Adult Asthma Scores—Development and Validation of Multivariable Scores to Identify Asthma in Surveys

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BACKGROUND: One of the questions in epidemiology is the identification of adult asthma in studies.

OBJECTIVE: To develop and validate multivariable scores for adult asthma identification in epidemiological studies and to explore cutoffs to rule in/rule out asthma, compared with asthma diagnosed by a physician after clinical examination and diagnostic tests, blinded to the self-administered questions. METHODS: We analyzed data (n = 711 adults) from a nationwide population-based study. The predictors were self-administered questions identified in a literature review (the Adult Asthma Epidemiological Score [A2 score]) and from the Global Allergy and Asthma Network of Excellence (GA2LEN) questionnaire (the GA2LEN Asthma Epidemiological Score [GA2LEN score]). Scores were developed using exploratory fac-tor analysis. Internal consistency, discriminative power, and diagnostic accuracy were assessed.

RESULTS: The A2 score comprises 8 questions (including "Did a physician confirm you had asthma?") and the GA2LEN score comprises 6 questions (including "Have you ever had asthma?"). Both had high Cronbach α (0.89 and 0.85, respectively, for the A2 score and the GA2LEN score) and good area under the receiver-operating characteristic curve (90.4% and 89.0%). The scoring is the sum of positive answers. Asthma is present (rule in) for scores of 4 or more (specificity, 99.2%; PPV, 93.3% and 91.7%; accuracy, 89.4% and 87.4%, respectively, for the A2 score and the GA2LEN score). Asthma is excluded (rule out) for A2 scores of 0 to 1 and a GA2LEN score of 0 (sensitivity, 93.1%; NPV, 98.2% and 98.0%; accuracy 89.4% and 82.8%, respec-tively, for the A2 score and the GA2LEN score).

CONCLUSIONS: These practical scores can be used to rule in/rule out asthma in epidemiological studies and clinical screening/triage settings. They may help physicians in primary care or other specialties to screen patients with asthma using a simple score with a high level of discrimination and to identify the best candidates to be referred for a diagnostic workup. Moreover, their use may contribute to reducing the inconsistencies of operacional definitions of asthma across studies and surveys.

Key words: *Asthma; Questionnaire survey; Factor analysis; statistical; Validation studies; Epidemiology*

What is already known about this topic? Estimates obtained in surveys are highly dependent on the set of questions used for the operational definition of asthma. The identification of asthma in epidemiological studies is still an issue.

What does this article add to our knowledge? We developed 2 short, easy, self-reported scores, with very good properties to rule in/rule out asthma.

How does this study impact current management guidelines? This study provides validated screening tools to be used in adult asthma surveys and clinical screening/triage settings.

Abbreviations used

A2 score- Adult Asthma Epidemiological Score
AUC- area under the ROC curve
COPD- chronic obstructive pulmonary disease
ECRHS- European Community Respiratory Health Survey
GA2LEN- Global Allergy and Asthma Network of Excellence
GA2LEN score- GA2LEN Asthma Epidemiological Score
ICAR- Control and Burden of Asthma and Rhinitis
NPV- negative predictive value
PPV- positive predictive value
ROC- receiver-operating characteristic

INTRODUCTION

Asthma is an important public health problem that affects people of all ages and causes significant health resource utilization.[1] Its prevalence varies widely in different regions, and a "precise and universally accepted definition of asthma" is still lacking.[2] In fact, estimates obtained in epidemiological studies, on both adults[3] and children,[4] are highly dependent on the set of questions used for the operational definition of asthma.

In a clinical context, the initial diagnosis of asthma is based on identifying a pattern of respiratory symptoms, supported by pulmonary function tests, including the study of airflow obstruction reversibility and/or bronchial hyperresponsiveness.[1] However, because these procedures are seldom feasible in population-based studies, efforts have been made to find accurate definitions of asthma on the basis of questionnaires. In 2014, we proposed a set of questions to be reported in population-based studies on asthma prevalence on the basis of a literature review of the different asthma definitions used in epidemiological studies.[3]

Several prediction models have been previously developed to identify children with asthma-like symptoms. A systematic review[5] on prediction models for children reported extensive variability both on predictors and on outcome definitions and that none had the ability to rule in and rule out asthma simultaneously. In adults, Pekkanen et al[6] developed a continuous asthma score to define asthma on the basis of the European Community Respiratory Health Survey (ECRHS) questionnaire and used bronchial hyperreactivity as the comparator. This score showed good predictive capability in a prospective study when compared with self-reported use of asthma medication and asthma attacks and with bronchial hyperreactivity test at the end of follow-up.[7] However, its validity was not supported by the results in another population setting.[8] The ECRHS score was also compared with the self-reported previous diagnosis of asthma[8] but not against in-person physician diagnosis confirmed after clinical examination. This study argued on the use of a continuous score over a dichotomous definition of asthma, but in fact, the choice of a cutoff depends mainly on the aims of the classification. Self-reported questionnaires are tools used to identify asthma in prevalence studies assessing participants only once (eg, the Global Allergy and Asthma Network of Excellence [GA2LEN] survey[9]) and are also used as initial screening questionnaires, being a feasible and effective way for preselecting patients for additional diagnostic workup, including pulmonary function tests (eg, the ECRHS[10]). Screening questionnaires are often used in epidemiological studies on chronic obstructive pulmonary disease (COPD),[11,12] and their development was encouraged by the World Health Organization.[13]

To our knowledge, the existing score system for the identification of asthma in adults, based on self-administered questionnaires, has not been validated against actual diagnostic workup by a trained physician. Furthermore, it is lacking a screening questionnaire to rule in and rule out asthma, enabling its use both in population-based studies and in screening/triage clinical settings. We aimed to (1) develop and validate multivariable scores for adult asthma identification in epidemiological studies on the basis of answers to questions commonly used in these studies and (2) to explore the best cutoff to rule in asthma (preferable in prevalence studies) and to rule out asthma (preferable for screening/triage).

METHODS

Source of data

We used data from the Control and Burden of Asthma and Rhinitis (ICAR) study (PTDC/SAU-SAP/119192/2010), a nationwide population-based observational cross-sectional study conducted in Portugal (ClinicalTrials.gov: NCT01771120). The study was approved by a hospital ethics committee (*Comissão de Ética do Hospital São João EPE*, on October 17, 2011) and by the national data protection committee (no. 12372/2011). All participants signed the consent form.

Methods regarding sample size calculations, participants, and data collection in the ICAR study are described in the "Methods" section in this article's Online Repository at www.jaci-inpractice.org. Data collection included lung function and exhaled nitric oxide, skin prick tests, a structured clinical assessment, and standardized questionnaires. The structured clinical assessment was performed by a trained physician and included physical examination, use of health resources and medications because of asthma/rhinitis, and detailed personal and family medical history. In the ICAR study, self-administered questionnaires assessed disease symptoms and control, including the Portuguese version of the GA2LEN survey questionnaire[14] among other questionnaires.

Participants

We included participants from the general population aged 18 years and older from the ICAR study (n = 728). Considering an asthma prevalence of 23% (in the study sample), a specificity of 90%, and a maximum marginal error of estimate not exceeding 3% with a 95% CI, the required sample size was 498 participants.[15] Approximately 80% (n = 560) of the participants were randomly selected into a derivation cohort and 20% (n = 151) into a validation cohort.

Outcome and predictors

Asthma diagnosis (criterion standard) was defined by a physician on the basis of a structured clinical assessment of symptoms and detailed medical history, and supported by objective measurements (see the "Methods" section in this article's Online Repository), according to guidelines. The physician had no previous access to the results of the self-administered questionnaires.

The predictors were asthma-related questions from the self-administered questionnaires. Sixteen questions were selected as initial predictors, namely, (1) questions previously suggested in a literature review[2] and (2) questions on asthma from the GA2LEN questionnaire (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). On the basis of these predictors, 2 separate scores were built: the Adult Asthma Epidemiological Score (A2 score), based on the literature, and the GA2LEN Asthma Epidemiological Score (GA2LEN score), based on the GA2LEN questionnaire.

Subjects with missing data in any of the predictors were excluded from the analysis (n = 17 [2.3%]).

Statistical analysis methods

Categorical variables are presented as absolute frequencies and proportions. Comparisons of proportions and associations were tested. A P value of less than .05 was considered as statistically significant. Statistical analysis was performed using IBM SPSS Statistics, version 24.0 (IBM Corp, Armonk, NY).

An exploratory factor analysis was performed to construct a score reducing the number of predictors while retaining, as much as possible, the information contained in the initial combination of predictors, identifying the possible statistical redundancy of the predictors.[16] A factor analysis was run for the initial predictors (see Table E1 in this article's Online Repository). Principal-component analysis and oblimin rotation were used. Predictors with more than 95% responses in a single category were excluded. An item was considered redundant and was excluded if any 1 of the following occurred: highly intercorrelated (>0.900), considerable cross-loading (>0.300 in more than 1 factor), low item-total correlation (<0.400), or increased Cronbach α if the predictor was deleted.

Discriminative/predictive power of the scores was evaluated by receiver-operating characteristic (ROC) curve analysis. Internal consistency was assessed by Cronbach α. The diagnostic accuracy measures used were sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy.

The scores' performance was tested in the derivation and validation cohorts and compared with the ECRHS asthma score. The cutoff to rule in asthma was defined as the minimum number of positive answers to obtain a PPV of 85% or more simultaneously in both cohorts. The cutoff to rule out asthma was defined as the maximum number of positive answers to obtain an NPV of 95% or more simultaneously in both cohorts.

For each of the 2 scores, 2 scoring methods were tested: the weighted sum, obtained by multivariable logistic regression of the included predictors, and the direct sum of the included predictors. The scores obtained by both the scoring methods were compared by the Spearman correlation factor. The values for the area under the ROC curve (AUC) for the scores obtained by both the methods were also compared.

RESULTS

This study included 711 participants (see Figure 1), with a median age (percentile 25 to percentile 75) of 42 (32-55) years,

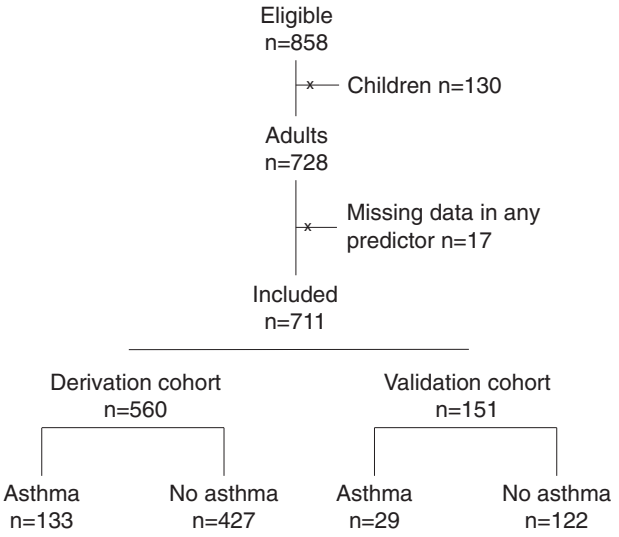

FIGURE 1. Participants' flowchart.

and 447 (63%) were females. The number of participants with asthma was 162 (23%). No statistically significant differences were observed between the derivation and the validation cohorts regarding sex, age, geographic region of residence, and presence of asthma ($P > .1$). Specifically, no differences between the cohorts were observed in the proportion of participants with asthma (23.8% vs 19.2%; $P = .24$).

In the derivation cohort, having asthma was highly associated with all the initial predictors but not with the demographic variables (Table I). In general, the ability to identify patients with asthma using any asthma predictor alone was low (PPV < 70%; see Table E2 in this article's Online Repository at www.jaci-inpractice.org).

Scores specifications and performance

On the basis of the initial set of questions (see Table E1 in this article's Online Repository), 2 scores were developed to identify the presence of asthma (Table II). The A2 score and the GA2LEN score derivations were obtained by exploratory factor analysis (see the "Exploratory factor analysis" section in this article's Online Repository at www.jaci-inpractice.org). The final A2 score included 8 predictors in 2 factors with eigenvalues of 3.997 (predictors 2-5 and 10; Table II) and 3.535 (predictors 6-8). The final GA2LEN score included 6 predictors in 2 factors with eigenvalues of 2.954 (predictors 6-8; Table II) and 2.860 (predictors 1, 4, and 5).

The discriminative properties of the developed scores were similar, with an AUC of about 90% (Figure 2). The A2 score had higher Cronbach α than the GA2LEN score (0.887 vs 0.852, respectively; Figure 2).

The scores obtained by the weighted sum (Table II) were highly correlated with those obtained by the direct sum (Spearman correlation coefficient >0.98; $P < .001$). As so, the final result was the direct sum of the positive answers to the questions selected for each score, ranging from 0 to 8 for the A2 score and from 0 to 6 for the GA2LEN score.

Diagnostic accuracy measures were assessed for both scores and cohorts (Table III; see also Table E3 in this article's Online Repository at www.jaci-inpractice.org). As expected, the

TABLE I. Characterization of the cohorts

Characteristic	Derivation cohort				Validation cohort			
		Asthma presence				Asthma presence		
	Total (n = 560)	No (427 [76.3%])	Yes (133 [23.8%])	*P* value	Total (n = 151)	No (122 [80.8%])	Yes (29 [19.2%])	*P* value
Demographic characteristics								
Age (y), median (P25-P75)	41.5 (32-55)	43 (32-56)	37 (31-55)	.119*	42 (33-52)	43 (32-54)	40 (33-48)	.501*
Sex, n (%)				.302†				.903‡
Female	360 (64.6)	279 (65.8)	81 (60.9)		87 (57.6)	70 (57.4)	17 (58.6)	
Male	197 (35.4)	145 (34.2)	52 (39.1)		64 (42.4)	52 (42.6)	12 (41.4)	
Region, n (%)				.561§				.701§
North	285 (50.9)	216 (50.6)	69 (51.9)		80 (53.0)	66 (54.1)	14 (48.3)	
Center	35 (6.3)	27 (6.3)	8 (6.0)		11 (7.3)	10 (8.2)	1 (3.4)	
Lisbon	183 (32.7)	139 (32.6)	44 (33.1)		36 (23.8)	27 (22.1)	9 (31.0)	
Alentejo	26 (4.6)	18 (4.2)	8 (6.0)		10 (6.6)	6 (4.9)	4 (13.8)	
Algarve	31 (5.5)	27 (6.3)	4 (3.0)		14 (9.3)	13 (10.7)	1 (3.4)	
Predictors, n (%)								
1. Have you ever had asthma?‖¶	138 (24.6)	36 (8.4)	102 (76.7)	<.001†	30 (19.9)	10 (8.2)	20 (69.0)	<.001†
2. Did a physician confirm you had asthma?‖	132 (23.6)	30 (7.0)	102 (76.7)	<.001†	29 (19.2)	10 (8.2)	19 (65.5)	<.001†
3. Do you still have asthma (previously diagnosed by a physician)?‖	104 (18.6)	14 (3.3)	90 (67.7)	<.001†	24 (15.9)	6 (4.9)	18 (62.1)	<.001‡
4. Have you ever been hospitalized because of asthma?¶	40 (7.1)	10 (2.3)	30 (22.6)	<.001†	8 (5.3)	2 (1.6)	6 (20.7)	.001‡
5. Have you had any asthma attack in the last 12 mo?‖¶	51 (9.1)	7 (1.6)	44 (33.1)	<.001†	7 (4.6)	1 (0.8)	6 (20.7)	<.001‡
6. Are you currently taking any medicines including inhalers, aerosols, or tablets for asthma?‖¶	66 (11.8)	5 (1.2)	61 (45.9)	<.001†	11 (7.3)	1 (0.8)	10 (34.5)	<.001‡
7. Have you ever had wheezing or whistling in the chest at any time in the last 12 mo?‖¶	178 (31.8)	85 (19.9)	93 (69.9)	<.001†	38 (25.2)	17 (13.9)	21 (72.4)	<.001†
8. Have you had this wheezing or whistling when you did not have a cold?‖¶	104 (18.6)	41 (9.6)	63 (47.4)	<.001†	18 (11.9)	4 (3.3)	14 (48.3)	<.001‡
9. Have you been at all breathless when the wheezing noise was present?‖¶	118 (21.1)	41 (9.6)	77 (57.9)	<.001†	24 (15.9)	7 (5.7)	17 (58.6)	<.001‡
10. Have you had an attack of shortness of breath after exercise in the last 12 mo?‖	45 (8.0)	16 (3.7)	29 (21.8)	<.001†	9 (6.0)	1 (0.8)	8 (27.6)	<.001‡
11. Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 mo?‖	78 (13.9)	26 (6.1)	52 (39.1)	<.001†	13 (8.6)	2 (1.6)	11 (37.9)	<.001‡
12. Have you woken up with the feeling of tightness in your chest at any time in the last 12 mo?‖¶	98 (17.5)	59 (13.8)	39 (29.3)	<.001†	25 (16.6)	15 (12.3)	10 (34.5)	.010‡
13. Have you been woken up by an attack of shortness of breath at any time in the last 12 mo?‖¶	57 (10.2)	23 (5.4)	34 (25.6)	<.001†	14 (9.3)	8 (6.6)	6 (20.7)	.029‡
14. Have you been woken up by an attack of coughing at any time in the last 12 mo?‖¶	226 (40.4)	156 (36.5)	70 (52.6)	.001†	54 (35.8)	37 (30.3)	17 (58.6)	.004†
15. In the last 12 mo, have you had a dry cough during the night, apart from a cough associated with a cold or a chest infection?‖	222 (39.6)	144 (33.7)	78 (58.6)	<.001†	59 (39.1)	40 (32.8)	19 (65.5)	.001†
16. Did you have phlegm when coughing for at least 3 mo in the last year?¶	19 (3.4)	8 (1.9)	11 (8.3)	.001†	4 (2.6)	2 (1.6)	2 (6.9)	.167‡

P25-P75, percentile 25 to percentile 75.
*Mann-Whitney *U* test.
†Chi-square test.
‡The Fisher exact test.
§Linear-by-linear test.
‖Initial predictors used to develop the A2 score.
¶Initial predictors used to develop the GA2LEN score.

TABLE II. Association of the variables included in the final multivariable scores with the presence of asthma as assessed by the physician

Predictors	A2 score		GA2LEN score	
	aOR	95% CI	aOR	95% CI
1. Have you ever had asthma?	*	*	13.36	6.79-26.27
2. Did a physician confirm you had asthma?	7.91	3.17-19.77	†	†
3. Do you still have asthma (previously diagnosed by a physician)?	4.28	1.33-13.79	†	†
4. Have you had any asthma attack in the last 12 mo?	0.51	0.15-1.78	1.07	0.36-3.18
5. Are you currently taking any medicines including inhalers, aerosols, or tablets for asthma?	4.07	1.23-13.47	6.02	2.01-18.00
6. Have you ever had wheezing or whistling in the chest at any time in the last 12 mo?	3.23	1.25-8.36	3.35	1.32-8.47
7. Have you had wheezing or whistling when you did not have a cold?	1.35	0.55-3.30	1.36	0.58-3.22
8. Have you been at all breathless when the wheezing noise was present?	1.13	0.42-3.00	1.37	0.55-3.42
9. Have you had an attack of shortness of breath after exercise in the last 12 mo?	*	*	†	†
10. Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 mo?	2.05	0.85-4.98	†	†
Constant	0.05		0.05	

aOR, Adjusted odds ratio.
*Question tested but not included in the final score.
†Question not included in GA2LEN questionnaire.

definitions requiring more positive answers have higher specificity and PPV but lower sensitivity, indicating that the probability of having asthma increases with an increasing score.

On the basis of a PPV of 85% or more in both cohorts, we considered asthma to be present in patients with a sum of 4 or more positive answers (Table III). Using this cutoff in the derivation cohort, the A2 score and the GA2LEN score had high accuracy (87.9% and 85.9%), high specificity (96.7% and 97.7%), and a sensitivity of 59.4% and 48.1%, respectively (see Table E3 in this article's Online Repository). In the validation cohort, for the same cutoff based on PPV, the A2 score had a slightly higher accuracy compared with the GA2LEN score (89.4% vs 87.4%; Figure 3, *C*) and a higher sensitivity (48.3% vs 37.9%; Figure 3, *A*), but the same specificity (99.2%; Figure 3, *A*) (see Table E3 in this article's Online Repository) and false-positive rate (1%; Figure 3, *E*).

The cutoff to rule out asthma was based on an NPV of 95% or more in both cohorts, which corresponds to a sum of less than 2 positive answers for the A2 score and 0 for the GA2LEN score (Table III). Using this cutoff in the derivation cohort, the A2 score had a higher accuracy compared with the GA2LEN score (84.3% vs 78.2%) and a higher specificity (83.8% vs 74.5%; Figure 3, *A*), but both scores had high sensitivity (85.7% and 90.2%, respectively; Figure 3, *A*) (see Table E3 in this article's Online Repository). For this cutoff in the validation cohort, the A2 score had a higher accuracy compared with the GA2LEN score (89.4% vs 82.8%; Figure 3, *B*), but both scores had the same sensitivity (93.1%; Figure 3, *A*) (see Table E3 in this article's Online Repository); the scores also had similar NPVs (98.2% vs 98.0%, respectively, for the A2 score and the GA2LEN score; Table III) and the same false-negative rate (7%; Figure 3, *D*).

DISCUSSION

We developed and validated 2 multivariable scores, on the basis of self-administered questions, for the identification of asthma cases in epidemiological studies. The scores obtained

A

	AUC using direct sum, % (95% CI)	AUC using weighted score, % (95% CI)	Number of items	Cronbach α (95% CI)
A2 score	90.4 (87.0-93.9)	91.3 (87.9-94.7)	8	0.887 (0.872-0.900)
GA2LEN score	89.0 (85.4-92.5)	90.5 (87.0-94.0)	6	0.852 (0.832-0.870)

B

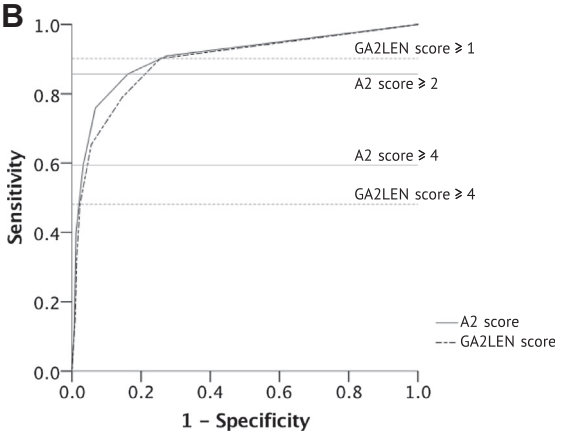

FIGURE 2. **(A)** Discriminative properties and internal consistency. **(B)** ROC curve of the scores, using participants from the derivation cohort (n = 560).

TABLE III. Predictive values in derivation and validation cohorts

Score (no. of positive answers)	Derivation cohort (n = 560)			Validation cohort (n = 151)		
	n (%)	PPV % (95% CI)	NPV % (95% CI)	n (%)	PPV % (95% CI)	NPV % (95% CI)
A2 score						
Possible Asthma						
≥2*	183 (32.7)	62.3 (56.8-67.5)	95.0 (92.5-96.6)	41 (27.2)	65.9 (53.8-76.1)	98.2 (93.4-99.5)
≥3	130 (23.2)	77.7 (70.8-83.4)	92.6 (90.2-94.4)	24 (15.9)	79.2 (60.8-90.3)	92.1 (87.6-95.1)
Probable Asthma						
≥4†	93 (16.6)	85.0 (76.8-90.6)	88.4 (86.2-90.4)	15 (9.9)	93.3 (65.7-99.0)	89.0 (85.0-92.0)
≥5	70 (12.5)	88.6 (79.2-94.0)	85.5 (83.4-87.4)	12 (7.9)	91.7 (59.7-98.8)	87.1 (83.5-89.4)
≥6	58 (10.4)	91.4 (81.2-96.3)	84.1 (82.1-85.8)	10 (6.6)	90.0 (54.3-98.6)	85.8 (82.6-88.5)
≥7	39 (7.0)	89.7 (76.0-96.0)	81.2 (79.6-82.7)	7 (4.6)	85.7 (42.9-98.0)	84.0 (81.4-86.4)
8	20 (3.6)	85.0 (62.8-95.0)	78.5 (77.4-79.6)	2 (1.3)	100.0	81.9 (80.4-83.3)
GA2LEN score						
Possible Asthma						
≥1*	229 (40.9)	52.4 (48.1-56.7)	96.1 (93.6-97.6)	51 (33.8)	52.9 (43.7-62.0)	98.0 (92.8-99.5)
≥2	167 (29.8)	62.9 (57.0-68.4)	92.9 (90.4-94.8)	31 (20.5)	71.0 (55.8-82.6)	94.2 (89.4-96.9)
≥3	111 (19.8)	78.4 (70.7-84.5)	89.8 (87.4-91.7)	21 (13.9)	81.0 (60.7-92.1)	90.8 (86.4-93.8)
Probable Asthma						
≥4†	74 (13.2)	86.5 (77.2-92.4)	85.8 (83.7-87.7)	12 (7.9)	91.7 (59.7-98.8)	85.8 (83.7-87.7)
≥5	50 (8.9)	88.0 (76.2-94.4)	82.6 (80.8-84.2)	10 (6.6)	90.0 (54.3-98.6)	85.8 (82.6-88.5)
6	24 (4.3)	83.3 (63.5-93.5)	78.9 (77.7-80.1)	3 (2-0)	66.7 (15.8-95.5)	81.8 (80.2-83.2)

A2 score, Adult Asthma Epidemiological Score; *GA2LEN score*, Global Allergy and Asthma Network of Excellence Asthma Epidemiological Score; *PPV*, Positive predictive value; *NPV*, negative predictive value.

*Cutoff of ≥2 (for the A2 score) and of ≥1 (for the GA2LEN score) for considering possible asthma (NPV of 95% or more, simultaneously in derivation and validation cohorts).

†Cutoff of ≥4 for considering probable asthma (PPV 85% or more, simultaneously in derivation and validation cohorts).

have very good properties to rule in/rule out asthma, providing, for the first time, validated screening tools to be used in adult asthma epidemiological studies and clinical screening/triage settings.

The performance of asthma prediction scores has been studied mostly for childhood asthma. Smit et al[5] assessed 12 prediction models for children and reported a sensitivity ranging from 15% to 75% and a specificity ranging from 35% to 100%. In

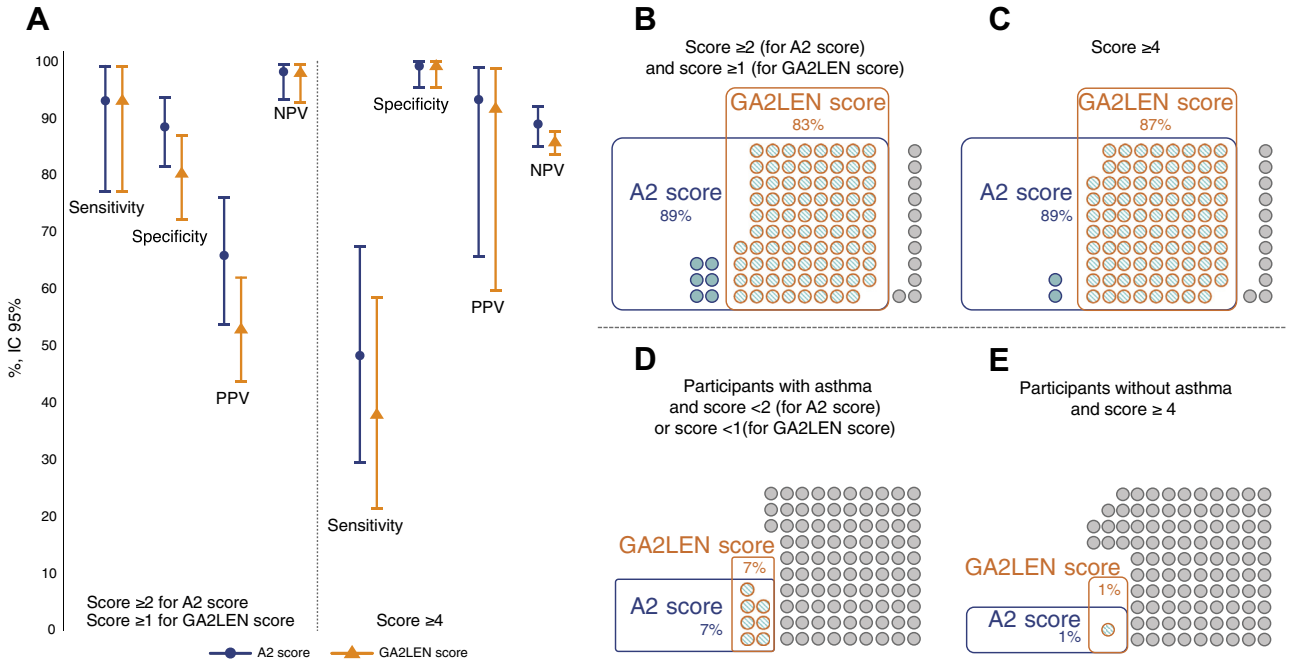

FIGURE 3. Diagnostic accuracy measures (**A**) and accuracy (**B** and **C**) of the 2 scores in patients from the validation cohort for considering possible asthma (values ≥2 in the A2 score or values ≥1 in the GA2LEN score) and probable asthma (values ≥4); false-negative rate (**D**) and false-positive rate (**E**).

prevalence studies, a questionnaire with high specificity (few false positives) and PPV for asthma diagnosis is preferable. Both our scores had high specificity for asthma diagnosis, which is related to the choice of a PPV-based cutoff to rule in asthma. However, if our interest is to screen subjects to undergo a confirmatory clinical evaluation, a questionnaire with high sensitivity (few false negatives) and NPV is preferable in the first stage. In this case, we can also use these scores to rule out asthma with the NPV-based cutoff. A meta-analysis on screening tests for COPD diagnostic accuracy determined a pooled sensitivity of 64.5% (95% CI, 59.9%-68.8%) and a specificity of 65.2% (52.9%-75.8%) for the COPD Diagnostic Questionnaire[12]; more recently, the development and validation study of the Salzburg COPD screening questionnaire reported a sensitivity of 69.1% (56.6%-79.5%) and an NPV of 91.8% (87.5%-95.7%).[11] The values of sensitivity and NPV obtained for our scores, considering the cutoff to rule out asthma, were superior to those for the screening tests for COPD. These findings indicate that the A2 score and the GA2LEN score may be used for asthma screening, for instance, in clinical screening/triage settings to identify the patients who could benefit from complete diagnostic workup. They may help physicians in primary care or other specialties to screen patients with asthma using a simple score with a high level of discrimination and to identify the best candidates to be referred for a diagnostic workup.

Pekkanen et al[6] developed the ECRHS asthma score using the question "Have you ever had asthma?" and with bronchial hyperreactivity as the comparator. It includes 8 questions (see the "ECRHS score" section and Table E1 in this article's Online Repository). Applying the ECRHS asthma score to our data and comparing it with the scores developed in the present study, we found that the A2 score has the same number of questions as the ECRHS asthma score, but shows better discriminative properties, better internal consistency, and better diagnostic accuracy measures. However, the GA2LEN score has the advantage of being shorter than the ECRHS asthma score, with comparable diagnostic accuracy measures and better discriminative properties and internal consistency (see the "ECRHS score" section and Table E4 in this article's Online Repository at www.jaci-inpractice.org).

The A2 score includes questions on previous physician diagnosis ("Did a physician confirm you had asthma?" and "Do you still have asthma (previously diagnosed by a physician)?"), whereas the GA2LEN score asks "Have you ever had asthma?" which can be preferable in settings with significant underdiagnoses or difficult access to health care. Moreover, the A2 score has 1 additional question: "Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 months?" The GA2LEN score may be considered to be more practical than the A2 score, because it is shorter and 1 positive answer is enough to consider possible asthma. The questions included in the A2 score that are not in the GA2LEN score are part of the ECRHS[10] and the National Health and Nutrition Examination Survey.[17]

This study has its strengths and limitations. In the present study, the Global Initiative for Asthma guidelines[1] for asthma diagnosis were followed by trained physicians, supported by objective measurements, and blinded to the results of previous self-administered questionnaires. A limitation of this study is that we did not validate the scores in other populations and settings, limiting its generalization. New studies using these scores are being designed, and their application to other data sets is warranted for external validation. To improve the robustness of the validation results, we used bootstrap resampling techniques, obtaining very similar results to those reported for the validation cohort (data not shown). Another limitation is the use of PPV-/NPV-based cutoffs, which are measurements highly dependable on asthma prevalence, and therefore these cutoff values may not be transferable to other settings. As so, presenting the results as continuous, before its dichotomization, is advisable when applying the scores. Despite these limitations, this study proposes scores developed on the basis of real-life data from the general population and on asthma diagnosis by a specialist that can be used for either asthma identification or asthma screening/triage.

CONCLUSIONS

Two scores based on self-administered questions were developed and validated compared with physician-led asthma diagnostic workup. These scores are short, easy to use, and can be applied to identify the likely presence of asthma (prevalence) or absence (screening) of asthma in epidemiological studies and clinical screening/triage settings. The A2 score may be preferred in studies aiming at maximum accuracy; however, the GA2LEN score is shorter and would be preferable for communities in which there may be difficulties related to physician diagnosis of asthma. Asthma presence can be considered for results of 4 or more in either the A2 score or the GA2LEN score and can be excluded for results of 0 in the GA2LEN score or of 0 to 1 in the A2 score. For results in between, asthma is possible but requires a confirmatory clinical evaluation. Nevertheless, the presentation of the results as a continuum score before dichotomization using a cutoff is advisable. The use of the A2 score and the GA2LEN score may contribute to reducing the inconsistencies of asthma definitions across studies and surveys and have the potential to be used in clinical settings for screening/triage of asthma, where they may contribute toward identifying the best candidates to be referred for diagnostic workup.

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Conflicts of interest: J. Bousquet received personal fees outside the submitted work from Chiesi, Cipla, Hikma, Menarini, Mundipharma, Mylan, Novartis, Sanofi-Aventis, Takeda, Teva, Uriach, and Kyomed. J. A. Fonseca received fees outside the submitted work from ALK, AstraZeneca, Boehringer Ingelheim, Chiesi, Diater, GSK, HAL Allergy, Laboratórios Vitória, Leti, Menarini, Mundipharma, Novartis, and Teva. The rest of the authors declare that they have no relevant conflicts of interest.

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ONLINE REPOSITORY

METHODS

This section describes in detail the methods of the ICAR study.

The ICAR was a nationwide population-based observational cross-sectional study. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki, consistent with good clinical practice and the applicable regulatory requirements, and was approved by a hospital ethics committee (*Comissão de Ética do Hospital São João EPE*, on October 17, 2011) and by the national data protection committee (no. 12372/2011). The study protocol containing standard operational procedures was registered in ClinicalTrials.gov (NCT01771120). All participants signed the consent form.

Sample size

The ICAR sample size calculations were based on the comparison of quality of life measured by the World Health Organization's Quality of Life (WHOQOL-BREF)[E1] questionnaire. Considering previous participation and expressed willingness, we estimate a nonparticipation rate of 33%. We have assumed a WHOQOL-BREF SD of 3.0 units, on the basis of the previous reports for different domains and populations.[E1,E2] Consequently, to identify a change of 1 unit in the WHOQOL-BREF quality-of-life scores, in a 2-sided test, for a type I error probability of 0.05 and a statistical power of 80, 142 individuals in each group are required. We include individuals without respiratory symptoms at a 2:1 ratio to other groups. As so, we calculated a sample of 750 individuals divided into 4 patient groups: (1) patients with a self-reported diagnosis of asthma alone (n = 150), (2) patients with a self-reported diagnosis of rhinitis alone (n = 150), (3) patients with a self-reported diagnosis of asthma and rhinitis (n = 150), and (4) patients with no history of respiratory symptoms or diseases (n = 300).

Participants and data collection

In the ICAR study, all subjects who have been included in the INAsma (*Inquérito Nacional sobre Asma*) study[E3,E4] and who have expressed their willingness to participate in a clinical assessment were eligible along with their family members. Furthermore, local media and posters were used to disseminate the study and invite participants. Persons who did not understand spoken Portuguese and who had cognitive or physical conditions that could hamper their participation in the study were excluded.

Data were collected between October 30, 2012, and July 12, 2014, in 2 allergy clinics (Lisbon and Porto) or by using a mobile diagnostic unit, on the basis of the participants' geographical proximity.

Participants were screened by telephonic interview into 1 of the 4 groups. A total of 858 participants, either with asthma and/or rhinitis or with no previous history of respiratory symptoms or diseases (aged between 3 and 89 years), were included from 90 Portuguese cities.

Data collection comprised anthropometric measurements, lung function and exhaled nitric oxide tests, skin prick tests, a structured clinical assessment, and standardized questionnaires. Anthropometric measurements of height, weight, and waist/hip circumference followed the procedures manual of the National Health and Nutrition Examination Survey.[E5] Lung function tests included spirometry with postbronchodilator reversibility (EasyOne Pro, ndd, Zurich, Switzerland, and Jaeger IOS, CareFusion, San Diego, Calif), carbon monoxide in exhaled air (SmokeCheck, Micro Medical, Kent, UK), and exhaled nitric oxide (NIOX Mino, Aerocrine AB, Solna, Sweden), and were done according to standardized methods.[E6-E8] Atopy was determined with skin prick tests. Blood sampling allowed for the determination of total IgE, eosinophilic cationic protein, and C-reactive protein. The structured clinical assessment performed by a trained physician included physical examination, comorbidities screening (eg, gastroesophageal reflux and anxiety/depression), use of health resources and medications because of asthma/rhinitis, assessment of the degree of control of the allergic diseases, family history, environmental exposures (at home and workplace), and social habits. In the ICAR study, self-administered questionnaires included the assessment of the following:

1. disease symptoms and control, using the Portuguese versions of the GA2LEN survey questionnaire,[E9] the allergy airway diseases screening (ASF) questionnaire,[E10] visual analog scales, the Control of Allergic Rhinitis and Asthma Test,[E11] the Control of Allergic Rhinitis and Asthma Test for kids,[E12] and the Allergic Rhinitis Control Test[E13];
2. quality of life, using the Portuguese versions of the EuroQol 5-dimensional questionnaire,[E14] the WHOQOL-BREF,[E1] the Mini Asthma Quality of Life Questionnaire,[E15] the Mini Rhinoconjunctivitis Quality of Life Questionnaire,[E16] and the Paediatric Asthma Caregiver's Quality of Life Questionnaire[E17];
3. work/school absenteeism and impairment, using the Work Productivity and Activity Impairment questionnaire[E18];
4. adherence to prescribed treatment, using the Medication Adherence Report Scale[E19]; and
5. physical activity, using the International Physical Activity Questionnaire.[E20]

EXPLORATORY FACTOR ANALYSIS

This section contains complementary material on exploratory factor analysis results.

The A2 score derivation was obtained by exploratory factor analysis as follows. The predictors "asthma diagnosis by a physician" and "asthma self-report" were highly correlated and had similar loading factors; however, because "asthma diagnosis by a physician" improved the Cronbach α of the final score, it was included, whereas "asthma self-report" was excluded. "Waking up with chest tightness" and "dry cough during the night not associated with infection" were excluded because they had a low item-total correlation. The best Cronbach α was obtained when "waking up with an attack of cough," "waking up with an attack of shortness of breath," and "having an attack of shortness of breath after exercise" were excluded. The final A2 score included 8 predictors in 2 factors with eigenvalues of 3.997 (predictors 2-5 and 10; Table II) and 3.535 (predictors 6-8).

For the GA2LEN score, "phlegm when coughing" was excluded because it had more than 95% responses in a single category; "waking up with chest tightness" and "hospitalization because of asthma" were excluded because they had a low item-total correlation. The best Cronbach α was obtained when "waking up with an attack of cough" and "waking up with an attack of shortness of breath" were excluded. The final GA2LEN score included 6 predictors in 2 factors with eigenvalues of 2.954 (predictors 6-8; Table II) and 2.860 (predictors 1, 4, and 5).

TABLE E1. Initial predictors (Portuguese and English versions) used to develop the multivariable prediction models and predictors included in the ECRHS asthma score previously developed

Portuguese version of the predictors	Predictors	From literature, as suggested by Sá-Sousa et al (A2 score)	From GA2LEN questionnaire (GA2LEN score)	Asthma score based on ECRHS
1. *Já alguma vez teve asma?*	1. Have you ever had asthma?	×	×	×
2. *Alguma vez um médico lhe disse que tem asma?*	2. Did a physician confirm you had asthma?	×		
3. *Ainda tem asma?*	3. Do you still have asthma?	×		
4. *Alguma vez esteve hospitalizado por asma?*	4. Have you ever been hospitalized because of asthma?		×	
5. *Teve um ataque de asma nos últimos 12 meses?*	5. Have you had any asthma attack in the last 12 mo?	×	×	×
6. *Presentemente está a tomar remédios (inaladores, aerossóis ou comprimidos) para a asma?*	6. Are you currently taking any medicines including inhalers, aerosols, or tablets for asthma?	×	×	×
7. *Alguma vez teve chiadeira ou pieira no peito nos últimos 12 meses?*	7. Have you ever had wheezing or whistling in the chest at any time in the last 12 mo?	×	×	
8. *Teve a chiadeira ou a pieira sem estar constipado?*	8. Have you had this wheezing or whistling when you did not have a cold?	×	×	
9. *Teve falta de ar quando a chiadeira estava presente?*	9. Have you been at all breathless when the wheezing noise was present?	×	×	×
10. *Alguma vez foi acordado devido a um ataque de falta de ar, depois de atividade física moderada ou intensa, nos últimos 12 meses?*	10. Have you had an attack of shortness of breath after exercise in the last 12 mo?	×		×
11. *Alguma vez teve uma crise de falta de ar, que surgiu durante o dia, quando estava em repouso, nos últimos 12 meses?*	11. Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 mo?	×		×
12. *Acordou com a sensação de aperto no peito nos últimos 12 meses?*	12. Have you woken up with the feeling of tightness in your chest at any time in the last 12 mo?	×	×	×
13. *Alguma vez foi acordado devido a um ataque de falta de ar nos últimos 12 meses?*	13. Have you been woken up by an attack of shortness of breath at any time in the last 12 mo?	×	×	×
14. *Alguma vez foi acordado devido a um ataque de tosse nos últimos 12 meses?*	14. Have you been woken up by an attack of coughing at any time in the last 12 mo?	×	×	
15. *Alguma vez teve tosse seca durante a noite nos últimos 12 meses, não contando com a tosse associada a constipação ou infeção?*	15. In the last 12 mo, have you had a dry cough during the night, apart from a cough associated with a cold or a chest infection?	×		
16. *Na maioria dos dias produz muco do seu peito durante um período de três meses por ano?*	16. Did you have phlegm when coughing for at least 3 mo in the last year?		×	

TABLE E2. Diagnostic accuracy measures for each predictor in the derivation and validation cohorts

	Derivation cohort (n = 560)				Validation cohort (n = 151)			
Predictor	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**PPV (95% CI)**	**NPV (95% CI)**	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**PPV (95% CI)**	**NPV (95% CI)**
1. Have you ever had asthma?	76.7 (69.0-83.8)	91.6 (88.7-94.0)	73.9 (66.2-80.8)	92.7 (89.9-94.9)	69.0 (51.0-91.8)	91.8 (86.1-95.8)	66.7 (48.9-81.7)	92.6 (87.0-96.4)
2. Did a physician confirm you had asthma?	76.7 (69.0-83.8)	93.0 (90.3-95.1)	77.3 (69.6-83.9)	92.8 (90.0-95.0)	65.5 (47.4-91.8)	91.8 (86.1-95.8)	65.5 (47.4-81.0)	91.8 (86.1-95.8)
3. Do you still have asthma (previously diagnosed by a physician)?	67.7 (59.4-75.2)	96.7 (94.7-98.1)	86.5 (79.1-92.2)	90.6 (87.7-93.0)	62.1 (43.9-78.2)	95.1 (90.3-98.0)	75.0 (55.7-89.2)	91.3 (85.6-95.4)
4. Have you ever been hospitalized because of asthma?	22.6 (16.0-30.1)	97.7 (95.9-98.8)	75.0 (60.3-86.6)	76.3 (72.6-79.6)	20.7 (8.8-37.5)	98.4 (95.0-99.7)	75.0 (40.9-95.3)	80.8 (74.0-86.5)
5. Have you had any asthma attack in the last 12 mo?	33.1 (25.5-41.3)	98.4 (96.9-99.3)	86.3 (75.1-93.9)	82.5 (79.1-85.6)	20.7 (8.8-37.5)	99.2 (96.4-100.0)	85.7 (50.6-99.1)	84.0 (77.5-89.4)
6. Are you currently taking any medicines including inhalers, aerosols, or tablets for asthma?	45.9 (37.5-54.4)	98.8 (97.5-99.6)	92.4 (84.4-97.2)	85.4 (82.1-88.4)	34.5 (19.0-52.6)	99.2 (96.4-100.0)	90.9 (65.7-99.5)	86.4 (80.1-91.4)
7. Have you ever had wheezing or whistling in the chest at any time in the last 12 mo?	69.9 (61.8-77.3)	80.1 (76.1-83.7)	52.2 (44.9-59.5)	89.5 (86.2-92.3)	72.4 (54.7-86.3)	86.1 (79.2-91.4)	55.3 (39.5-70.3)	92.9 (87.2-96.7)
8. Have you had wheezing or whistling when you did not have a cold?	47.4 (39.0-55.8)	90.4 (87.4-93.0)	60.6 (51.0-69.6)	84.6 (81.2-87.8)	48.3 (30.8-66.0)	96.7 (92.5-99.0)	77.8 (55.7-92.5)	88.7 (82.6-93.3)
9. Have you been at all breathless when the wheezing noise was present?	57.9 (49.4-66.1)	90.4 (87.4-93.0)	65.3 (56.4-73.5)	87.3 (84.0-90.2)	58.6 (40.5-75.2)	94.3 (89.2-97.5)	70.8 (51.2-86.3)	90.6 (84.7-94.8)
10. Have you had an attack of shortness of breath after exercise in the last 12 mo?	21.8 (15.4-29.3)	96.3 (94.2-97.8)	64.4 (49.9-77.3)	79.8 (76.2-83.1)	27.6 (13.7-45.3)	99.2 (96.4-100.0)	88.9 (59.5-99.3)	85.2 (78.8-90.4)
11. Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 mo?	39.1 (31.1-47.5)	93.9 (91.4-95.9)	66.7 (55.8-76.5)	83.2 (79.9-86.4)	37.9 (21.8-56.1)	98.4 (95.0-99.7)	84.6 (59.6-97.3)	87.0 (80.7-91.1)
12. Have you woken up with the feeling of tightness in your chest at any time in the last 12 mo?	29.3 (22.0-37.4)	86.2 (82.7-89.2)	39.8 (30.5-49.7)	79.7 (75.8-83.2)	34.5 (19.0-52.6)	87.7 (81.1-92.7)	40.0 (22.5-59.5)	84.9 (78.0-90.4)
13. Have you been woken up by an attack of shortness of breath at any time in the last 12 mo?	25.6 (18.7-33.4)	94.6 (92.2-96.5)	59.6 (46.7-71.8)	80.3 (76.7-83.6)	20.7 (8.8-37.5)	93.4 (88.1-96.9)	42.9 (19.8-68.3)	83.2 (76.4-88.8)
14. Have you been woken up by an attack of coughing at any time in the last 12 mo?	52.6 (44.2-61.0)	63.5 (58.8-67.9)	31.0 (25.2-37.2)	81.1 (76.7-85.1)	58.6 (40.5-75.2)	69.7 (61.2-77.4)	31.5 (20.2-44.5)	87.6 (80.1-93.2)
15. In the last 12 mo, have you had a dry cough during the night, apart from a cough associated with a cold or a chest infection?	58.6 (50.2-66.8)	66.3 (61.7-70.7)	35.1 (29.1-41.6)	83.7 (79.5-87.4)	65.5 (47.4-81.0)	67.2 (58.6-75.1)	32.2 (21.2-44.7)	89.1 (81.7-94.4)
16. Did you have phlegm when coughing for at least 3 mo in the last year?	8.3 (4.4-13.7)	98.1 (96.5-99.1)	57.9 (35.8-78.0)	76.3 (72.6-79.6)	6.9 (1.2-19.8)	98.4 (95.0-99.7)	50.0 (10.7-89.3)	80.8 (74.0-86.5)

TABLE E3. Diagnostic accuracy measures in derivation and validation cohorts

Score (no. of positive answers)	Derivation cohort (n = 560)						Validation cohort (n = 151)					
	n (%)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy %	n (%)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy %
A2 score												
Possible Asthma												
≥2*	183 (32.7)	85.7 (78.6-91.2)	83.8 (80.0-87.2)	62.3 (56.8-67.5)	95.0 (92.5-96.6)	84.3	41 (27.2)	93.1 (77.2-99.2)	88.5 (81.5-93.6)	65.9 (53.8-76.1)	98.2 (93.4-99.5)	89.4
≥3	130 (23.2)	75.9 (67.8-82.9)	93.2 (90.4-95.4)	77.7 (70.8-83.4)	92.6 (90.2-94.4)	89.1	24 (15.9)	65.5 (45.7-82.1)	95.9 (90.7-98.7)	79.2 (60.8-90.3)	92.1 (87.6-95.1)	90.0
Probable Asthma												
≥4†	93 (16.6)	59.4 (50.5-67.8)	96.7 (94.6-98.2)	85.0 (76.8-90.6)	88.4 (86.2-90.4)	87.9	15 (9.9)	48.3 (29.5-67.5)	99.2 (95.5-100.0)	93.3 (65.7-99.0)	89.0 (85.0-92.0)	89.4
≥5	70 (12.5)	46.6 (37.9-55.5)	98.1 (96.3-99.2)	88.6 (79.2-94.0)	85.5 (83.4-87.4)	85.9	12 (7.9)	37.9 (20.7-57.7)	99.2 (95.5-100.0)	91.7 (59.7-98.8)	87.1 (83.5-89.4)	87.4
≥6	58 (10.4)	39.9 (31.5-48.7)	98.8 (97.3-99.6)	91.4 (81.2-96.3)	84.1 (82.1-85.8)	84.8	10 (6.6)	31.0 (15.3-50.8)	99.2 (95.5-100.0)	90.0 (54.3-98.6)	85.8 (82.6-88.5)	86.1
≥7	39 (7.0)	26.3 (19.1-34.7)	99.1 (97.6-99.7)	89.7 (76.0-96.0)	81.2 (79.6-82.7)	81.8	7 (4.6)	20.7 (7.99-39.7)	99.2 (95.5-100.0)	85.7 (42.9-98.0)	84.0 (81.4-86.4)	84.1
8	20 (3.6)	12.8 (7.6-19.7)	99.3 (98.0-99.9)	85.0 (62.8-95.0)	78.5 (77.4-79.6)	78.8	2 (1.3)	6.9 (0.9-22.8)	100.0 (97.0-100.0)	100.0	81.9 (80.4-83.3)	82.1
GA2LEN score												
Possible Asthma												
≥1*	229 (40.9)	90.2 (83.8-94.7)	74.5 (70.1-78.5)	52.4 (48.1-56.7)	96.1 (93.6-97.6)	78.2	51 (33.8)	93.1 (77.2-99.1)	80.3 (72.2-87.0)	52.9 (43.7-62.0)	98.0 (92.8-99.5)	82.8
≥2	167 (29.8)	79.0 (71.0-85.5)	85.5 (81.8-88.7)	62.9 (57.0-68.4)	92.9 (90.4-94.8)	83.9	31 (20.5)	75.9 (56.5-89.7)	92.6 (86.5-96.6)	71.0 (55.8-82.6)	94.2 (89.4-96.9)	89.4
≥3	111 (19.8)	65.4 (56.7-73.4)	94.4 (91.8-96.4)	78.4 (70.7-84.5)	89.8 (87.4-91.7)	87.5	21 (13.9)	58.6 (38.9-76.5)	96.7 (91.8-99.1)	81.0 (60.7-92.1)	90.8 (86.4-93.8)	89.4
Probable Asthma												
≥4†	74 (13.2)	48.1 (39.4-57.0)	97.7 (95.7-98.9)	86.5 (77.2-92.4)	85.8 (83.7-87.7)	85.9	12 (7.9)	37.9 (20.7-57.7)	99.2 (95.5-100.0)	91.7 (59.7-98.8)	85.8 83.7-87.7	87.4
≥5	50 (8.9)	33.1 (25.2-41.8)	98.6 (97.0-99.5)	88.0 (76.2-94.4)	82.6 (80.8-84.2)	83.0	10 (6.6)	31.0 (15.3-50.8)	99.2 (95.5-100.0)	90.0 (54.3-98.6)	85.8 (82.6-88.5)	86.1
6	24 (4.3)	15.0 (9.4-22.3)	99.1 (97.6-99.7)	83.3 (63.5-93.5)	78.9 (77.7-80.1)	79.1	3 (2-0)	6.9 (0.9-22.8)	99.2 (95.5-100.0)	66.7 (15.8-95.5)	81.8 (80.2-83.2)	81.5

A2 score, Adult Asthma Epidemiological Score; *GA2LEN score*, Global Allergy and Asthma Network of Excellence Asthma Epidemiological Score; *PPV*, Positive predictive value; *NPV*, negative predictive value.

*Cutoff of ≥2 (for the A2 score) and of ≥1 (for the GA2LEN score) for considering possible asthma (NPV of 95% or more, simultaneously in derivation and validation cohorts).

†Cutoff of ≥4 for considering probable asthma (PPV 85% or more, simultaneously in derivation and validation cohorts.

TABLE E4. Diagnostic accuracy measures of the ECRHS asthma score previously developed, using participants from the derivation and validation cohorts

Score (no. of positive answers)	Derivation cohort (n = 560)						Validation cohort (n = 151)					
	n (%)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy %	n (%)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy %
Possible Asthma												
≥1*	244 (43.6)	87.2 (80.3-92.4)	70.0 (65.4-74.3)	47.5 (43.6-51.5)	94.6 (91.8-96.5)	74.1	60 (39.7)	93.1 (77.2-99.2)	73.0 (64.2-80.6)	45.0 (37.6-52.7)	97.8 (92.1-99.4)	76.8
≥2	147 (26.3)	74.4 (66.2-81.6)	88.8 (85.4-91.6)	67.4 (60.8-73.3)	91.8 (89.8-93.7)	85.4	29 (19.2)	72.4 (52.8-87.3)	93.4 (87.5-97.1)	72.41 (56.4-84.2)	93.4 (88.8-96.3)	89.4
≥3	89 (15.9)	54.1 (45.3-62.8)	96.0 (93.7-97.7)	80.9 (72.2-87.4)	87.1 (84.8-89.0)	86.1	16 (10.6)	51.7 (32.5-70.6)	99.2 (95.5-100.0)	93.8 (67.4-99.1)	89.6 (85.6-92.7)	90.1
Probable Asthma												
≥4†	68 (12.1)	45.9 (37.2-54.7)	98.4 (96.7-99.3)	89.7 (80.3-94.9)	85.4 (83.3-87.2)	85.9	12 (7.9)	37.9 (20.7-57.7)	99.2 (95.5-100.0)	91.7 (59.7-98.8)	87.1 (83.5-89.9)	87.4
≥5	44 (7.9)	28.6 (21.1-37.1)	98.6 (97.0-99.5)	86.4 (73.3-93.6)	81.6 (79.9-83.2)	82.0	6 (4)	17.2 (5.9-35.8)	99.2 (95.5-100.0)	83.3 (37.8-97.6)	83.5 (81.0-85.6)	83.4
≥6	34 (6.1)	22.6 (15.8-30.6)	99.1 (97.6-99.7)	88.2 (72.9-95.4)	80.4 (78.9-81.8)	80.9	5 (3.3)	13.8 (3.9-31.7)	99.2 (95.5-100.0)	80.0 (31.7-97.2)	82.9 (80.7-84.9)	82.8
≥7	18 (3.2)	12.0 (7.0-18.8)	99.5 (98.3-99.9)	88.9 (65.1-97.2)	78.4 (77.3-79.5)	78.8	3 (2.0)	10.3 (2.2-27.4)	100.0 (97.0-100.0)	100.0	82.4 (80.6-84.2)	82.8
8	7 (1.3)	4.5 (1.7-9.6)	99.8 (98.7-100)	85.7 (42.2-98.0)	77.0 (76.4-77.7)	77.1	2 (1.3)	6.9 (0.9-22.8)	100.0 (97.0-100.0)	100.0	81.9 (80.4-83.3)	82.1

ECRHS, European Community Health Survey; *PPV*, positive predictive value; *NPV*, negative predictive value.
*Cut-off of ≥1 for considering possible asthma (NPV of 95% or more, simultaneously in derivation and validation cohorts).
†Cutoff of ≥4 for considering probable asthma (PPV 85% or more, simultaneously in derivation and validation cohorts).

THE ECRHS SCORE

This section contains details on the previously developed ECRHS asthma score and the application of this score to our data. The previously developed ECRHS asthma score[E21] has 8 questions:

1. Have you been at all breathless when the wheezing noise was present?
2. Have you woken up with the feeling of tightness in your chest at any time in the last 12 months?
3. Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 months?
4. Have you had an attack of shortness of breath after exercise in the last 12 months?
5. Have you been woken up by an attack of shortness of breath at any time in the last 12 months?
6. Have you ever had asthma?
7. Have you had any asthma attack in the last 12 months?
8. Are you currently taking any medicines including inhalers, aerosols, or tablets for asthma?

We applied the ECRHS asthma score to our data, and its performance was tested in the derivation and validation cohorts. The AUC obtained by applying the previously developed ECRHS asthma score to our data was 86.8% (95% CI, 82.8%-90.8%) and the Cronbach α was 0.826 (95% CI, 0.804-0.847). The diagnostic accuracy measures are described in Table E4.

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