

# Rhinitis and Asthma Patient Perspective (RAPP): Clinical Utility and Predictive Value



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**What is already known about this topic?** The RhinAsthma Patient Perspective is a well-validated questionnaire to assess the health-related quality of life of patients with asthma and comorbid allergic rhinitis in daily practice. It is available in Italian, English, Spanish, Portuguese, and Polish.

**What does this article add to our knowledge?** In addition to detecting the impact of disease from the patient's perspective, the RhinAsthma Patient Perspective provides an estimate of the risk for uncontrolled allergic rhinitis and asthma.

**How does this study impact current management guidelines?** The RhinAsthma Patient Perspective can be used to support shared clinical management.

**BACKGROUND:** RhinAsthma Patient Perspective (RAPP) is the only validated tool for assessing of health-related quality of life (HRQoL) related to asthma and rhinitis in individual patients.

**OBJECTIVE:** To compare the HRQoL burden among countries and explore the usefulness of RAPP as a complementary measure in disease management.

**METHODS:** In this post hoc analysis of the RAPP International Study, the enrolled population was clustered into patients with controlled rhinitis and controlled asthma (CA/CR), uncontrolled rhinitis and controlled asthma (CA/UR), controlled rhinitis and uncontrolled asthma (UA/CR), and uncontrolled rhinitis and uncontrolled asthma (UA/UR).

**RESULTS:** We recruited 575 adult patients. Significant differences among countries were observed in the mean RAPP score (from 15.7 in Spain to 18.7 in the Philippines) although

the percentage of subjects with an optimal HRQoL (RAPP <15) was not significantly different. Compared with patients with AR and asthma disease control, those with UR/CA, CR/UA, and UR/UA had significantly higher RAPP scores (4.7, 5, and 9.8, respectively). The best cutoffs for detecting uncontrolled diseases were RAPP of 15 or greater (SE = 75%; specificity = 69%; and area under the receiver operating characteristic curve [AUC] = 0.78) for AR; RAPP of 16 or greater (SE = 78%; specificity = 76%; and AUC = 0.83) for asthma; and RAPP of 18 or greater (SE = 86%; specificity = 87%; and AUC = 0.92) for both AR and asthma.

**CONCLUSIONS:** These findings provide a better understanding of the individual burden of HRQoL related to asthma and rhinitis in daily practice. In addition, the RAPP estimates how much of the risk for uncontrolled disease depends on uncontrolled AR and asthma, allowing its use as a clinical

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*Abbreviations used*

ACT- Asthma Control Test  
AR- Allergic rhinitis  
AUC- area under the receiver operating characteristic curve  
CR/CA- Controlled rhinitis and controlled asthma  
CR/UA- Controlled rhinitis and uncontrolled asthma  
HRQoL- Health-related quality of life  
PRO- Patient-reported outcome  
RAPP- RhinAsthma Patient Perspective  
SE- Sensitivity  
SP- 1-Specificity  
UR/CA- Uncontrolled rhinitis and controlled asthma  
UR/UA- Uncontrolled rhinitis and uncontrolled asthma  
VAS- Visual analog scale

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**Key words:** Allergic rhinitis; Asthma; Clinical practice; Health-related quality of life; Questionnaire

## INTRODUCTION

Health-related quality of life (HRQoL)<sup>1</sup> is a patient-reported outcome (PRO)<sup>2-4</sup> of critical importance in managing chronic disease. It is traditionally included in research studies and clinical trials to assess the impact of respiratory allergy and its treatment from the patient perspective. Starting in the 1990s, owing to the development of questionnaires specific to asthma,<sup>5</sup> allergic rhinitis (AR),<sup>6</sup> and both conditions,<sup>7-9</sup> a growing number of studies have included an assessment of HRQoL as an end point, allowing us to determine the subjective disease burden.<sup>10,11</sup> Moreover, HRQoL data from research have been used to compare treatment options in effectiveness trials and integrate existing measurements of safety and efficacy in the drug development process and regulatory review.<sup>12</sup>

There has been increasing interest in incorporating PROs into clinical practice with greater awareness of the importance of patient-oriented approaches.<sup>13-17</sup> For health care professionals, PROs are a supportive tool during clinical consultation to detect and manage disease better as well as its treatment-related effects.<sup>18</sup> Moreover, the routine collection of PROs improves communication<sup>19</sup> and shared decision-making<sup>20</sup> and has a positive impact on patient outcomes.<sup>21</sup>

The National Quality Forum<sup>22</sup> and the International Society for Quality of Life Research<sup>23</sup> developed specific guidance to assess patients' perspectives properly in routine care settings. The availability of questionnaires with well-defined psychometric and practical features is the first step toward the adoption and inclusion of PROs in clinical practice.

RhinAsthma Patient Perspective (RAPP)<sup>24</sup> was originally developed and validated in Italy for implementation in a real-world setting to assess the HRQoL of adult patients with AR and asthma. It was devised based on the concept of united airway diseases. Allergic rhinitis and asthma represent different manifestations of a single underlying disease.<sup>25,26</sup> They often coexist; up to 80% of asthma patients experience AR, and greater than

40% of AR patients have asthma.<sup>27</sup> Moreover, the impact of comorbid asthma and AR on clinical outcomes, PROs, and costs has been well-characterized.<sup>28-30</sup>

The RAPP satisfies psychometric criteria<sup>22</sup> and pragmatic characteristics<sup>31</sup> requested for use in clinical practice. It is short (eight items), user-friendly, and simple to score. The scores range from 8 to 40 (higher scores indicate a greater impact on HRQoL), and a cutoff point of 15 showed the best sensitivity (SE) and specificity in discriminating the achievement of an optimal HRQoL. Moreover, the high responsiveness to change and the minimal important difference (two points) increase the interpretability and actionability of the questionnaire and allow its use in making clinical decisions. A specific version for children<sup>32</sup> is available in Italy.

A recent multinational project aimed at transcultural adaptation and validation of the RAPP in English,<sup>33</sup> Spanish,<sup>34</sup> Portuguese,<sup>35</sup> and Polish<sup>36</sup> confirmed that the questionnaire has the recommended psychometric properties in each language (see Appendix E1 in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org) for the full questionnaire and Appendix E2 in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org) for a summary of the validation process).

The results of this international study offered the opportunity to compare HRQoL in the involved countries and explore RAPP's usefulness as a complementary measure in disease management. To achieve this goal, the ability of RAPP to differentiate patients with impaired HRQoL owing to uncontrolled AR, uncontrolled asthma, or both was explored.

## METHODS

### Study design and participants

This is a post hoc analysis of the RAPP International study, which was a multicenter, observational perspective study approved by the Ethics Committee of the University of Genoa (Approval No. P.R. 333REG2106) and ratified by the local ethics committees. The methodology and the results were previously described elsewhere.<sup>33-36</sup> In brief, for each country, adult patients with a diagnosis of asthma and rhinitis according to Global Initiative for Asthma<sup>37</sup> and Allergic Rhinitis and its Impact on Asthma<sup>38</sup> documents, who were attending a specialist center for a visit, were asked to enroll in the study. Patients were evaluated twice, with an interval of 4 weeks between visits. At each visit, patients completed the RAPP<sup>24</sup> and three other validated PROs: Short Form-12,<sup>39</sup> a questionnaire to assess health status; the Asthma Control Test (ACT),<sup>40</sup> to evaluate the level of asthma control; and the symptomatologic visual analog scale (VAS), a well-accepted measure to monitor AR control.<sup>41</sup> At the second visit, patients were asked to complete a global rating scale<sup>42</sup> to detect any change in health.

Between the visits, patients received treatment according to current guideline recommendations.

Analyzed end points of this post hoc analysis were (1) differences in terms of patient characteristics and RAPP scores across countries and (2) the usefulness of RAPP as a complementary tool in managing disease in patients with upper and lower respiratory allergy. To this aim, recruited patients were divided into four classes according to the level of control for the upper<sup>43</sup> and lower<sup>40</sup> airways: controlled rhinitis and controlled asthma (ACT >19 and VAS ≤5 [CR/CA]), uncontrolled rhinitis and controlled asthma (ACT >19 and VAS >5 [UR/CA]), controlled rhinitis and uncontrolled asthma (ACT ≤19 and VAS ≤5 [CR/UA]), and uncontrolled rhinitis and uncontrolled asthma (ACT ≤19 and VAS >5 [UR/UA]).

TABLE I. Patient characteristics by center

Characteristic	Philippines (n = 150; 26.1%)	Poland (n = 127; (22.1%)	Portugal (n = 149; (25.9%)	Spain (n = 149; (25.9%)	<i>P</i> *
Age, y	39.3 (15.5)	34.8 (12.5)	36.8 (13.2)	37.7 (10.3)	.054
Female sex	111 (74.0)	68 (53.5)	98 (65.8)	93 (62.4)	<b>.005</b>
BMI, kg/m <sup>2</sup>	26.6 (7.3)	25.3 (4.6)	24.5 (3.9)	25.1 (5.8)	.118
Education					<b>&lt;.001</b>
Primary/middle school	73 (48.7)	66 (52.0)	65 (43.6)	39 (26.2)	
Graduate	77 (51.3)	61 (48.0)	84 (56.4)	110 (73.8)	
Employment status					<b>&lt;.001</b>
Unemployed/retired	66 (44.0)	32 (25.2)	46 (30.9)	30 (20.1)	
Employed	84 (56.0)	95 (74.8)	103 (69.1)	119 (79.9)	
Smoking habits					<b>&lt;.001</b>
Never-smoker	106 (70.7)	92 (72.4)	128 (85.9)	91 (61.1)	
Current smokers	27 (18.0)	19 (15.0)	6 (4.0)	28 (18.8)	
Ex-smoker	17 (11.3)	16 (12.6)	15 (10.1)	30 (20.1)	
Atopy	149 (99.3)	127 (100.0)	141 (94.6)	142 (95.3)	<b>.003</b>
Rhinitis					<b>&lt;.001</b>
Intermittent	59 (39.3)	47 (37.0)	43 (28.9)	87 (58.4)	
Persistent	91 (60.7)	80 (63.0)	106 (71.1)	62 (41.6)	
Rhinitis severity					<b>&lt;.001</b>
Mild	107 (71.3)	52 (40.9)	60 (40.3)	135 (90.6)	
Moderate	43 (28.7)	75 (59.1)	89 (59.7)	14 (9.4)	
Asthma severity (Global Initiative for Asthma)					<b>&lt;.001</b>
Step 1	86 (57.3)	9 (7.1)	59 (39.6)	102 (68.5)	
Step 2	2 (1.3)	37 (29.1)	31 (20.8)	16 (10.7)	
Step 3	33 (22.0)	15 (11.8)	18 (12.1)	18 (12.1)	
Step 4	29 (19.3)	27 (21.3)	35 (23.5)	11 (7.4)	
Step 5	0 (0.0)	39 (30.7)	6 (4.0)	2 (1.3)	
ACT total score	18.2 (4.0)	20.9 (3.7)	22.0 (3.2)	23.0 (3.4)	<b>&lt;.001</b>
VAS	4.7 (2.6)	3.3 (2.9)	5.0 (2.5)	5.3 (2.8)	<b>&lt;.001</b>
Rhinitis/asthma control					<b>&lt;.001</b>
VAS ≤5/ACT >19 (CR/CA)	54 (36.0)	72 (56.7)	76 (51.0)	61 (40.9)	
VAS >5/ACT >19 (UR/CA)	7 (4.7)	19 (15.0)	44 (29.5)	64 (43.0)	
VAS ≤5/ACT ≤19 (CR/UA)	34 (22.7)	24 (18.9)	10 (6.7)	5 (3.4)	
VAS >5/ACT ≤19 (UR/UA)	55 (36.7)	12 (9.4)	19 (12.8)	19 (12.8)	
RAPP total score	18.7 (6.4)	16.6 (6.9)	16.9 (5.5)	15.7 (4.6)	<b>&lt;.001</b>
HRQoL					.136
Impaired HRQoL (RAPP ≥15)	100 (66.7)	69 (54.3)	90 (60.4)	83 (55.7)	
Optimal HRQoL (RAPP <15)	50 (33.3)	58 (45.7)	59 (39.6)	66 (44.3)	

ACT, Asthma Control Test; CA, controlled asthma; CR, controlled rhinitis; HRQoL, health-related quality of life; RAPP, RhinAsthma Patient Perspective; UA, uncontrolled asthma; UR, uncontrolled rhinitis; VAS, visual analog scale.

Significant *P* values are shown in bold. Data are reported as means (SDs) for quantitative variables and n (%) for categorical variables.

\*Kruskal-Wallis (quantitative variables), chi-square (categorical variables), or Fisher's exact test (for atopy and asthma severity).

A convenient data sampling method was used to recruit a total of 150 patients in each country. Because the current analysis was post hoc, no sample size calculations were required; therefore, all analyses are only descriptive, as are the calculated *P* values.

### Statistical analysis

Patient characteristics were summarized through means and SDs for quantitative variables and through absolute numbers and percentages (frequencies) for categorical variables. Comparisons among centers were carried out using Kruskal-Wallis test for quantitative variables and chi-square test for categorical variables. We used Fisher's exact test when one or more cells of the contingency table were less than 5.

Pairwise group differences in the RAPP total score were assessed through Tukey's honest multiple comparisons by means of 95% familywise confidence intervals (CIs).

The ability of RAPP to discriminate between each disease status (UR/CA, CR/UA, and UR/UA) and the baseline status (CR/CA) was assessed by receiver operating characteristic curves, representing 1-specificity (SP) and SE for different RAPP cutoffs. The discriminating ability was considered fair when the 95% CI of the area under the receiver operating characteristic curve (AUC) did not include 0.5. For each receiver operating characteristic curve, the best cutoff was identified as the RAPP total score maximizing Youden's *J* statistic (SE plus SP). For each detected cutoff, we reported SE, SP, overall accuracy, and the odds ratio (OR) from the 2 × 2 confusion

matrix. We also adjusted the OR by age, sex, body mass index, education, employment status, smoking habits, atopy, rhinitis severity, and asthma severity through multivariable logistic regression models.

All statistical analyses were performed using R software (version 4.0.2, R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at *P* less than .05.

## RESULTS

### Patient characteristics and RAPP scores across countries

A total of 575 patients were recruited: 150 from the Philippines (26.1%), 127 from Poland (22.1%), 149 from Portugal (25.9%), and 149 from Spain (25.9%). On average, patients were younger in Poland (34.8 years). A higher percentage of females were recruited in the Philippines (74.0%). Table I lists patient characteristics by center. A lower percentage of current smokers was observed in Portugal. Almost all subjects were atopic (from 94.6% in Portugal to 100% in Poland). The highest percentage of uncontrolled asthma was observed in the Philippines (59.4%), whereas the highest percentage of uncontrolled rhinitis was observed in Spain (55.8%). Significant center differences were observed in the mean RAPP total score (from 15.7 in Spain to 18.7 in the Philippines), even when the percentage of subjects with a good HRQoL (RAPP <15) was not significantly different.

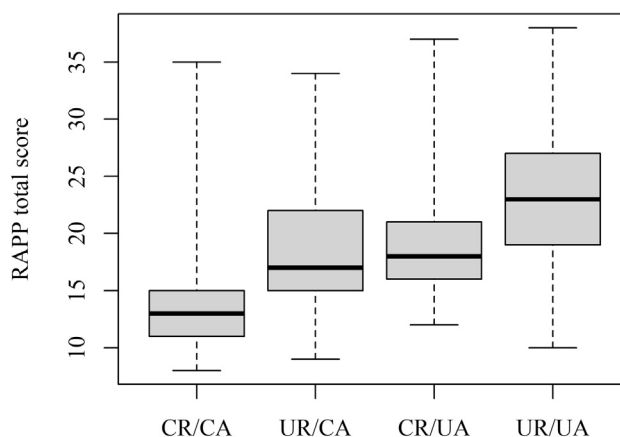
### Analysis according to disease control

A total of 263 subjects (45.7%) were in the CR/CA group (both diseases controlled); 134 subjects (23.3%) were in the UR/CA group (uncontrolled rhinitis only). A total of 73 subjects were in the CR/UA group (uncontrolled asthma only), whereas 105 subjects were in the UR/UA group (both diseases uncontrolled). Figure 1 represents the RAPP total score distribution by class. Mean (SD) RAPP total scores by group were 13.5 (SD, 4.1) in CR/CA, 18.1 (SD, 5.1) in UR/CA, 18.5 (SD, 4.4) in CR/UA, and 23.3 (SD, 5.8) in UR/UA. Table II lists pairwise mean differences among the four classes. Mean RAPP total scores were significantly different for all class pairs except for CR/UA and UR/CA.

### Receiver operating curve analyses

Figure 2 shows the ROC curves for the three disease outcomes. When having uncontrolled rhinitis was used as the outcome, the AUC was 0.78 (95% CI, 0.73-0.83). When having uncontrolled asthma was used as the outcome, the AUC was 0.83 (95% CI, 0.78-0.87). When having both diseases uncontrolled was used as the outcome, the AUC was 0.92 (95% CI, 0.89-0.95).

Table III lists the optimal RAPP cutoffs and the relevant performance indicators for each disease outcome. The best cutoff for detecting uncontrolled rhinitis (UR/CA vs CR/CA) was RAPP of 15 or greater (SE, 75%; SP, 69%; accuracy, 71%; OR = 6.8; adjusted OR = 7.0). The best cutoff for detecting uncontrolled asthma (CR/UA vs CR/CA) was RAPP of 16 or greater (SE, 78%; SP, 76%; accuracy, 76%; OR = 11.1; adjusted OR = 14.4). The best cutoff for detecting an uncontrolled status of both diseases (UR/UA vs CR/CA) was RAPP of 18 or greater (SE, 86%; SP, 87%; accuracy, 86%; OR = 39.1; adjusted OR = 42.0).



**FIGURE 1.** RhinAsthma Patient Perspective (RAPP) total score distribution by disease class. Boxplots represent the median (central line), 25th through 75th percentiles (box), and min-max (whiskers) of the RAPP total score. CR/CA, controlled rhinitis and controlled asthma; CR/UA, controlled rhinitis and uncontrolled asthma; UR/CA, uncontrolled rhinitis and controlled asthma; UR/UA, uncontrolled rhinitis and uncontrolled asthma.

**TABLE II.** Pairwise group differences in RhinAsthma Patient Perspective total score and 95% family-wise confidence intervals from Tukey's honest multiple comparisons

Group comparison	Mean RAPP total score difference (95% confidence interval)
UR/CA vs CR/CA	<b>4.7 (3.4-5.9)</b>
CR/UA vs CR/CA	<b>5 (3.4-6.6)</b>
UR/UA vs CR/CA	<b>9.8 (8.4-11.2)</b>
CR/UA vs UR/CA	0.3 (-1.5 to 2.1)
UR/UA vs UR/CA	<b>5.1 (3.5-6.7)</b>
UR/UA vs CR/UA	<b>4.8 (3-6.7)</b>

CA, controlled asthma; CR, controlled rhinitis; UA, uncontrolled asthma, UR, uncontrolled rhinitis.

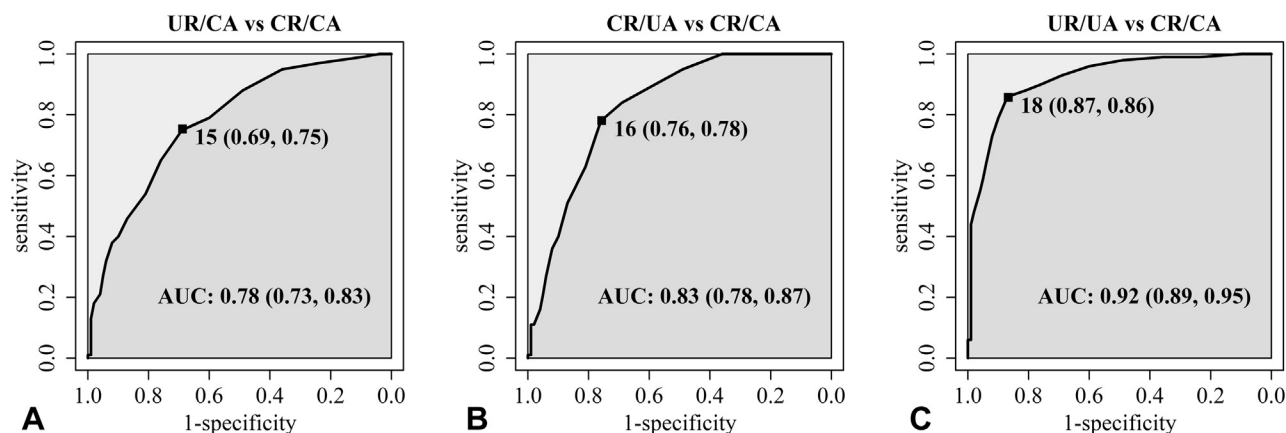
Significant differences are shown in bold.

## DISCUSSION

The impact of asthma and comorbid rhinitis on the symptoms, control, and HRQoL are a main component of disease management. Patient-reported outcomes are increasingly being recommended as a part of routine practice to provide a standardized method for detecting the patient's perspective.<sup>2</sup> User guides to implement PROs in clinical practice have well defined the psychometric standards and practical characteristics that the questionnaires should have.<sup>22,23</sup>

In recent years, the pathogenic view of AR and asthma has changed, and epidemiologic and clinical evidence has confirmed the link between the upper and lower airways.<sup>25-27</sup> In light of the concept of united airway disease, the clinical routine should guarantee an integrated approach to optimize outcomes.

The RAPP<sup>24</sup> is the first validated tool for the individual assessment of HRQoL in managing upper and lower respiratory allergy; it is available in five languages.<sup>24,33-36</sup> The tool is clinically applicable in daily practice: patients may fill in and score it in a few minutes, and the result interpretation is immediate.



**FIGURE 2.** Receiver operating characteristic curves. Predictor: RhinAsthma Patient Perspective total score. (A) The uncontrolled rhinitis and controlled asthma (UR/CA) group rather than the baseline group (controlled rhinitis and controlled asthma [CR/CA], ie, both diseases controlled). (B) The controlled rhinitis and uncontrolled asthma (CR/UA) group rather than the baseline group. (C) The uncontrolled rhinitis and uncontrolled asthma (UR/UA) group (both diseases uncontrolled) rather than the baseline group.

**TABLE III.** Area under receiver operating characteristic curve and performance indicators associated with optimal RhinAsthma Patient Perspective (RAPP) cutoff, by disease outcome: sensitivity, specificity, overall accuracy, and odds ratio

Performance indicators associated RAPP cutoff points	UR/CA vs CR/CA	CR/UA vs CR/CA	UR/UA vs CR/CA
Area under receiver operating characteristic curve (95% CI)	0.78 (0.73-0.83)	0.83 (0.78-0.87)	0.92 (0.89-0.95)
Cutoff point	RAPP $\geq$ 15	RAPP $\geq$ 16	RAPP $\geq$ 18
Sensitivity	75%	78%	86%
Specificity	69%	76%	87%
Overall accuracy	71%	76%	86%
Odds ratio (95% CI)	6.8 (4.3-11.0)	11.1 (6.1-21.2)	39.1 (20.9-77.5)
Adjusted* odds ratio (95% CI)	7.0 (4.2-11.9)	14.4 (7.3-29.9)	42.0 (20.4-94.4)

CA, controlled asthma; CI, confidence interval; CR, controlled rhinitis; UA, uncontrolled asthma; UR, uncontrolled rhinitis.

\*Adjusted by age, sex, body mass index, education, employment status, smoking habits, atopy, rhinitis severity, and asthma severity through multivariable logistic regression models.

Disease control is the key outcome in treating asthma and AR.<sup>44</sup> Reaching this goal offers the opportunity to reduce or even avoid the impact of respiratory allergies on HRQoL.

This post hoc analysis of a large cross-sectional study provided new insights into the HRQoL of patients with AR and asthma in a real-life setting.

Our results indicate that the rate of patients who achieved disease control varies and is significantly different across countries, ranging from 36% to 56.7% for both AR and asthma controlled, from 4.7% to 43% for AR or asthma uncontrolled, and from 5.5% to 6.9% for both uncontrolled. These findings are in agreement with results of numerous studies evaluating control in respiratory allergies. The Recognise Asthma and Link to Symptoms and Experience study<sup>45</sup> reported uncontrolled asthma in 45% and 49.7% of patients in Europe and Asia, respectively. In a large multicenter study performed in 12 European countries, the percentage of patients with suboptimal asthma control was 56.7%.<sup>46</sup> Available literature data on AR control showed that this goal is achieved in approximately 40% to 45% of patients,<sup>47,48</sup> independent of treatment. The high variability we found could be the result of the different socio-demographic (sex, age, education level, and employment status) and clinical (atopy and disease severity) features of patients in

each center. The limited number of selection criteria (adult age, AR and asthma diagnosis according guidelines, and willingness to participate in the study) affected eligibility for recruitment. However, the statistical analyses we performed in each country during the validation process excluded the possible effect of sociodemographic features on RAPP answers.

In contrast, the percentage of subjects with an optimal HRQoL was not significantly different across countries. More than half of patients still failed to achieve this goal; percentages ranged from 54.3% to 66.7%.

Failure to reach optimal HRQoL is strictly related to the level of AR and asthma control.

Median RAPP scores lower than 15, indicating optimal HRQoL, were detected only for patients in whom AR and asthma were controlled. This result is in line with previous studies showing an association between disease control and HRQoL.<sup>49</sup> Moreover, the comparison across classes of disease control allowed us to detect how much the RAPP score increased when patients were not controlled, all largely exceeding the minimal important difference. Indeed, having uncontrolled AR or asthma, compared with achieving control in both diseases, resulted in 4.7 and 5 extra points, respectively. This slight difference confirms how, from patients' viewpoint, when disease control is not

achieved, no matter if it is related to upper and lower respiratory tracts, HRQoL scores become worse. In patients with both uncontrolled AR and asthma, RAPP was 5.1 points higher than in patients with uncontrolled AR and controlled asthma and 4.8 points higher than in patients with controlled AR and uncontrolled asthma. The findings indicate that both AR and asthma control are perceived by patients in terms of HRQoL, with differences that are statistically as well as clinically significant.

No statistically significant difference was detected in the mean RAPP score between patients who achieved control in one of the two diseases. However, ROC analyses identified increasing cut-offs values of the RAPP score<sup>15,16,18</sup> associated with an increasing ability (in terms of SE, specificity, and AUC) to forecast uncontrolled rhinitis, uncontrolled asthma, or uncontrolled rhinitis and asthma) (Figure 2). In particular, a RAPP score of 18 or greater (namely, four points higher than the optimal HRQoL) increases the odds of having uncontrolled rhinitis and asthma by 39.1 times. After adjusting for sociodemographic and clinical outcomes through multivariable logistic regression models, the OR improved. These results suggest that independent of the characteristics of patients, the RAPP score is able to predict the likelihood of uncontrolled AR and asthma. A simple tool such as RAPP could easily be incorporated into the routine assessment of patients with upper and lower respiratory allergy to tailor treatment decisions to patients' needs.

Some limitations should be considered in the evaluation of our results. Patient selection bias cannot be excluded, because patients were recruited from specialist centers and the sample was nonrandomized. In addition, the data were analyzed for the whole study population; however, there were some country-specific variations among respondents in terms of demographic and clinical characteristics.

These findings provide a better understanding of the clinical relevance of HRQoL assessment in daily practice. In addition to detecting the impact of disease from the patient's perspective, RAPP provides an estimate of risk for uncontrolled AR and asthma. This information, available in real time, gives clinical meaning to subjective experience about disease and treatment, and can be used to support shared disease management.

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## ONLINE REPOSITORY

### APPENDIX E1. RHINASTHMA PATIENT PERSPECTIVE

The following questionnaire will evaluate the impact of rhinitis and asthma in daily life. Please indicate how much you have been bothered during the past 2 weeks by:

1. Stuffy or runny nose, sneezing, or itchy nose
2. Itchy eyes, watery eyes, sore eyes, and eye redness
3. Difficulty concentrating
4. Wheezing, cough, chest tightness, or shortness of breath
5. Problems in sleeping (ie, night awakenings)
6. Having to avoid certain areas and environments
7. Having to take drugs
8. Limitation in performing some activities (ie, working, studying, sports)

Score scale:

1. Nothing at all
2. A little
3. Enough
4. Much
5. Very much

### APPENDIX E2. CROSS-CULTURAL ADAPTATION AND VALIDATION OF RHINASTHMA PATIENT PERSPECTIVE IN ENGLISH, SPANISH, PORTUGUESE, AND POLISH<sup>E1-E4</sup>

#### Adaptation process

The original Italian version was independently translated. The process of cross-cultural adaptation was conducted according to international guidelines with two forward and backward translations.

#### Validation process

The following psychometric properties were evaluated:

- Scale dimension by mean of explorative and confirmative factor analysis.
- Internal consistency using Cronbach alpha on the whole test.
- Reliability by means of interclass coefficient and Lin's concordance correlation coefficient.
- Convergent validity using Spearman's between RhinAsthma Patient Perspective and Short Form-12.
- Discriminant validity by means of analysis of variance (Fisher's test) comparing patients according to Asthma Control Test, Global Initiative for Asthma, and Allergic Rhinitis and its Impact on Asthma classification of severity.
- Responsiveness by analyzing correlation between changes in RhinAsthma Patient Perspective scores and changes in global rating scale, visual analog scale, and Asthma Control Test by means of nonparametric test (Spearman correlation coefficient).
- Minimal important difference was determined by applying the receiver operating characteristics curve method. The entire cohort for one dichotomization point (ie, no change versus any improvement or deterioration) was adopted.

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