

Validation of the German version of the Asthma Impairment and Risk Questionnaire (AIRQ)

Validierung der deutschen Version des Asthma Impairment and Risk Questionnaires (AIRQ)



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ABSTRACT

Background The Asthma Impairment and Risk Questionnaire (AIRQ), a 10-item, equally weighted, yes/no tool assessing symptom impairment and risk of exacerbations in patients with asthma aged ≥ 12 years, was developed and validated in a US patient population to evaluate varying levels of asthma control. This study aimed to validate the German language version of the AIRQ in patients aged ≥ 12 years with different levels of asthma control.

Methods A cross-sectional, observational, multi-centre study comprising a single visit was conducted in multiple specialised asthma centres and general practices in Germany. A total of 300 patients completed the following measures: 1) Patient Sociodemographic and Clinical Questionnaire, 2) AIRQ, 3) Asthma Control Test (ACT), and 4) Asthma Control Questionnaire (ACQ-6). Logistic regression analyses were conducted to assess the AIRQ score cut points with the greatest predictive validity in discriminating between different control levels relative to a standard of ACT plus prior-year exacerbations or ACQ-6 plus prior-year exacerbations.

Results The German version of the AIRQ demonstrated a robust capability to correctly identify well-controlled versus not well- or very poorly controlled (AUC values of 0.90 or higher) and well- or not well-controlled versus very poorly controlled asthma (AUC values of 0.89 or higher).

Conclusions The German version of the AIRQ is a suitable tool to identify adults with varying levels of asthma control, which in turn can help to accurately identify patients with uncontrolled asthma in clinical practice.

ZUSAMMENFASSUNG

Hintergrund Der Asthma Impairment and Risk Questionnaire (AIRQ), ein 10 Punkte umfassendes, gleichgewichtetes Ja/Nein-Tool zur Beurteilung der Symptombeeinträchtigung und des Risikos von Exazerbationen bei Patienten mit Asthma im Alter von ≥ 12 Jahren, wurde in einer US-amerikanischen Patientenpopulation entwickelt und validiert, unterschiedliche Grade der Asthmakontrolle zu bewerten. Ziel dieser Studie war es, die deutschsprachige Version des AIRQ bei Patienten im Alter von ≥ 12 Jahren mit unterschiedlichem Grad der Asthmakontrolle zu validieren.

Methoden Eine beobachtende, multizentrische Querschnittsstudie mit einem einzigen Besuch wurde in mehreren spezialisierten Asthmazentren und Allgemeinpraxen in Deutschland durchgeführt. Insgesamt 300 Patienten absolvierten die folgenden Maßnahmen: 1) Soziodemografischer und klinischer Patientenfragebogen, 2) AIRQ, 3) Asthmakontrolltest (ACT) und 4) Asthmakontrollfragebogen

(ACQ-6). Logistische Regressionsanalysen wurden durchgeführt, um die Schnittpunkte des AIRQ-Scores mit der größten prädiktiven Validität bei der Unterscheidung zwischen verschiedenen Kontrollniveaus im Vergleich zu einem Standard aus ACT plus Exazerbationen des Vorjahres oder ACQ-6 plus Exazerbationen des Vorjahres zu ermitteln.

Ergebnisse Die deutsche Version des AIRQ zeigte eine robuste Fähigkeit, gut kontrolliertes von nicht gut oder sehr schlecht kontrolliertem Asthma (AUC-Werte von 0,90 oder höher) sowie gut oder nicht gut kontrolliertes von sehr schlecht kontrolliertem Asthma (AUC-Werte von 0,89 oder höher) korrekt zu unterscheiden.

Schlussfolgerungen Die deutsche Version des AIRQ ist ein geeignetes Instrument zur Identifizierung von Erwachsenen mit unterschiedlichem Grad der Asthmakontrolle, was wiederum dazu beitragen kann, Patienten mit unkontrolliertem Asthma in der klinischen Praxis akkurat zu identifizieren.

Background

The goal of asthma therapy is to achieve disease control, which includes symptom relief, lung function improvement, and exacerbation prevention [1]. Uncontrolled asthma is burdensome for patients, putting them at increased risk for frequent exacerbations, greater healthcare resource utilisation, and limitations in activities compared to those with well-controlled disease [2, 3]. However, even patients with good symptom control can experience severe exacerbations [1]. In addition, asthma control is often overestimated by patients and health care professionals, which underscores the importance of changing the current practice of how patients with uncontrolled asthma are identified and monitored [4–7]. Validated questionnaires are available to assess asthma control in a standardised manner, including the Asthma Control Test (ACT) and the Asthma Control Questionnaire (ACQ) [1, 8, 9]. Although asthma control comprises both impairment and risk of adverse outcomes, both control measures only evaluate impairment [8, 9]. A composite control measure capable of identifying uncontrolled asthma more accurately than the current impairment measures may be helpful to reduce morbidity from uncontrolled disease.

The Asthma Impairment and Risk Questionnaire (AIRQ) is a 10-item yes/no composite asthma control tool. It was designed to assess symptoms over the past two weeks and exacerbations over the past 12 months [10–12]. It also predicts exacerbations in the coming 12 months and the probability of time to first exacerbation [13]. The AIRQ was evaluated in a US adult and adolescent patient population of all asthma severities, yielding receiver operating characteristic area-under-the-curve (ROC AUC) values of 0.94 for discriminating between well-controlled and not well- or very poorly controlled asthma and 0.93 for discriminating between well- or not well-controlled and very poorly controlled asthma. The good validity and clinical utility of the AIRQ for identifying patients with uncontrolled asthma justify translation into other languages and validation in other

populations. The locally adapted Spanish version of the AIRQ, for example, was able to demonstrate that it is a valid instrument that yields similar measurement properties to the original English version [14].

The present study aimed to validate the German language version of the AIRQ by determining the performance characteristics of the German AIRQ score and identifying the cut points of control with the greatest predictive validity in terms of discriminating patients with varying levels of asthma control relative to ACT score (primary objective) and ACQ-6 score (secondary objective). The exploratory objectives were to assess the agreement between the asthma control level determined by AIRQ, ACT, and ACQ-6 scores and the patient's asthma control level as perceived by physicians as well as to assess the agreement between AIRQ score, ACT score plus prior-year exacerbations validation standard, and ACQ-6 score plus prior-year exacerbations secondary standard.

Methods

Study design

This was a cross-sectional, observational, multi-centre study consisting of a single visit and targeted enrolment of adults and adolescents aged ≥ 12 years with a clinically confirmed asthma diagnosis in Germany.

Study setting

The aim was to enrol 300 patients from about ten specialised asthma centres and general practices in Germany. Best efforts were made to recruit equal numbers of patients across ACT score group ranges (≥ 20 [well-controlled], 16–19 [not well-controlled], and ≤ 15 [very poorly controlled]) to ensure the inclusion of different levels of asthma control and severity in the study population. Site staff collected all necessary information from patients' medical records to determine their eligibili-

ty for enrolment. ACT scores from the past two weeks were used to verify that the patient fell into a group that was still open for enrolment. Although patients on a biologic treatment for asthma were permitted to enrol, the number of patients on biologics was monitored so that no more than 10% of participants on any biologic therapy were permitted to participate. Enrolment of eligible patients was competitive between study sites; however, inclusion materials provided to each site after training and initiation were limited to approximately 40 sets. Adult and adolescent patients with a confirmed asthma diagnosis were subsequently screened, and those who met all inclusion criteria were invited to participate. Adult patients and parents of adolescent patients provided written informed consent, with adolescents providing assent.

Participants

Inclusion criteria comprised: 1) aged ≥ 12 years at the time of consent, 2) physician-diagnosed asthma, 3) medical asthma therapy according to current treatment guidelines, 4) willingness and ability to provide written informed consent, and 5) ability to read, understand, and speak German sufficiently to complete all the questionnaires. Patients were excluded from the study if they met any of the following criteria: 1) any past or present chronic lower respiratory diagnosis other than asthma including but not limited to: pulmonary fibrosis, bronchial carcinoma, obesity-induced hypoventilation syndrome, cystic fibrosis, lung cancer, and others that – in the investigator's opinion – were in conflict with inclusion and proper interpretation of the results, 2) cognitive impairment, psychiatric diseases, severe hearing or vision impairment, and/or insufficient knowledge of the German language, if the study physician believed that these factors might influence the ability to provide written consent and impair correct completion and assessment of the questionnaires, and/or 3) current participation in an interventional clinical trial. To ensure a study population with a variety of levels of asthma control and grades of severity, best efforts were made to recruit an equal number of patients with ACT scores of ≥ 20 , 16–19, or ≤ 15 .

Assessments

Patients completed the following measures: patient sociodemographic and clinical questionnaire, AIRQ (German version, **Supplementary Figure 1**), ACT, and ACQ-6. Retrospective exacerbation data were documented from patient records. An exacerbation was defined as a change in asthma control requiring: 1) a course of oral corticosteroids (OCS) for at least three days and/or steroid injection, or 2) an emergency room, urgent care, or unplanned office visit for an asthma exacerbation (not associated with a hospitalization), or 3) a hospital stay for asthma for >24 hours.

Statistical methods

All analyses were conducted using SAS version 9.4. Frequencies and percentages were used to describe categorical variables. Two-sided 95% confidence intervals (CIs) were presented where appropriate. Continuous variables were described as means and standard deviations as well as medians and interquartile ranges,

minimum and maximum. Logistic regression analyses were conducted to assess the AIRQ score cut points with the greatest predictive validity in discriminating between patients with different control levels compared to either the ACT score plus prior-year exacerbations standard used in the original English language AIRQ validation [11] or a secondary standard of ACQ-6 score plus prior-year exacerbations. Agreement between AIRQ, ACT, and ACQ-6 scores and patients' asthma control level as perceived by physicians was descriptively analysed using contingency tables. Also, the level of agreement between AIRQ score and the ACT score plus prior-year exacerbations standard and the ACQ-6 score plus prior-year exacerbations was descriptively analysed and compared using Krippendorff's alpha coefficient.

Primary analyses

Univariate logistic regression analyses were carried out to determine the cut points with the greatest validity relative to the ACT plus prior-year exacerbations standard. Two logistic models were conducted to distinguish 1) well-controlled from not well-controlled or very poorly controlled asthma, and 2) well-controlled or not well-controlled from very poorly controlled asthma. The likelihood ratio for a positive test (LR+), likelihood ratio for a negative test (LR-), sensitivity, specificity, positive predictive value, negative predictive values, Akaike information criterion (AIC), and receiver operating characteristic (ROC) curve were also calculated.

Secondary analyses

Similar analyses were conducted to achieve the secondary objective. Univariate logistic regression models were used comparing 1) well-controlled from not well-controlled or very poorly controlled asthma, and 2) well-controlled or not well-controlled from very poorly controlled asthma to determine performance characteristics of the AIRQ relative to the ACQ-6 plus prior-year exacerbations secondary standard.

Exploratory analyses

In addition to the primary and secondary analyses, additional exploratory analyses were carried out. The pairwise level of agreement between the AIRQ, ACT, and ACQ-6 score, as well as the physician's perception of asthma control were descriptively analysed and compared using weighted kappa. The magnitude of the kappa coefficient (k), which ranges from below 0 (agreement is worse than random) to 1 (complete agreement), is usually interpreted as follows: poor ($k < 0.20$), weak (k between 0.21 and 0.40), moderate (k between 0.41 and 0.60), good (k between 0.61 and 0.80), and very good (k between 0.81 and 1.00) [15]. The proportion of patients classified as well-controlled based on their treating physician, the ACT, ACQ-6, and AIRQ assessments, and the number of documented prior-year exacerbations was also descriptively compared. Based on the agreement between AIRQ score and physician assessment of control, two groups (concordant and discordant) were created, and sociodemographic and clinical characteristics of the groups were compared. A patient was assigned to the concordant group when the physician's assessment of a patient's asthma control was equal to the AIRQ assessment. Otherwise, the patient was

assigned to the discordant group. In addition, the agreement between AIRQ score, the ACT score plus prior-year exacerbations standard, and the ACQ-6 score plus prior-year exacerbations secondary standard was descriptively calculated and compared using Krippendorff's alpha coefficient.

Results

The data collection period started on 19 July 2021 with the first patient in and ended on 9 November 2021 with the last patient having enrolled in the cohort. The number of patients included in the all patients enrolled set was 311. Of these, a total of 11 patients were excluded due to the respective ACT score group being closed for enrolment (6 patients) or due to not meeting inclusion/exclusion criteria (5 patients). Therefore, the full analysis set (FAS) included 300 patients.

Demographic and other baseline characteristics

Over half of the patients in the FAS were female (61.3%) (► **Table 1**). The median age of the patients was 55 years. The median age at initial asthma diagnosis was 32 years. Only one patient was aged <18 years. A majority (87.7%) of the participants had at least one comorbidity. Of the 300 patients, 293 (97.7%) were treated with inhaled corticosteroids (ICS) in concordance with current guidelines. Most (70.0%) were treated with ICS in combination with a long-acting beta-agonist (LABA), and 86.7% were treated with any LABA medication (including ICS/LABA). A total of 30 patients (10.0%) were on biologic therapy as defined by the protocol.

Among the 300 patients, asthma was defined as well-controlled in 99 patients (33.0%), not well-controlled in 99 (33.0%), and very poorly controlled in 102 (34%) according to ACT score (► **Table 2**).

A total of 57 (19.0%) patients had at least one severe exacerbation during the previous year. 38 (12.7%) patients had an exacerbation requiring short-term oral corticosteroids (OCS) treatment for at least three days and/or an increase in long-term OCS dose, 27 (9.0%) patients had an exacerbation requiring an emergency room or unplanned office visit or treatment with a systemic corticosteroid, and 9 (3.0%) patients had an exacerbation that resulted in hospitalisation for ≥ 24 hours. Patients may be grouped in multiple categories depending on the type of exacerbation.

Primary analysis

The AIRQ model yielded a ROC of 0.91 to identify well-controlled versus not well- or very poorly controlled and a ROC of 0.90 to identify well- or not well-controlled versus very poorly controlled asthma, as reflected by the ACT plus prior-year exacerbations standard (► **Fig. 1**). An AIRQ score cut point of ≥ 2 for identifying well-controlled patients versus all others yielded a sensitivity of 85.8%, a specificity of 82.3%, and positive and negative predictive values of 91.1% and 73.1%, respectively. A cut point of ≥ 5 showed a sensitivity of 64.8%, a specificity of 91.8%, and positive and negative predictive values of 81.0% and 82.9%, respectively, for identifying very poorly controlled patients versus all others.

Secondary analysis

The AIRQ model yielded a ROC of 0.91 to identify well-controlled versus not well- or very poorly controlled asthma, and of 0.90 to identify well- or not well-controlled versus very poorly controlled asthma as reflected by the ACQ-6 plus prior-year exacerbations secondary standard (► **Fig. 2**). An AIRQ score cut point of ≥ 2 for identifying well-controlled patients versus all others yielded a sensitivity of 80.3%, a specificity of 88.7%, and positive and negative predictive values of 95.8% and 58.3%, respectively. A cut point of ≥ 5 showed a sensitivity of 51.6%, a specificity of 97.2%, and positive and negative predictive values of 95.2% and 65.3%, respectively, for identifying very poorly controlled patients versus all others.

Exploratory analysis

Among the 300 patients in the FAS, 142 (47.3%) were rated by their treating physician as having well-controlled asthma, whereas the number of patients with well-controlled asthma based on the ACT, ACQ-6, and AIRQ assessments was 102 (34.0%), 75 (25.0%), and 108 (36.0%), respectively (► **Table 3**). The weighted kappa (95% CI) measure of agreement between patients' asthma control level as perceived by physicians and the asthma control level determined by the assessments was 0.47 (0.40–0.55) for the AIRQ score and 0.57 (0.50–0.64) for the ACT score; whereas the agreement between the physician's perception of patient asthma control and the ACQ-6 score was weak, with a kappa coefficient (95% CI) of 0.36 (0.30–0.43).

Further exploratory results showed that the agreement between the AIRQ score and the ACT score plus prior-year exacerbations standard was good, with a kappa coefficient (95% CI) of 0.63 (0.55–0.69). The agreement between the AIRQ score and the ACQ-6 score plus prior-year exacerbations secondary standard was moderate, with a kappa coefficient (95% CI) of 0.53 (0.46–0.59). Additionally, there was substantial agreement between the AIRQ score, the ACT score plus prior-year exacerbations standard, and the ACQ-6 score plus prior-year exacerbations secondary standard as indicated by Krippendorff's alpha coefficient (95% CI) of 0.69 (0.65–0.72).

Among the population of physician-rated well-controlled patients, 7.0% had at least one documented prior-year exacerbation; the proportion of well-controlled asthma participants based on the ACT score, ACQ-6 score, and AIRQ score assessments who had at least one prior-year exacerbation was 5.9% (6/102), 5.3% (4/75), and 4.6% (5/108), and the number of participants with at least two prior-year exacerbations was 1% (1/102), 1.3% (1/75), and 0% (0/108), respectively.

Discussion

This cross-sectional study aimed to determine the performance characteristics of the German AIRQ and to identify the pre-defined cut points of control with the greatest predictive validity in terms of discrimination. Demographic characteristics at the reference date suggest that the study sample is a middle-aged adult population of patients with asthma and comorbidities, with the majority being treated with ICS monotherapy or ICS in

► **Table 1** Sociodemographic and clinical characteristics of patients reported at reference date.

Characteristics	Full Analysis Set (FAS)	
	N	%
Sociodemographic and clinical characteristics		
Sex	300	
Male	116	38.7
Female	184	61.3
Age at reference date	300	
Median (Q1, Q3)	55 (43; 64)	
<18 years	1	0.3
18–35 years	40	13.3
36–55 years	111	37.0
56–75 years	124	41.3
>75 years	24	8.0
Working status	300	
Employed, full-time	112	37.3
Employed, part-time	54	18.0
Homemaker	9	3.0
Student	9	3.0
Unemployed	10	3.3
Retired	83	27.7
Disabled	6	2.0
Other	17	5.7
Comorbidities¹	300	
Do not know/no comorbidities	37	12.3
With comorbidities ¹	263	87.7
Allergy diagnosed by blood or skin testing	130	43.3
Allergic rhinitis ²	142	47.3
Heart disease ³	32	10.7
Anxiety	30	10.0
Anaphylaxis ⁴	42	14.0
Arthritis	16	5.3
Aspirin sensitivity ⁵	27	9.0
Atopic dermatitis/eczema	20	6.7
Chronic bronchitis	54	18.0
Chronic obstructive pulmonary disease (COPD)	20	6.7
Chronic sinusitis	21	7.0
Depression	32	10.7
Diabetes	23	7.7
Emphysema	6	2.0
GORD (heartburn/reflux)	37	12.3
Hypertension	69	23.0

► **Table 1** (Fortsetzung)

Characteristics	Full Analysis Set (FAS)	
	N	%
Nasal polyps	26	8.7
Sleep apnoea	23	7.7
Stroke	3	1.0
Other	41	13.7
Clinician-reported age at initial diagnosis (years)	294	
Median (Q1, Q3)	32 (15; 46)	
Years since initial diagnosis	294	
Median (Q1, Q3)	18 (8; 31)	
Spirometry performed in the last year	300	
Yes	297	99.0
No	3	1.0
Asthma medication	300	
ICS (monotherapy)	38	12.7
LABA (monotherapy)	6	2.0
OCS (monotherapy)	0	0
Biologics (monotherapy)	1	0.3
ICS + LABA	210	70.0
ICS + OCS	1	0.3
ICS + LABA + OCS	15	5.0
ICS + LABA + biologics	26	8.7
ICS + LABA + OCS + biologics	3	1.0
Exacerbations experienced in the last year		
Number of patients with a severe exacerbation ⁶	57	19.0
Number of patients with an exacerbation requiring short-term OCS treatment for at least three days AND/OR an increase in the OCS dose	38	12.7
Number of patients with an exacerbation requiring a visit to an emergency room (≥ 24 hours), unplanned office visit or treatment with systemic corticosteroid	27	9.0
Number of patients with an exacerbation that resulted in hospitalisation for asthma for ≥ 24 hours	9	3.0
Number of severe exacerbations		
Mean (SD)	0.4 (0.94)	
Median (Q1, Q3)	0 (0; 0)	
Min, max	0 (7)	
Number of exacerbations requiring short-term OCS treatment for at least three days AND/OR an increase in the OCS dose ⁷		
Mean (SD)	1.1 (1.32)	
Median (Q1, Q3)	1 (0; 1)	
Min, max	0 (6)	

► **Table 1** (Fortsetzung)

Characteristics	Full Analysis Set (FAS)	
	N	%
Number of exacerbations requiring a visit to an emergency room (≥ 24 hours), unplanned office visit or treatment with systemic corticosteroid ⁷		
Mean (SD)	0.7 (1.02)	
Median (Q1, Q3)	0 (0; 1)	
Min, max	0 (4)	
Abbreviations: FAS, full analysis set; GORD, gastro-oesophageal reflux disease; ICS, inhaled corticosteroids; LABA, long-acting beta-agonist; OCS, oral corticosteroids. ¹ Note that patients may have several comorbidities; therefore, the total number of comorbidities does not add up to the total number of patients ² Nasal allergies, "hay fever" ³ History of heart attack, heart failure, or heart valve problems ⁴ Severe allergic reaction to a food, bee sting, allergy shot, medication, or other ⁵ Or other nonsteroidal anti-inflammatory drugs that cause hives, swelling, or breathing problems ⁶ The total number of patients who experience any severe exacerbation may not be equal to the sum of the number of patients who experience an OCS exacerbation, emergency visit exacerbation and hospitalisation exacerbation since one patient can have multiple types of exacerbations ⁷ Among patients suffering any severe exacerbations		

► **Table 2** Study population.

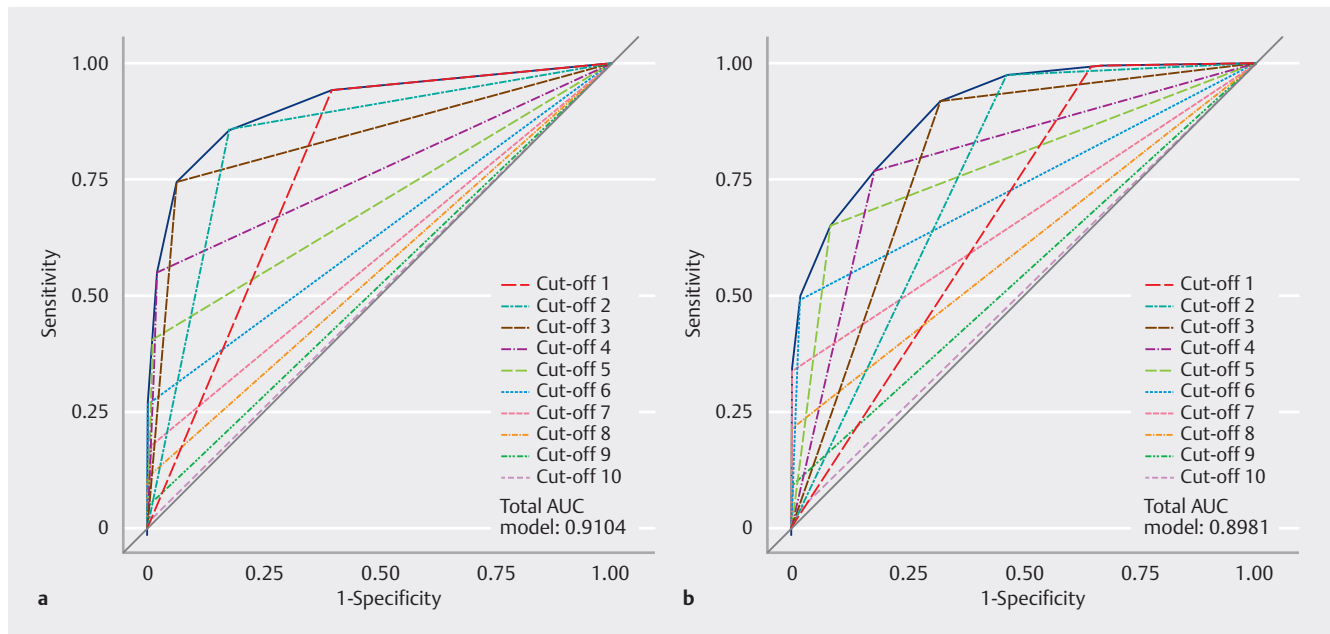
Study population	Patients remaining		Patients excluded	
	N patients	% patients	N patients	% patients
<i>All patients enrolled set</i>	311	100.0%		
ACT score group completed	305	98.1%	6	1.9%
Retrospectively excluded due to inclusion/exclusion criteria	300	96.5%	11	3.5%
<i>Full analysis set</i>	300	100.0%		
On biologic medication	30	10.0%	270	90.0%
Well-controlled: ACT score ≤ 15 points	99	33.0%	201	67.0%
Not well-controlled: ACT score 16–19 points	99	33.0%	201	67.0%
Very poorly controlled: ACT score ≥ 20 points	102	34.0%	198	66.0%
Abbreviations: ACT, Asthma Control Test				

combination with other asthma therapies in concordance with current guidelines [1]. The AIRQ performed well with respect to the ACT plus prior-year exacerbations standard and ACQ-6 plus prior-year exacerbations standard in identifying the different degrees of asthma control. Overall, the results of the present study confirmed the results of the original AIRQ validation study conducted among US patients [11], despite differences in health care systems and asthma management guidelines [16]. Thereby, the simple binary assessment allows for a broad coverage of asthma symptoms as described during the development and implementation of the AIRQ [11], without compromising the validity of the results.

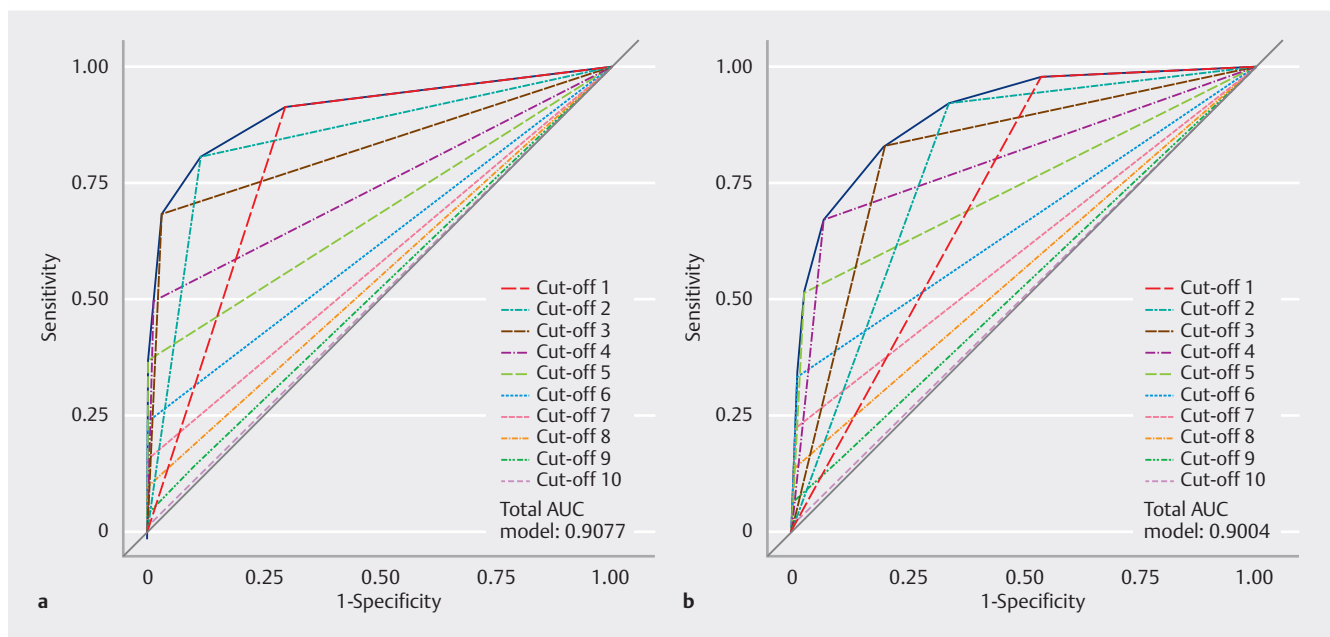
Aside from these confirmatory results of the AIRQ, it is remarkable that the agreement between physician-rated asthma control and the AIRQ, the ACT plus prior-year exacerbations standard, and the ACQ-6 plus prior-year exacerbations standard was found to be only moderate. This means that physicians often

overestimate the level of disease control in patients and are not fully aware of exacerbations in the previous year. This might indicate that a structured history taking of exacerbations is needed. These results are in line with previous data that showed only moderate concordance between physician-perceived and patient-perceived asthma control as measured by ACT or ACQ-6. However, that study was not powered for this analysis, and its informative value may thereby be limited [17, 18].

It is notable that there was a good agreement between the outcomes of the three questionnaires when the ACT and the ACQ-6 were complemented by the prior-year exacerbations standard. The AIRQ covers the prior-year exacerbations by default through questions eight to ten, while the ACT and ACQ-6 do not cover exacerbations. Interestingly, the agreement was high even though the questionnaires have different recall times of one, two or four weeks for the ACQ-6, AIRQ, and ACT, respectively, and partially cover different asthma symptoms.



► **Fig. 1** ROC curves and AUC of the German AIRQ based on patients' ACT score plus prior-year exacerbation history. To distinguish (a) well-controlled versus not well-controlled or very poorly controlled asthma, and (b) well-controlled or not well-controlled versus very poorly controlled asthma. Abbreviations: ACT, Asthma Control Test; AIRQ, Asthma Impairment and Risk Questionnaire; AUC, area under the curve; ROC, receiving operator characteristic.



► **Fig. 2** ROC curves and AUC of the German AIRQ based on patients' ACQ-6 score plus prior-year exacerbation history. To distinguish (a) well-controlled versus not well-controlled or very poorly controlled asthma, and (b) well-controlled or not well-controlled versus very poorly controlled asthma. Abbreviations: ACQ-6, 6-item Asthma Control Questionnaire; AIRQ, Asthma Impairment and Risk Questionnaire; AUC, area under the curve; ROC, receiving operator characteristic.

Most prominent differences between the questions are the inclusion of cough as a measure of asthma control in the AIRQ, but not in the ACT or the ACQ-6, and that one occurrence of sleep disturbance within the recall period is allowed for complete asthma control in the AIRQ.

There were some limitations of our study. The statistical analysis was of descriptive nature, thereby, no conclusions can be drawn on the significance of the analysis. The cross-sectional nature of the study requires assessment of the current level of asthma control using exacerbation data from a retrospective

► **Table 3** Physician, ACT, ACQ-6 and AIRQ assessment of asthma control.

Full Analysis Set												
Assessment of asthma control												
	AIRQ Score			ACT score			ACQ-6 score			Physician		
	N	%	95% CI	N	%	95% CI	N	%	95% CI	N	%	95% CI
Well-controlled	108	36.0%	30.6%; 41.7%	102	34.0%	28.7%; 39.7%	75	25.0%	20.2%; 30.3%	142	47.3%	41.6%; 53.2%
≥ 1 documented prior-year exacerbation	5	4.6%	1.5%; 10.5%	6	5.9%	2.2%; 12.4%	4	5.3%	1.5%; 13.1%	10	7.0%	3.4%; 12.6%
≥ 2 documented prior-year exacerbation	0	0%	0%; 3.4%	1	1.0%	0.0%; 5.3%	1	1.3%	0.0%; 7.2%	0	0%	0%; 2.6%

Abbreviations: ACQ-6, 6-item Asthma Control Questionnaire; ACT, Asthma Control Test; AIRQ, Asthma Impairment and Risk Questionnaire CI, confidence interval

chart review and the current ACT score (i. e., assessing symptom impairment over the past two weeks). Therefore, the likelihood of future adverse events or the response to treatment changes could not be assessed in this study. In contrast to the US validation study, in which 17.4% of the participants were aged 12–17, our study had only one participant aged < 18 years. Inclusion of almost exclusively adults in the patient population results in limited applicability to adolescents. Additional validation of the German version of the AIRQ in patients with asthma aged < 18 years is needed.

In conclusion, the AIRQ appears to be a robust tool for identifying patients with varying levels of asthma control. In clinical practice, the implementation of the AIRQ may help to identify patients with uncontrolled asthma more accurately and might provide another opportunity for clinicians to assess the appropriateness for maintenance of or changes to treatment. Future large-scale studies in real-life practice settings are needed to demonstrate the impact of AIRQ usage on the reduction of morbidity and mortality in uncontrolled disease.

Declarations

Ethic approval and consent to participate

Each patient gave informed consent to participate in this study, and the trial has been reviewed by the ethics committee of the chamber of physicians Schleswig-Holstein under the number 073/21 I. They had no obligations to the study.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Conflict of Interest

F. Kannies has served as a speaker and on advisory boards from AstraZeneca, Mundipharma, Novartis, GSK and Teva. M. Lommatzsch has served as a speaker and on advisory boards for ALK, Allergopharma, AstraZeneca, Bencard Allergie, Berlin-Chemie, Boehringer Ingelheim, Bosch, Chiesi, Circassia, GSK, HAL Allergy, Janssen-Cilag, MSD, Mundipharma, Novartis, Nycomed/Takeda, Sanofi, Teva, and UCB. T. Schultz has served as a speaker and on advisory boards and has received research support from AstraZeneca, Berlin-Chemie, Boehringer Ingelheim, Chiesi, Esanum, GSK, Meda, Mundipharma, Novartis, Omnia-med, TEVA, UCB and various professional associations. H. Timmermann has served as a speaker and lecturer and received consultant fees and/or research grants from AstraZeneca, Almirall, Astellas Pharma, Bayer, Boehringer Ingelheim, Berlin-Chemie, GSK, Leti Pharma, Meda, Mundipharma, Novartis, Nycomed, Pfizer, Sanofi, Takeda, and TEVA. O. Schmidt received fees for lectures or consulting from AstraZeneca, Boehringer Ingelheim, Chiesi, Novartis, and Sanofi. S. Heindl has served as speaker and received consultation fees from AstraZeneca, GSK, Sanofi and Klosterfrau Melisengeist. H.J. Baumann has served as a speaker and lecturer and received consultant fees and/or research grants from AstraZeneca, Boehringer Ingelheim, Berlin-Chemie, Chiesi, GSK, Novartis, Orion Pharma and Pfizer. R. Buhl has received grants from Boehringer Ingelheim, GSK, Novartis, and Roche, as well as personal fees from AstraZeneca, Berlin-Chemie, Boehringer Ingelheim, Chiesi, Cipla, GSK, Novartis, Sanofi, Roche and Teva. S. Korn has served as a speaker received consultation fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Novartis, and Sanofi. K. Defosse and F. Höing are employees of AstraZeneca. C. Taube has no competing interests to declare.

References

- [1] Global Initiative for Asthma (GINA). The Global Strategy for Asthma Management and Prevention. 2022
- [2] Suruki RY, Daugherty JB, Boudiaf N et al. The frequency of asthma exacerbations and healthcare utilization in patients with asthma from the UK and USA. *BMC Pulm Med* 2017; 17: 74
- [3] Sullivan PW, Slejko JF, Ghushchyan VH et al. The relationship between asthma, asthma control and economic outcomes in the United States. *J Asthma* 2014; 51: 769–778
- [4] Fuhlbrigge AL, Adams RJ, Guilbert TW et al. The burden of asthma in the United States: level and distribution are dependent on interpretation of the national asthma education and prevention program guidelines. *Am J Respir Crit Care Med* 2002; 166: 1044–1049 doi:10.1164/rccm.2107057
- [5] Murphy KR, Meltzer EO, Blaiss MS et al. Asthma management and control in the United States: results of the 2009 Asthma Insight and Management survey. *Allergy Asthma Proc* 2012; 33: 54–64 doi:10.2500/aap.2011.32.3518
- [6] Sastre J, Fabbri LM, Price D et al. Insights, attitudes, and perceptions about asthma and its treatment: a multinational survey of patients from Europe and Canada. *World Allergy Organ J* 2016; 9: 13
- [7] Kritikos V, Price D, Papi A et al. A multinational observational study identifying primary care patients at risk of overestimation of asthma control. *NPJ Prim Care Respir Med* 2019; 29: 43 doi:10.1038/s41533-019-0156-4
- [8] Nathan RA, Sorkness CA, Kosinski M et al. Development of the Asthma Control Test: a survey for assessing asthma control. *J Allergy Clin Immunol* 2004; 113: 59–65 doi:10.1016/j.jaci.2003.09.008
- [9] Juniper EF, O'Byrne PM, Guyatt GH et al. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999; 14: 902–907 doi:10.1034/j.1399-3003.1999.14d29.x
- [10] Lee TY, Petkau J, Sadatsafavi M. Long-Term Natural History of Severe Asthma Exacerbations and Their Impact on the Disease Course. *Ann Am Thorac Soc* 2022; 19: 907–915 doi:10.1513/AnnalsATS.202012-1562OC
- [11] Murphy KR, Chipps B, Beuther DA et al. Development of the Asthma Impairment and Risk Questionnaire (AIRQ): A Composite Control Measure. *J Allergy Clin Immunol Pract* 2020; 8: 2263–2274.e5
- [12] Reibman J, Chipps BE, Zeiger RS et al. Relationship Between Asthma Control as Measured by the Asthma Impairment and Risk Questionnaire (AIRQ) and Patient Perception of Disease Status, Health-Related Quality of Life, and Treatment Adherence. *J Asthma Allergy* 2023; 16: 59–72
- [13] Beuther DA, Murphy KR, Zeiger RS et al. Asthma Impairment and Risk Questionnaire (AIRQ) Control Level Predicts Future Risk of Asthma Exacerbations. *J Allergy Clin Immunol Pract* 2022; 10: 3204–3212.e2
- [14] Pérez de Llano L, Martínez Moragón E, Entrenas LM et al. Validation of the Asthma Impairment and Risk Questionnaire (AIRQ) in Spain: a useful tool to assess asthma control in adolescent and adult patients. *J Investig Allergol Clin Immunol* 2022; 33: 397–400
- [15] Altman DG. *Practical Statistics for Medical Research*. New York (US): CRC Press; 1990
- [16] National Heart, Lung, and Blood Institute. 2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. Published December 2020. Accessed May 05, 2021: <https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>
- [17] Fuhlbrigge A, Marvel J, Electricwala B et al. Physician-Patient Concordance in the Assessment of Asthma Control. *J Allergy Clin Immunol Pract* 2021; 9: 3080–3088.e3081
- [18] Matsunaga K, Hamada K, Oishi K et al. Factors Associated with Physician-Patient Discordance in the Perception of Asthma Control. *J Allergy Clin Immunol Pract* 2019; 7: 2634–2641