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ORIGINAL RESEARCH

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

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Purpose: Critical asthma outcomes highlighted in clinical guidelines include asthma-related quality of life, asthma exacerbations, and asthma control. An easy-to-implement measure of asthma control that assesses both symptom impairment and exacerbation risk and reflects the impact of asthma on patients' lives is lacking. Hence, the objective of this study was to assess the Asthma Impairment and Risk Questionnaire (AIRQ®) construct validity relative to patient self-perception of asthma status and validated disease-specific patient-reported outcome (PRO) measures.

Patients and methods: Baseline data were analyzed from patients (aged ≥ 12 years) with asthma participating in a 12-month observational study assessing the ability of AIRQ to predict exacerbations. At entry, patients completed a sociodemographic questionnaire, AIRQ, 3 questions addressing self-perceived asthma status, Saint George's Respiratory Questionnaire (SGRQ), mini-Asthma Quality of Life Questionnaire (AQLQ), and Adult Asthma Adherence Questionnaire (AAAQ). Descriptive statistics were calculated for demographic and clinical characteristics. AIRQ construct validity was evaluated by assessing correlations between total AIRQ score and patient self-assessments, SGRQ, mini-AQLQ, and AAAQ scores. Comparisons of SGRQ, mini-AQLQ, and AAAQ total and component/domain scores by AIRQ control category were performed using general linear models and Scheffe's post hoc adjustments for pairwise comparisons.

Results: A total of 1112 patients were enrolled: 70% female, 78% White, mean (standard deviation) age 43.9 (19.5) years. There were highly significant correlations between AIRQ score and patient self-perception of overall control ($r = 0.69$; $p < 0.001$), total SGRQ ($r = 0.74$, $p < 0.001$), and mini-AQLQ ($r = -0.78$, $p < 0.001$) scores. As AIRQ control category worsened, so did total and domain SGRQ, mini-AQLQ, and AAAQ impediment-to-inhaled-corticosteroid-adherence scores (all pairwise comparisons $p < 0.001$).

Conclusion: Findings demonstrate the construct validity of AIRQ relative to patient self-perception of asthma status, disease-specific PRO measures, and treatment adherence barriers. AIRQ can be a useful instrument to raise awareness of the unrecognized impacts of asthma on patients' lives.

Keywords: exacerbation, patient-reported outcomes, construct validity, impact of asthma

Introduction

Asthma has a significant, severity-correlated, detrimental impact on an individual's health-related quality of life (HRQoL).[1,2] Patients with poorly controlled asthma experience worse HRQoL, physical and mental health, work

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productivity, and activity impairment than patients with controlled asthma.[3] Models project that from 2019 to 2038, over half of all patient-days for adolescents and adults with asthma in the United States (US) will be uncontrolled if no change occurs in asthma prevalence and current asthma management, resulting in over one trillion dollars of cumulative direct and indirect costs.[4] To address asthma morbidity, the National Asthma Education and Prevention Program's 2020 Focused Updates to the Asthma Management Guidelines highlight asthma-related quality of life, exacerbations, and control as the three critical outcomes that should be used to assess management recommendations.[5] Further, the Global Initiative for Asthma (GINA) emphasizes that assessing patient preferences and goals is a key component of a successful asthma-management strategy.[6]

The Asthma Impairment and Risk Questionnaire (AIRQ®) was developed by a network of 190 US-based scientific experts and primary- and specialty-care clinicians as a first step in addressing the current and projected rising morbidity from uncontrolled asthma. These healthcare professionals concluded that a novel, easily implemented, composite questionnaire that can effectively identify uncontrolled asthma and be used as a shared decision-making tool at point-of-care was required to mitigate the burden of disease. AIRQ is a 10-item, yes/no, low-literacy-demand tool that assesses both the impairment and risk domains of asthma control.[7] It differs from other widely used asthma control tools validated for adolescents and adults, such as the Asthma Control Test (ACT)[8] and the Asthma Control Questionnaire (ACQ),[9] in that AIRQ item responses are yes/no versus the Likert scale format in the ACT and ACQ. Additionally, the ACT and ACQ were validated against expert opinion on patient level of control based on Expert Guidelines criteria, whereas AIRQ questions and cut points of control levels were modeled against a composite standard of impairment (ACT score) and risk (prior-year exacerbation history). The five ACT and seven ACQ items assess only the impairment domain of control over prior 4-week and 1-week time intervals, respectively, whereas the seven AIRQ symptom-based questions use a prior 2-week recall period, and the three risk-based questions cover prior 12-month exacerbation history. Cognitive interviewing and observation of questionnaire completion were performed to evaluate and establish comprehension and user experience; electronic, paper-and-pencil, and interviewer administration; (English and Spanish translation) and all methods of administration showed similar performance.[7]

In contrast to asthma-specific HRQoL measures, the AIRQ is intended to serve as a multidomain assessment tool for identifying patients with uncontrolled asthma based on impairment and risk, and as a predictor of future exacerbation risk and poor HRQoL. Significant relationships between AIRQ control levels and patient and physician perception of asthma control, lung function (pre- and post-bronchodilator 1-second forced expiratory volume [FEV_1]), number of prior-year oral corticosteroid bursts, and healthcare utilization for an asthma exacerbation have been previously demonstrated.[7] Patient-reported outcome (PRO) measures are traditionally utilized to assess the benefit or risk of a given treatment[10] and can provide useful information regarding patient perspectives of the effectiveness and impact of a given management intervention for clinical decision-making.[11–14]

Despite the value of using PRO measures, there are barriers to their implementation in a real-world clinical setting. The most widely used PRO instruments for assessing asthma-specific HRQoL are the Saint George's Respiratory Questionnaire (SGRQ) and the Asthma Quality of Life Questionnaire (AQLQ) (including the mini-AQLQ). However, the SGRQ has been criticized as too time consuming to be completed during most clinical visits, taking approximately 8–15 minutes to complete, and is also best scored using a computer.[13,15] Challenges with the mini-AQLQ include licensing requirements and potentially difficult electronic administration.[14] Additionally, SGRQ and mini-AQLQ are more commonly used in research settings than in clinical practice, again because of licensing requirements and also per suggested use by tool developers; therefore, primary care clinicians may be unfamiliar with how to implement or interpret these tools.[16,17] A measurement of asthma control at each clinical encounter is recommended by the National Asthma Education and Prevention Program (NAEPP 2007)[18] expert opinion guidelines and by the GINA 2022[6] report; thus, an easily implemented control assessment that also reflects HRQoL may have an important role in practice to heighten awareness of the impact of asthma on patients' quality of life.

Significant correlations have been found between existing tools assessing asthma control (ie, ACT, ACQ, Asthma Therapy Assessment Questionnaire [ATAQ]), patient self-perception of asthma burden, and disease-specific PRO measures for adolescents and adults with asthma.[9,19–22] However, the generalizability of these findings is limited by homogeneous and small-sized samples,[9,23] country- and healthcare-coverage-specific results,[21,22] age-inclusion

limitations,[24] and/or the need for further multifactorial modeling.[22] Additionally, because the ACT, ACQ, and ATAQ address only symptom impairment and omit the exacerbation risk component of asthma control, the relationship between composite control tools and validated, disease-specific, PRO measurements is unknown.[22]

The objective of this analysis was to assess the cross-sectional construct validity of the AIRQ relative to patient self-perception of asthma control, validated asthma-specific HRQoL measures, and treatment-adherence barriers.

Methods

This is a cross-sectional analysis of the baseline data of patients aged ≥12 years with physician-diagnosed asthma who enrolled in a 12-month prospective, observational study to assess the ability of the AIRQ to predict future exacerbations.

Study Participants

Between May 2019 and November 2019, patients were recruited from 24 geographically diverse specialty care (allergy/immunology or pulmonology) sites and 1 specialty-affiliated primary care clinical site in the US. Eligible patients (aged ≥12 years) had physician-diagnosed asthma, were currently taking GINA guideline-appropriate asthma controller therapy[6] and had varying levels of asthma control based on screening ACT scores before enrollment. Sites were required to have access to patient medical records for ≥12 months before enrollment to provide objective documentation of exacerbations and level of asthma therapy at enrollment. Patients were excluded if they had a diagnosis of a chronic lower respiratory condition other than asthma, prior bronchial thermoplasty, chronic oral corticosteroid use (≥3 months of continuous oral corticosteroid use at doses of ≥10 mg/day) or were currently or actively planning to become pregnant.

Adult patients and parents of adolescent patients provided written informed consent, with adolescents providing assent. The study protocol received central institutional review board (E&I IRB; Independence, MO, USA) approval on March 26, 2019. This study was performed according to ethical principles consistent with the Declaration of Helsinki, International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Good Clinical Practices, Good Pharmacoepidemiology Practices, the Health Insurance Portability and Accountability Act (HIPAA), and applicable legislation for observational studies.

Data Collection and PRO Measures

At enrollment and before an encounter with their physician, patients completed the AIRQ, together with a sociodemographic questionnaire, 3 self-perception questions (global asthma control, health risk from asthma, and asthma symptom severity), and the following PRO measures: SGRQ, mini-AQLQ, and Adult Asthma Adherence Questionnaire (AAAQ).

Each patient's physician completed a chart review and documented the number of asthma exacerbations in the prior 12 months. An exacerbation was defined as a change in asthma clinical status requiring a course of systemic corticosteroids (oral steroids for ≥3 days), or an emergency department, urgent care, or unplanned office visit for an asthma exacerbation, or a hospital stay for asthma of >24 hours. Patients and their study clinicians were not provided with summated scores or any interpretations of the AIRQ or other PRO measures to prevent biases to subsequent HRQoL assessments.

AIRQ Summary

The 10 AIRQ questions address symptoms, activity limitation, sleep, rescue medication use, social activities, exercise, difficulty controlling asthma, and exacerbations (Figure 1). The recall period for impairment items is the prior 2 weeks and the recall period for risk items is the prior 12 months. Scores range from 0 to 10, based on the number of "yes" responses to the AIRQ items, with higher scores indicating worse asthma control (ie, 0 to 1: well-controlled, 2 to 4: not well-controlled, 5 to 10: very poorly controlled).

AIRQ® (Asthma Impairment and Risk Questionnaire)

PRECISION

For use by health care providers with their patients 12 years and older who have been diagnosed with asthma. AIRQ® is intended to be part of an asthma clinic visit.

Please answer all of the questions below.

In the past 2 weeks, has coughing, wheezing, shortness of breath, or chest tightness:

1. Bothered you during the day on **more than 4 days**?	Yes	No
2. Woke you up from sleep **more than 1 time**?	Yes	No
3. Limited the activities you want to do **every day**?	Yes	No
4. Caused you to use your rescue inhaler or nebulizer **every day**?	Yes	No


Primatene® MIST (Amphastar Pharmaceuticals) or Epinephrine


ProAir® HFA (Teva Respiratory, LLC) or Albuterol sulfate


ProAir RespiClick® (Teva Respiratory, LLC) or Albuterol sulfate


Proventil® HFA (Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.) or Albuterol sulfate


Ventolin® HFA (GlaxoSmithKline) or Albuterol sulfate


Xopenex HFA® (Sunovion Pharmaceuticals Inc.) or Levalbuterol tartrate


Albuterol sulfate or Xopenex® (Sunovion Pharmaceuticals Inc.) or Levalbuterol HCl

Please see all prescribing information for all products.

In the past 2 weeks:

5. Did you have to limit your social activities (such as visiting with friends/relatives or playing with pets/children) because of your asthma?	Yes	No
6. Did coughing, wheezing, shortness of breath, or chest tightness limit your ability to exercise?	Yes	No
7. Did you feel that it was difficult to control your asthma?	Yes	No

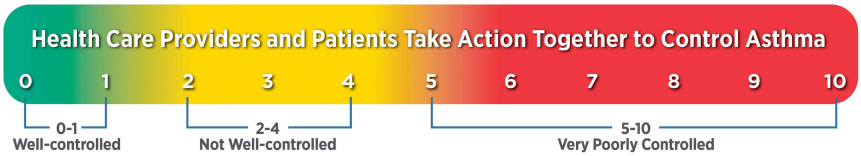
In the past 12 months, has coughing, wheezing, shortness of breath, or chest tightness:

8. Caused you to take steroid pills or shots, such as prednisone or Medrol®*?	Yes	No
9. Caused you to go to the emergency room or have unplanned visits to a health care provider?	Yes	No
10. Caused you to stay in the hospital overnight?	Yes	No

Total YES Answers ☐

What Does My AIRQ® Score Mean?

The AIRQ® is meant to help your health care providers talk with you about your asthma control. The AIRQ® does not diagnose asthma. Whatever your AIRQ® score (total **YES** answers), it is important for your health care team to discuss the number and answers to each of the questions with you. All patients with asthma, even those who may be well-controlled, can have an asthma attack. As asthma control worsens, the chance of an asthma attack increases.[1] Only your medical provider can decide how best to assess and treat your asthma.



*Medrol® (Pfizer, Inc.) or methylprednisolone

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[1]Global Strategy for Asthma Management and Prevention: ©2021 Global Initiative for Asthma

Figure 1 Asthma Impairment and Risk Questionnaire (AIRQ®). AIRQ® is a trademark of AstraZeneca. The AIRQ® is reproduced with permission from AstraZeneca. AstraZeneca is the copyright owner of the AIRQ®. However, third parties will be allowed to use the AIRQ® free of charge. The AIRQ® must always be used in its entirety. Except for limited reformatting, the AIRQ® may not be modified or combined with other instruments without prior written approval. The ten questions of the AIRQ® must appear verbatim, in order, and together as they are presented and not divided on separate pages. All copyright and trademark information must be maintained as it appears on the bottom of the AIRQ® and on all copies. The layout of the final authorized AIRQ® may differ slightly, but the item wording will not change.

Patient Self-Perception of Asthma Control Questionnaire Summary

Three 5-point Likert-scale items address patient self-perception of asthma control, health risk from asthma, and asthma symptom severity. The former 2 questions were tested in qualitative cognitive interviews with 30 patients with asthma aged ≥12 years,[7] and the latter question was developed in a parallel fashion. (Note, the patient perception of asthma control questionnaire is not a validated HRQoL measure.) Patient-perceived asthma control is rated as either completely controlled, well-controlled, somewhat controlled, poorly controlled, or not controlled; patient-perceived risk to their health from asthma is assessed as either no risk, a little risk, some risk, a lot of risk, or high risk; and patient-perceived asthma symptom severity is graded as either no current symptoms, mild symptoms, moderate symptoms, severe symptoms, or extremely severe symptoms. Numerical scoring of each of these questions ranges from 1 to 5, with higher scores representing worse disease status.

SGRQ Summary

The SGRQ is a validated 50-item questionnaire for measuring HRQoL in patients with airway diseases. It consists of a total score and component scores of respiratory symptoms, activity limitations, and psychosocial impacts in the prior 3 months.[11,25] Scores range from 0 to 100, with higher scores indicating more limitations.

Mini-AQLQ Summary

The mini-AQLQ is a 15-item questionnaire measuring HRQoL in patients with asthma based on a total score and domain scores of functional impairment due to symptoms, environmental stimuli, emotional function, and activity limitations within a 2-week recall period.[9] Scores range from 0 to 7, with lower scores reflecting greater impairment.

AAAQ Summary

AAAQ is a 5-item questionnaire for adult patients with asthma that measures general risk of nonadherence with a therapeutic regimen, as well as 4 specific barriers to medication adherence.[26] Items are scored using a 6-point Likert scale, with a cut-point threshold score of >1 on a general adherence question suggesting a possible adherence problem, and more-specific barriers to adherence being reflected by a score of ≤3 on items relating to inhaled corticosteroid use and ≤4 on self-perception of disease severity.

Statistical Analyses

Analyses were based on available data at study entry. Descriptive statistics were calculated for patient demographic and clinical characteristics at enrollment. AIRQ construct validity was evaluated by correlating AIRQ score with each of the 3 patient self-perception items of asthma control and the SGRQ, mini-AQLQ, and AAAQ total and domain scores using Spearman rank coefficients. Correlations were defined as weak, moderate, or strong if $r < 0.30$, 0.30–0.60, or >0.60, respectively.[27,28] The correlations for mini-AQLQ were negative as a result of the difference in scoring systems between AIRQ and the mini-AQLQ. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA). Comparisons of SGRQ and mini-AQLQ total and component/domain scores and AAAQ threshold scores on each barrier to adherence item by AIRQ control categories were performed using general linear models (PROC-GLM) with Scheffe's post hoc adjustment for pairwise comparisons. Significance was defined as $p \leq 0.05$.

Results

Patient Characteristics

Among 1112 patients enrolled, mean (standard deviation [SD]) age at study entry was 43.9 (19.5) years, 14.8% of participants were 12–17 years of age, 70.1% were female, 77.8% were White, 13.0% were Black, 6.6% were Hispanic or Latino, and 57.8% had less than a college degree education level (Table 1). Based on AIRQ scores at study entry, 35% (n = 389) of patients had asthma that was well-controlled (scores 0–1), 38% (n = 423) not well-controlled (scores 2–4), and 27% (n = 300) very poorly controlled (scores 5–10). Most patients had a body mass index (BMI) of >30 (46.6%), 25.1% had a BMI of 25 to 29.9, 23.2% had a BMI of 19 to 24.9, and 5.1% had a BMI < 19. Age and BMI increased with each worsening AIRQ control category ($p = 0.003$ and $p < 0.001$, respectively). Similar to findings in the AIRQ cross-sectional validation study,[7] percent predicted prebronchodilator FEV_1 also decreased with each worsening AIRQ control category ($p = 0.002$). For the entire group, 41.1% of patients had ≥1 chart-documented asthma exacerbation in the

12 months prior to study enrollment (mean [SD] number of exacerbations: 1.7 [0.8]). The proportion of patients experiencing any prior-year exacerbations and the mean number of exacerbations significantly increased as asthma-control category worsened ($p < 0.001$ and $p = 0.001$, respectively).

Table 1 Sociodemographic Characteristics Overall and by AIRQ Control Group at Entry

Parameter	All Enrolled (N = 1112)	Well-Controlled (AIRQ 0–1) (n = 389; 35.0%)	Not Well-Controlled (AIRQ 2–4) (n = 423; 38.0%)	Very Poorly Controlled (AIRQ 5–10) (n = 300; 27.0%)	P value
Age at enrollment, years, mean (SD)	43.9 (19.5)	42.0 (21.0)	43.6 (19.7)	47.0 (16.5)	0.003
Female sex, n (%)	779 (70.1)	248 (63.8)	280 (66.2)	251 (83.7)	< 0.001
Race, n (%)					0.002
Black or African American	145 (13.0)	43 (11.1)	42 (9.9)	60 (20.0)	
Other[a]	89 (8.0)	29 (7.5)	34 (8.0)	26 (8.7)	
White	865 (77.8)	310 (79.7)	343 (81.1)	212 (70.7)	
Missing	13 (1.2)	7 (1.8)	4 (0.9)	2 (0.7)	
Ethnicity, n (%)					0.764
Hispanic or Latino	73 (6.6)	25 (6.4)	28 (6.6)	20 (6.7)	
Missing	18 (1.6)	9 (2.3)	5 (1.2)	4 (1.3)	
Highest level of education, n (%)					< 0.001
Less than high school	146 (13.1)	66 (17.0)	59 (13.9)	21 (7.0)	
Secondary/high school	265 (23.8)	93 (23.9)	84 (19.9)	88 (29.3)	
Associate degree, technical or trade school	232 (20.9)	58 (14.9)	92 (21.7)	82 (27.3)	
College/University degree	278 (25.0)	87 (22.4)	122 (28.8)	69 (23.0)	
Postgraduate degree	178 (16.0)	78 (20.1)	62 (14.7)	38 (12.7)	
Missing	13 (1.2)	7 (1.8)	4 (0.9)	2 (0.7)	
Baseline ACT, mean (SD)	18.6 (4.6) (n = 1106)	22.4 (2.3) (n = 387)	18.8 (3.1) (n = 421)	13.3 (3.4) (n = 298)	< 0.001
Clinician-reported clinical characteristics					
BMI (kg/m^2), mean (SD)	30.6 (8.7)	28.8 (7.8)	30.3 (8.3)	33.4 (9.5)	< 0.001
FEV_1prebronchodilator % predicted, mean (SD)	88.6 (17.0)	91.4 (15.9)	88.6 (17.1)	85.1 (17.7)	0.002
Patients with ≥ 1 exacerbation in the prior 12 months, n (%)	457 (41.1)	60 (15.4)	186 (44.0)	211 (70.3)	< 0.001
Number of exacerbations in the prior 12 months, mean (SD)	1.7 (0.8)	1.4 (0.6)	1.7 (0.7)	1.8 (0.8)	0.001

Note: [a]"Other" includes Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Other.
Abbreviations: ACT, Asthma Control Test; AIRQ, Asthma Impairment and Risk Questionnaire; BMI, body mass index; FEV_1, forced expiratory volume in 1 second; SD, standard deviation.

AIRQ Construct Validity

Correlations of AIRQ Score with Patient Self-Perceptions of Asthma Status

Of the 1108 patients answering the 3 asthma status self-perception questions, approximately two-thirds chose responses indicative of controlled disease (eg, asthma was completely or well-controlled, posed no or little risk to their health, and currently caused no or mild symptoms; Table 2). Of note, although 30.9% of patients indicated that their asthma posed no risk to their health and 27.1% were not currently experiencing any asthma symptoms, only 15.8% indicated that their asthma was completely controlled. There were highly significant correlations between AIRQ score and patient self-perception of overall

control (r = 0.69; p < 0.001) and symptom severity (r = 0.62; p < 0.001), and moderately significant correlations with patient self-perceived health risk from asthma (r = 0.55; p < 0.001). With worsening self-perceived asthma control, risk, or symptom severity category, mean AIRQ score also increased (p < 0.001 for all).

Table 2 Relationship of AIRQ Score with Patient Self-Perception of Asthma Control (N = 1108)

Overall Asthma Control						
	Completely controlled	**Well controlled**	**Somewhat controlled**	**Poorly controlled**	**Not controlled**	**P value for F-test**
n (%)	175 (15.8)	511 (46.1)	346 (31.2)	64 (5.8)	12 (1.1)	
AIRQ score: mean (SD)	0.7 (1.0)	2.0 (1.8)	4.8 (2.2)	6.6 (2.1)	7.9 (1.8)	p < 0.001[a]
Risk to Health from Asthma						
	No risk	**A little risk**	**Some risk**	**A lot of risk**	**High risk**	**P value for F-test**
n (%)	343 (30.9)	405 (36.6)	280 (25.3)	62 (5.6)	18 (1.6)	
AIRQ score: mean (SD)	1.4 (1.6)	2.7 (2.2)	4.5 (2.5)	6.2 (2.2)	7.0 (2.1)	p < 0.001[b]
Severity of Asthma Symptoms						
	No current symptoms	**Mild**	**Moderate**	**Severe**	**Extremely severe**	**P value for F-test**
n (%)	300 (27.1)	461 (41.6)	281 (25.3)	64 (5.8)	2 (0.2)	
AIRQ score: mean (SD)	1.2 (1.5)	2.5 (2.1)	4.8 (2.2)	7.0 (2.0)	9.5 (0.7)	p < 0.001[c]

Notes: [a]All pairwise comparisons are significant at p < 0.001 except "poorly controlled" versus "not controlled" where p = 0.27. [b]All pairwise comparisons are significant at p < 0.001 except "a lot of risk" versus "high risk" where p = 0.70. [c]All pairwise comparisons are significant at p < 0.001 except "moderately severe" versus "extremely severe" where p = 0.02 and "very severe" versus "extremely severe" where p = 0.53.
Abbreviations: AIRQ, Asthma Impairment and Risk Questionnaire; SD, standard deviation.

Correlations of AIRQ Score with Asthma-Specific HRQoL

There were highly significant correlations between AIRQ score and SGRQ total score (r = 0.74; p < 0.001) and mini-AQLQ total score (r = −0.78; p < 0.001), as well as with SGRQ component of symptoms (r = 0.69; p < 0.001) and impacts (r = 0.73; p < 0.001), and mini-AQLQ domains of symptoms (r = −0.76; p < 0.001), activities (r = −0.69; p < 0.001), and emotions (r = −0.70; p < 0.001) (Table 3). Moderately significant correlations between AIRQ score and SGRQ activity component (r = 0.59; p < 0.001) and mini-AQLQ environment domain (r = −0.60; p < 0.001) were also observed.

Relationship Between AIRQ Control Category and HRQoL PRO Measures

Mean total and component SGRQ scores (Figure 2) were higher and mini-AQLQ scores (Figure 3) were lower with worsening AIRQ control category. Both SGRQ and AQLQ, total and component scores, trended in the direction of worse HRQoL across worsening AIRQ control categories (p < 0.001 for all pairwise comparisons).

Correlations and Relationships Between AIRQ and Barriers to Treatment-Adherence PRO Measures

Nonsignificant or weak correlations (ranging from r = −0.06 to r = 0.29) between total AIRQ score and AAAQ items were present, indicating that the AIRQ assesses a concept distinct from adherence (Table 3). Mean AIRQ scores differed significantly for patients who did or did not meet 3 of the 5 questions' minimum cut-off threshold scores for a barrier to adherence to inhaled corticosteroids (Figure 4A). For *My inhaled steroid causes side effects* and *I can't afford my inhaled steroid treatment*, higher AIRQ scores (ie, worse asthma control) were associated with barriers to adherence (p < 0.001 for each). For *My asthma is mild and does not require regular preventative treatment*, a lower

Table 3 Correlations of AIRQ Score with HRQoL and Barriers to Treatment Adherence

PRO	Scales	Correlation	P value
SGRQ	Total score (n = 1088)	0.74	< 0.001
	Symptoms (n = 1093)	0.69	< 0.001
	Activity (n = 1101)	0.59	< 0.001
	Impacts (n = 1102)	0.73	< 0.001
Mini-AQLQ (n = 759)	Total score	−0.78	< 0.001
	Symptoms	−0.76	< 0.001
	Activities	−0.69	< 0.001
	Emotions	−0.70	< 0.001
	Environment	−0.60	< 0.001
AAAQ (n = 1112)	Item 1 – I follow my medication plan	0.06	0.051
	Item 2 – I forget to take at least 1 dose of my inhaled steroid each day	−0.06	0.042
	Item 3 – My asthma is mild and does not require regular preventative treatment	0.29	< 0.001
	Item 4 – My inhaled steroid causes side effects	−0.23	< 0.001
	Item 5 – I cannot afford my inhaled steroid medication	−0.21	< 0.001

Note: Spearman rank coefficients used for P values.
Abbreviations: AAAQ, Adult Asthma Adherence Questionnaire; AIRQ, Asthma Impairment and Risk Questionnaire; AQLQ, Asthma Quality of Life Questionnaire; PRO, patient-reported outcome; SGRQ, St. George's Respiratory Questionnaire.

AIRQ score (ie, better asthma control) was associated with a barrier to inhaled corticosteroid adherence ($p < 0.001$). For these 3 items, the proportion of patients in each AIRQ control category that met the threshold scores for an adherence barrier differed significantly (Figure 4B), with increasing proportions of patients within worsening AIRQ

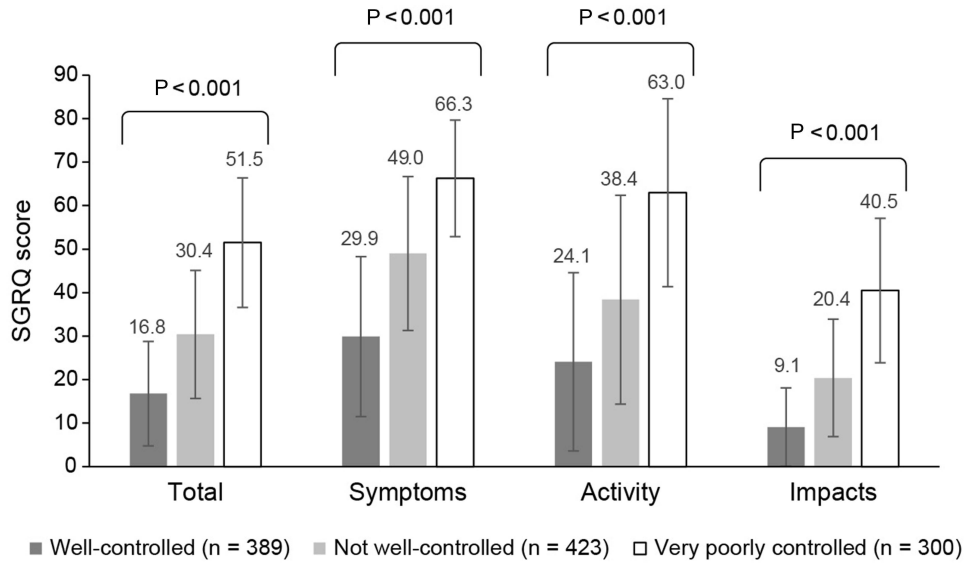

Figure 2 Mean (± SD) SGRQ total and component scores by AIRQ control group.
Abbreviations: AIRQ, Asthma Impairment and Risk Questionnaire; SGRQ, St. George's Respiratory Questionnaire; SD, standard deviation.

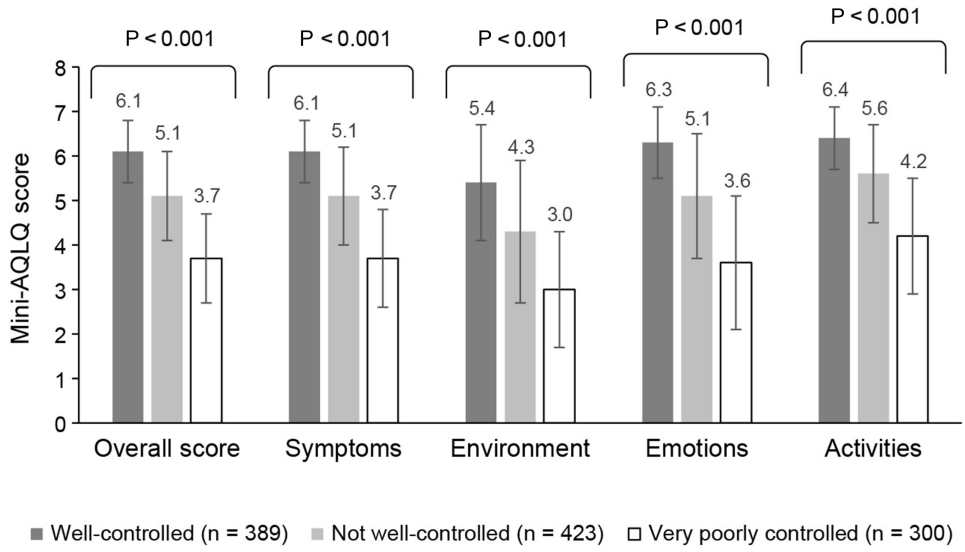

Figure 3 Mean (± SD) mini-AQLQ total and domain scores by AIRQ control group.
Abbreviations: AIRQ, Asthma Impairment and Risk Questionnaire; AQLQ, Asthma Quality of Life Questionnaire; SD, standard deviation.

control categories observed for items related to inhaled steroid side effects and inability to afford inhaled steroids ($p < 0.001$ for each), and increasing proportions of patients within improving AIRQ control categories meeting the adherence threshold barrier for the item related to self-perceived mild asthma not requiring regular preventative treatment ($p < 0.001$).

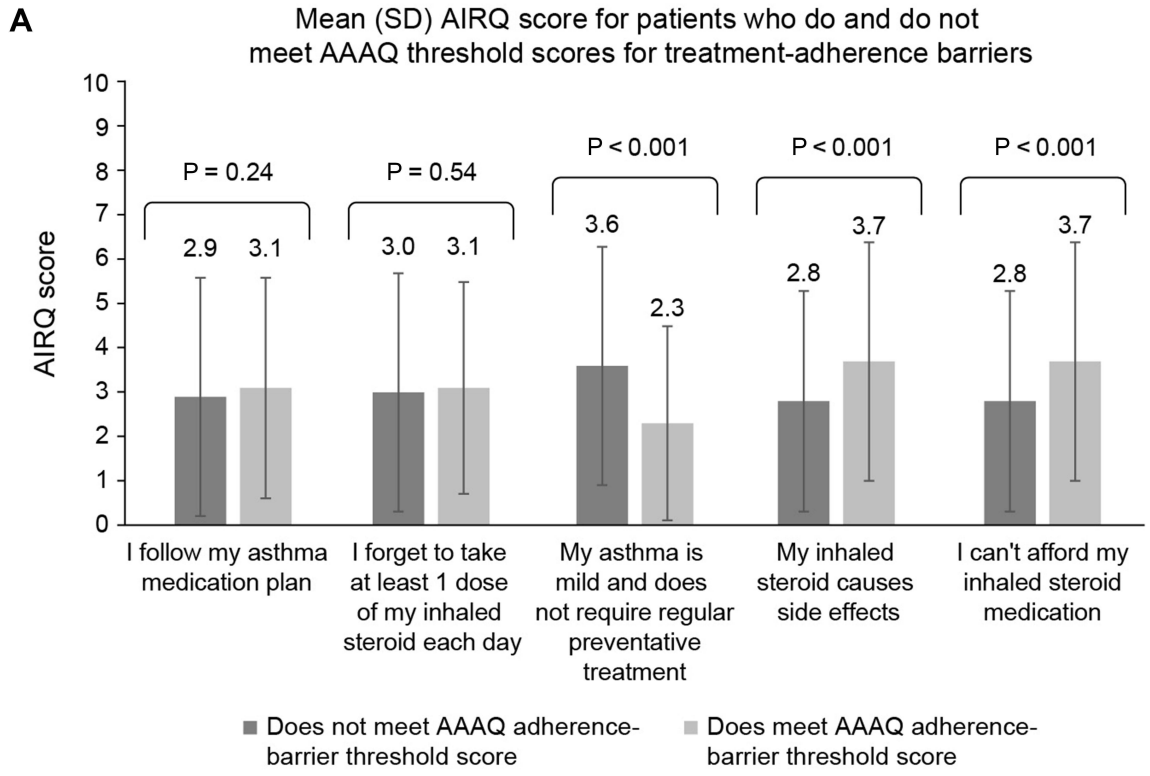

Figure 4 Continued.

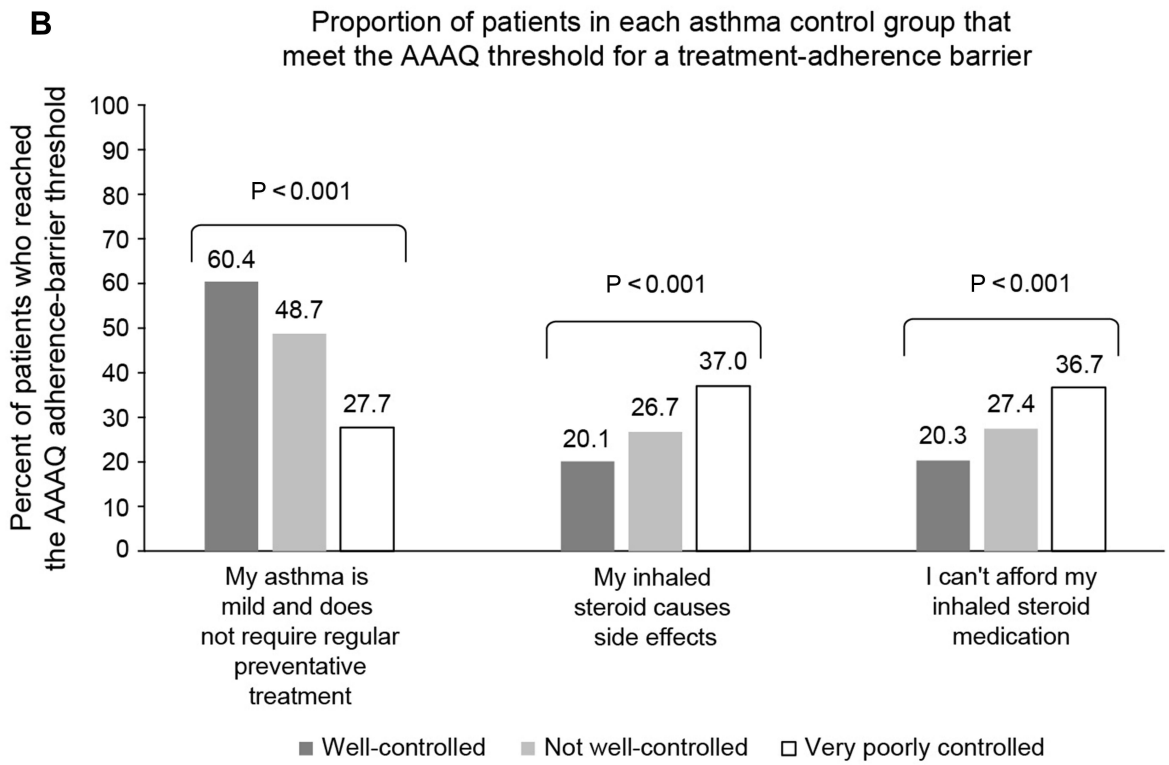

Figure 4 Relation of AIRQ and AAAQ thresholds for barriers to treatment adherence (**A**) AIRQ score and barriers to treatment adherence and (**B**) AIRQ control group and barriers to treatment adherence[a]. [a]The analysis was performed only for those items in which mean AIRQ score differed for patients who did or did not meet the cut-off threshold score of an adherence-to-treatment barrier. The statements "I follow my asthma medication plan" and "I forget to take at least 1 dose of my inhaled steroid each day" were not assessed because the mean score was not statistically significantly different.
Abbreviations: AAAQ, Adult Asthma Adherence Questionnaire; AIRQ, Asthma Impairment and Risk Questionnaire; SD, standard deviation.

Discussion

This analysis of 1112 US patients aged ≥12 years with physician-diagnosed asthma provides further construct validation of AIRQ and demonstrates significant relationships between AIRQ and validated disease-specific PRO measures of HRQoL and treatment adherence barriers, as well as with patients' self-perception of asthma control, risk to their health from asthma, and asthma symptom severity. These findings support the initial cross-sectional construct validation study of AIRQ in 442 patients with asthma aged ≥12 years with respect to lung function, exacerbation history, and patient and physician global assessment of asthma control.[7]

These observations expand upon the robust performance metrics of the AIRQ in differentiating levels of asthma control. The discriminant validity of the AIRQ was previously demonstrated in the cross-sectional study of 442 patients; results from this earlier study yielded receiver operating characteristic curves of 0.94 to discriminate well-controlled vs not well/very poorly controlled asthma and 0.93 to discriminate well/not well-controlled versus very poorly controlled asthma, relative to a 3-level composite standard of ACT score and chart-documented, prior-year exacerbations.[7] An AIRQ score cut-point of ≥2 "yes" responses for detecting not well-controlled/very poorly controlled asthma yielded a sensitivity of 0.90, whereas a cut-point of ≥5 "yes" responses yielded a specificity of 0.96 to identify very poorly controlled asthma.[7]

Current PRO measures used to assess patients with asthma have shown clinical relevance to measures of asthma control and are well established; however, studies demonstrating the validity of these tools are limited by small sample sizes and generalizability.[9,21–24] In 2005, Schatz et al evaluated the relationship between AQLQ and the Short Form-12 questionnaire, finding that validated tools used to assess HRQoL in people with asthma, including the AQLQ, are practical for use in clinical practice.[22,24] That study was limited by a homogeneous patient sample (a majority of White and well-educated patients located on the West Coast of the US).[22,24] Other studies assessing the utility of HRQoL instruments in people with asthma were limited by study-site location and healthcare-specific results.[21,23] An Iranian

study found that the AQLQ was a reliable tool for assessing HRQoL in children and adolescents, but the study was restricted to children aged 7–17 years living in Iran.[23] A 2008 study validated the Korean version of the ACT by demonstrating significant correlations with the AQLQ; however, this study was limited to a single study site in Seoul, Republic of Korea.[21] Further, a US study of HRQoL found correlations between the ACT and AQLQ but was limited by study-site region and required enrollment in a single health maintenance organization health plan.[29] Our current study was not limited by a small sample, restrictive patient age requirements, or healthcare coverage-specific results.

Comparisons of AIRQ with AAAQ reveal a narrative regarding asthma control, aspects of treatment, and disease state. Within improving AIRQ control categories, a greater proportion of patients described themselves as having mild disease. Depending upon the specific adherence barrier item, patients at either end of the control spectrum demonstrated a greater risk for nonadherence that could subsequently lead to enhanced disease morbidity. As asthma control ratings worsened, a greater proportion of patients reported having side effects from inhaled corticosteroids or an inability to afford their medication. An inverse relationship was found between better AIRQ control category and higher proportions of patients meeting the adherence barrier regarding self-perception of mild disease and not needing regular treatment. At first glance, this observation may appear counter-intuitive. However, for patients with milder asthma, this risk for nonadherence with preventative therapies may not pose a real-world negative impact on their asthma control, but instead likely reflects an accurate assessment of medication needs and the ability to successfully self-titrate inhaled corticosteroid therapies.[30] In contrast, the observations of patients with intolerable side effects or an inability to afford medication also having worse asthma control provides a potential for intervention. Reverse causality may be reflected in these results, as patients with severe disease that may not be steroid responsive may discontinue their inhaled corticosteroid due to lack of benefit. Overall, the relationship between adherence to therapy and asthma control is complex because asthma that is controlled with only intermittent symptoms may result in patients believing that there is no need to take daily maintenance medications or, conversely, poor adherence may lead to poor asthma control and lack of efficacy may cause a patient to discontinue ineffective treatments.[31]

A recent study of people with mild asthma treated with as-needed budesonide-formoterol versus twice-daily with budesonide alone found that as-needed asthma treatment was noninferior with respect to the rate of asthma exacerbations.[32] Further, despite recent GINA guidelines asserting that poor adherence is prevalent in up to 75% of patients with asthma, there is no established target or goal for optimal patient adherence.[30] Rather than a predetermined numerical goal, some literature suggests that optimal adherence should be determined by patient-treatment and disease-management goals.[30] Orienting patient adherence goals around patient perceptions of their disease status and quality of life may allow for more effective communication between patients and providers. As misperception of disease burden is common among patients with asthma,[33] using one tool—the AIRQ—may help initiate appropriately focused conversations about medication adherence by increasing awareness of disease status and helping to fill the gap between PRO measures and patient perceptions of disease.

Compared with existing tools, the AIRQ may offer a simple composite control assessment that also demonstrates a good correlation to HRQoL. Further, AIRQ assesses a breadth of the experiences people with asthma may regularly navigate, in comparison to other validated tools that may not capture the entire patient experience (such as social activity and exercise limitations). The AIRQ was developed through a needs-based, iterative process, informed by a diverse network of clinical experts, practitioners, asthma educators, and patient advocates in conjunction with rigorous testing and validation.[7] Given that the AIRQ is strongly correlated with patient self-perception of asthma control, measures of HRQoL, and medication adherence, both clinicians and patients can use the AIRQ to initiate conversations regarding shared decision-making for the optimization of asthma management. Additionally, the AIRQ is easily implemented as—unlike most control tools and PRO measures—it is free of charge for clinicians and independent researchers. A licensing agreement is requested to assure the integrity of the validation of the AIRQ, and it provides the requestor with paper and digital versions of the AIRQ and the Follow-up AIRQ[34] in English, Spanish, and German, if desired.

Strengths

The current analysis of baseline AIRQ data was conducted using a large patient sample size with varying levels of asthma control. The AIRQ was compared with several validated PRO measures for patients with asthma, as well as patient self-assessments of their disease status.

Limitations

This study was restricted to patients aged ≥12 years with physician-diagnosed asthma in the US and had a relatively homogeneous sample in terms of race and ethnicity. Additionally, the study had more female than male patients, and approximately 15% of the enrolled participants were aged 12–17 years; therefore, these results may not be generalizable to the total patient population. Nonetheless, the study's predominantly female population generally aligns with CDC-reported data of asthma prevalence (63%),[35] and the categorical age data for patients aged 12–17 years generally accords with a previous AIRQ study (17%).[7] Therefore, we believe the results do not diminish the utility of these data for informing decision-making in real-world clinical practice.

Although patients were required to be treated for >12 months at the study site or have electronic medical records that were accessible by the study clinicians, the data may not have included all prior exacerbations and actual level of pharmacotherapy utilized. The SGRQ and AAAQ are validated for adults and may not reflect HRQoL and potential for nonadherence in the adolescent population in this study. Additionally, most patients were recruited from specialty sites; therefore, the construct validity of the AIRQ for HRQoL may differ for patients with asthma treated in the primary care setting.

Conclusions

This cross-sectional analysis of patient-reported data from over 1100 individuals with asthma aged ≥12 years across disease severities supports the construct validity of the AIRQ with respect to validated measures of HRQoL and medication adherence barriers, as well as self-perceptions of disease control, health risk, and symptom severity. AIRQ scores and SGRQ total scores were significantly correlated. Both SGRQ and mini-AQLQ scores trended in the direction of worse HRQoL across worsening AIRQ control categories. However, there were weaker correlations between total AIRQ scores and AAAQ items, indicating that the AIRQ assesses a concept distinct from adherence. In addition to providing an assessment tool that identifies patients with uncontrolled asthma based on the domains of impairment and risk, the AIRQ heightens awareness of unrecognized impacts on daily life experienced by many patients with asthma.

Abbreviations

AAAQ, Adult Asthma Adherence Questionnaire; ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; AIRQ, Asthma Impairment and Risk Questionnaire; AQLQ, Asthma Quality of Life Questionnaire; ATAQ, Asthma Therapy Assessment Questionnaire; BMI, body mass index; FEV_1, 1-second forced expiratory volume; GINA, Global Initiative for Asthma; HRQoL, health-related quality of life; PRO, patient-reported outcome; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

J. Reibman has served on advisory boards for AstraZeneca, Novartis, and Genentech; has received grants from Novartis; and has received research support from AstraZeneca, Novartis, and Teva. B. Chipps has served as an advisor, consultant, and as a speaker for AstraZeneca, Boehringer Ingelheim, Circassia, Genentech, GSK, Novartis, Regeneron, and Sanofi. R. S. Zeiger has received grants from Aerocrine, Genentech, MedImmune/AstraZeneca, Merck, GSK, ALK Pharma, Teva, and the National Heart, Lung, and Blood Institute; and has received consultant fees from AstraZeneca, Genentech/Novartis, GSK, Merck, Regeneron, Teva, American College of Allergy Asthma and Immunology, and American Academy of Allergy, Asthma and Immunology. D. A. Beuther has participated in advisory boards for AstraZeneca and GSK. R. A. Wise has received consultant fees and honoraria from AstraZeneca, GSK, Novartis, Sanofi, 4DX, Contrafec, Bristol Myers Squibb, Savara, Puretech, Chiesi, Pulmonx, Galderma, Boehringer Ingelheim, Contrafect, Roche, Regeneron, AbbVie, Spiration, Sunovion, Merck, Circassia, Pneuma, Verona, Bonti, Denali, Aradigm, Mylan, Theravance, Propeller Health, Kiniksa, and Syneos. W. McCann has served as a consultant and speaker for AstraZeneca; has served as a speaker for Regeneron; and has served as a consultant for Aimmune. K. R. Murphy has served as a consultant and is a speaker for AstraZeneca, Boehringer Ingelheim, Genentech, Greer, Merck, Mylan, Novartis, Regeneron, Sanofi, Optinose, and Teva. M. George has served as a consultant for AstraZeneca, Teva, Genentech, and Sanofi Genzyme/Regeneron; and has served as a speaker for AstraZeneca and Genentech. I. Gilbert, J. M. Eudicone, and H. N. Gandhi are employees of AstraZeneca. G. Harding, K. Cutts, and K. Coyne are employees of Evidera, which was contracted by AstraZeneca for study design support and to collect and analyze data for this study. The authors report no other conflicts of interest in this work.

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