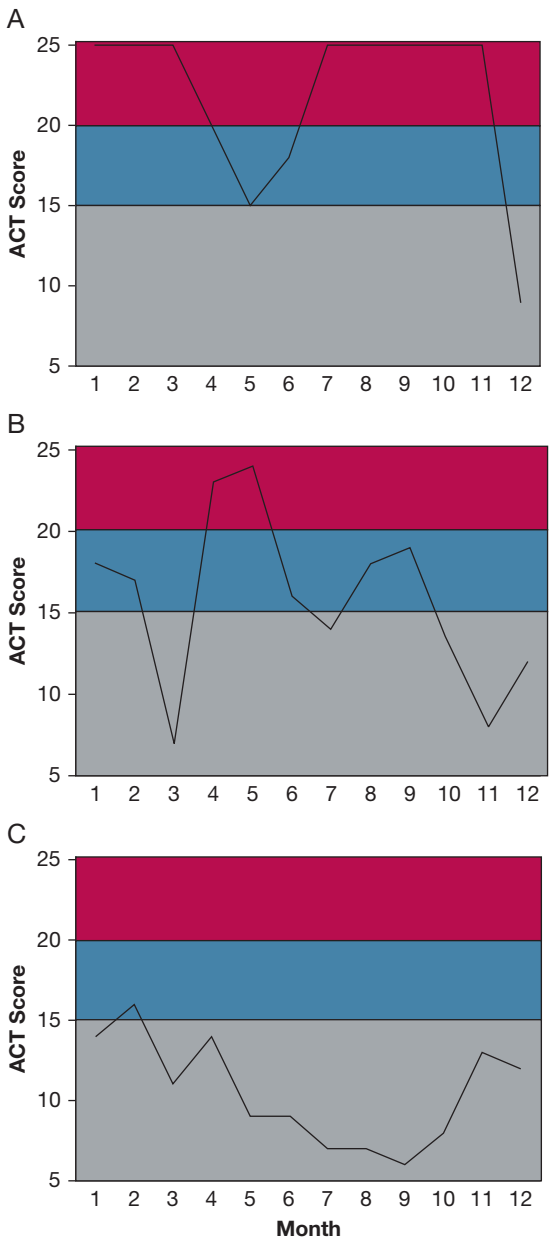

Figure 2 – *Examples of participants with high ACT variability. A, Participant who had many months of good control with episodic drops in control. B, Participant who fluctuated dramatically across months. C, Participant with high variability but no periods of good control. ACT = Asthma Control Test.*

exacerbation by 12 months of follow-up (Fig 3). Not surprisingly, the patients with asthma in the highest ACT CV tertile had more periods of worsening asthma symptoms (Table 4), regardless of whether these worsening symptoms met the threshold for a clinical exacerbation. When responding to questions in the IBS survey about perceived triggers of worsening asthma symptoms, patients with asthma in the highest ACT CV tertile more frequently identified cold and flulike illness as the precipitating cause (Table 4, e-Fig 1). In contrast, patients with asthma in the lowest ACT CV tertile more commonly identified weather changes as a precipitating cause (Table 4).

Discussion

In this study, we evaluated the utility of a monthly IBS platform to capture ACT data in a cohort of patients with asthma (many with severe disease) over a 1-year period. We found that half of the cohort engaged with the IBS platform and half did not, and predictors of engagement included multiple measures associated with higher socioeconomic status. Among patients with asthma who participated, we found that a subgroup had highly variable ACT scores, and these patients with labile asthma were characterized by obesity, metabolic dysfunction, and loss in asthma control precipitated by cold and flulike illness.

Roughly half of our cohort did not engage with the IBS platform, and although there was a higher rate of noncompliance with SARP visits among those who did not engage with the IBS survey, the vast majority of the IBS– participants were still able to adhere to other SARP activities (81%). Among the demographic factors associated with nonengagement were black race and a lack of higher education. There are potential methods of increasing participant adherence to IBS. First, our study did not compensate participants for completing the survey, and it is possible that a payment incentive could have improved engagement. In addition, the platform contained minimal interfacing with medical staff and did not provide any feedback on survey responses. Other Internet-based monitoring tools have incorporated feedback features[12] such as text messaging, and it is possible that these could have improved engagement with our IBS tool. Finally, recent data suggest that up to 15% of American adults do not use the Internet,[13] and it is possible that a lack of access to the Internet prohibited some subjects from participating in the IBS survey.

Internet-based technologies are a powerful tool to monitor asthma control, but it will be important to continue to explore the utility of these technologies and ensure that the data generated are generalizable. Our findings suggest that race and educational attainment significantly influence the use of Internet-based monitoring tools. Our findings also indicate that

TABLE 3] Demographics and Characteristics of Asthma and Asthma-Related Inflammation Associated With Variability of Control Over Time

Characteristics (as Measured at Baseline)	ACT CV Tertile 1 0%-10.6% (n = 68)	ACT CV Tertile 2 10.7%-21.6% (n = 67)	ACT CV Tertile 3 21.7%-67.3% (n = 67)	*P* Value[a]
	Mean ± SD or No. (%) or Median (IQR)			
Age, y	48.5 ± 14.3	49.2 ± 13.5	50.5 ± 12.5	.44
Age of asthma onset, y	15 (6-33)	14 (5-32)	12 (4-23)	.31
Female sex, No. (%)	45 (67)	44 (65)	54 (81)	.01
Race/ethnicity, No. (%)				.45
Asian	4 (6)	2 (3)	3 (4)	
Black	14 (21)	7 (10)	7 (10)	
White	48 (71)	54 (81)	52 (78)	
Mixed/other	2 (3)	4 (6)	5 (7)	
BMI, kg/m^2	30.2 ± 7.7	31.0 ± 6.9	34.6 ± 9.9	.004
Nasal polyps, No. (%)	11 (16)	18 (27)	19 (28)	.12
Chronic rhinosinusitis, No. (%)	21 (31)	33 (49)	39 (58)	.001
GERD, No. (%)	25 (37)	32 (48)	41 (61)	.006
Hypertension, No. (%)	17 (25)	23 (34)	29 (43)	.03
Diabetes, No. (%)	6 (9)	9 (13)	9 (13)	.30
ATS/ERS severe category, No. (%)				.02
Mild	19 (28)	7 (10)	11 (16)	
Moderate	16 (24)	17 (25)	10 (15)	
Severe	33 (49)	43 (64)	46 (69)	
Baseline ACT	20 (17-22)	18 (14-21)	15 (12-20)	< .0001
Asthma-related ED visit in past 12 m, No. (%)	4 (6)	20 (30)	22 (33)	< .001
Asthma-related hospitalization in past 12 m, No. (%)	3 (4)	11 (16)	9 (13)	.10
Lifetime history of asthma-related ICU stay, No. (%)	5 (7)	13 (19)	13 (19)	.05
Baseline FEV_1 %	77.1 ± 22.6	70.0 ± 20.7	73.5 ± 18.6	.30
Baseline FVC %	88.2 ± 17.5	81.7 ± 17.6	85.3 ± 16.0	.29
Exhaled nitric oxide, ppb	18.5 (13-31)	22 (13-39)	26 (14-42)	.11
IgE, IU/mL	150 (38-267)	145 (36-378)	98 (27-281)	.40
WBC count, $\times 10^6$/L	6.7 (5.6-8.0)	7.0 (5.7-8.3)	7.6 (6.0-9.9)	.07
Peripheral blood neutrophils, $\times 10^6$/L	3,966 (2,910-5,370)	4,008 (3,097-5,106)	4,402 (3,294-5,964)	.12
Peripheral blood eosinophils, $\times 10^6$/L	181 (125-347)	244 (144-378)	251 (124-456)	.25

CV = coefficient of variation, IgE = immunoglobulin E; ppb = parts per billion. See Table 1 legend for expansion of other abbreviations.
[a]Statistical comparison done using a nonparametric test for trend.

participants with increased disease morbidity are at higher risk for nonuse. The finding that patients with uncontrolled asthma are less likely to use IBS is concerning, because a primary objective of IBS is to characterize asthma exacerbations among a population with a higher proportion of subjects with severe asthma. Furthermore, nonadherence would limit the ability of IBS to serve as a recruitment tool to identify participants with exacerbation-prone disease. Nevertheless, the IBS survey did capture data in half of all adult enrolled participants. Additionally, 40% of IBS+ participants provided data about recent exacerbations. Although the agreement between the exacerbations reported using IBS and those reported at live encounters with SARP staff was good, the IBS tool captured data about each exacerbation, including triggers of exacerbation, which

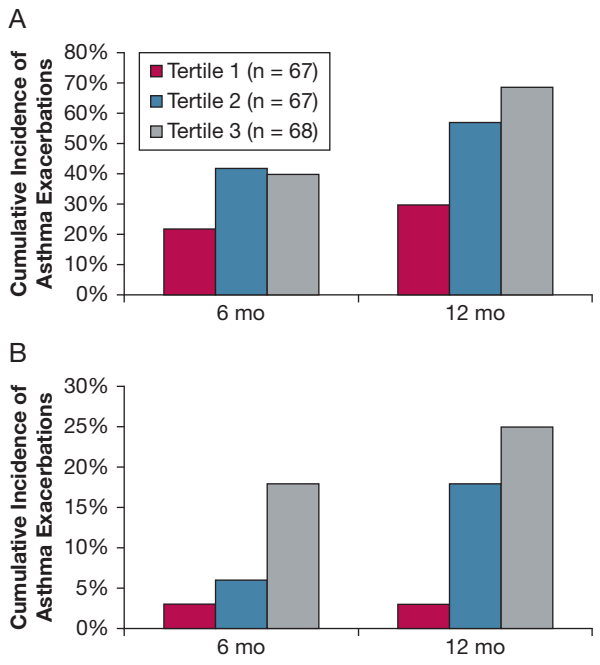

Figure 3 – *Cumulative incidence of asthma exacerbations at 6-month and 12-month follow-up stratified by Asthma Control Test (ACT) variability tertiles. Subjects with high ACT variability (tertile 3) experienced a higher incidence of severe and nonsevere asthma exacerbations at the 12-month follow up. A, Cumulative incidence of all asthma exacerbations, as defined by any of the following: (1) unscheduled visit to a physician's office, (2) oral corticosteroid burst, (3) ED visit, or (4) hospital admission. B, Cumulative incidence of severe asthma exacerbations, limited to one of the following: (1) ED visit or (2) hospital admission.*

would not have been practical given recall limitations at the live biannual encounters. Given that the IBS tool used here contained minimal interaction with medical staff and lacked any additional compensation, we consider that the adherence was good and that the IBS tool is practical for real-time sensing of exacerbations of asthma in research.

Through the use of IBS, we identified a subset of patients with asthma with highly variable ACT scores. Using less frequent monitoring systems, such as 6-month or annual questionnaires, missed identifying these patients with labile asthma. Participants with labile asthma more frequently met ATS/ERS criteria for severe asthma and experienced more exacerbations during the 12-month follow-up period. Furthermore, the IBS data allowed us to characterize asthma exacerbation triggers and show that cold and flulike illnesses were common causes of worsening asthma control. Conversely, neither low lung function nor degree of bronchodilator reversibility was a clinical feature of "patients with labile asthma." Thus, labile asthma seems to relate to factors associated with susceptibility to viral illnesses rather than factors associated with excessive airway narrowing or smooth muscle dysfunction.

Compared with patients with asthma who have minimal or moderate ACT score variability, patients with asthma with high ACT score variability were also characterized by obesity, hypertension, and a trend toward higher WBC counts, but they did not have prominent systemic or airway measures of type 2 inflammation. Our findings are consistent with studies that identify diabetes as a risk factor for the development of respiratory tract infections,[14] and our recent data that interleukin-6-associated systemic inflammation is associated with more severe asthma phenotypes.[7]

TABLE 4] Self-Reported Triggers of Worsening Asthma Symptoms Among Participants Who Reported at Least One Episode of Worsening Asthma

Asthma Trigger	ACT CV Tertile 1 0%-10.6% (n = 68)	ACT CV Tertile 2 10.7%-21.6% (n = 67)	ACT CV Tertile 3 21.7%-67.3% (n = 67)	*P* Value
≥ 1 episode of worsening asthma, No. (%)	51 (75)	64 (96)	66 (99)	< .0001
Triggers of worsening asthma, No. (%)				
Illness	33 (65)	39 (61)	54 (82)	.03
Airborne irritants	16 (31)	24 (38)	31 (47)	.08
Emotion	10 (20)	21 (33)	27 (41)	.02
Allergens	32 (63)	41 (64)	39 (59)	.66
Physical exertion	14 (27)	18 (28)	23 (35)	.37
Tobacco smoke	2 (4)	9 (14)	12 (18)	.02
Weather changes	18 (35)	15 (23)	12 (18)	.04
Unknown	6 (12)	16 (25)	20 (30)	.02
Other	2 (4)	6 (9)	7 (11)	.20

See Table 1 legend for expansion of abbreviations.

Conclusions

We demonstrate that an IBS tool is effective for monitoring asthma control in patients with severe disease, but that demographic factors such as race and education influence engagement with the tool. The use of the IBS tool in the SARP-3 cohort identifies a subgroup of patients with asthma who have highly variable asthma control and are characterized by metabolic dysfunction and increased susceptibility to loss of asthma control triggered by cold and flulike illnesses. IBS has the potential to identify patients who are at risk for the development of asthma exacerbations, and IBS could enable providers to target asthma interventions, including higher inhaled corticosteroid doses, to prevent future exacerbations in these patients.

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