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VALUE IN HEALTH

Development and Validation of a New Spanish Instrument to Measure Health-Related Quality of Life in Patients with Allergic Rhinitis: The ESPRINT Questionnaire

The ESPRINT Study Group* and Investigators**

ABSTRACT

Objectives: To develop and validate an instrument to measure health-related quality of life (HRQOL) specific to patients with allergic rhinitis (AR) and primarily for use in Spanish and Spanish-speaking populations.

Methods: An initial item pool was generated from literature review, focus groups with AR patients, and consultations with clinical experts. Item reduction was performed using clinimetric and psychometric approaches after administration of the item pool to 400 AR patients. The resulting instrument's internal consistency, test–retest (2–4 weeks) reliability, known groups and convergent validity, and sensitivity to change were tested in a longitudinal, observational, multicenter study in 210 AR patients who also completed the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ).

Results: The new questionnaire took a mean (SD) of 7.1 (5.4) minutes to answer. Floor and ceiling effects were less than 15% on all dimensions. Cronbach's alpha values and intraclass correlation coefficient values for six of the seven dimensions and the overall score exceeded 0.70. Statistically significant differences ($P < 0.01$) were observed on all ESPRINT-28 dimensions and the overall score between patients with mild (mean overall score 1.97, SD 0.99), moderate (mean overall score 2.78, SD 0.88), and severe AR (mean overall score 3.89, SD 0.87). Patients with persistent AR had worse scores ($P < 0.05$) on all dimensions than patients with intermittent AR. Correlations between the ESPRINT-28 and the RQLQ were generally as expected. Effect sizes for score changes between the two study visits ranged from 0.96 to 1.76 for individual dimensions and the overall score.

Conclusions: This new, Spanish-developed instrument to measure HRQOL in AR patients has shown good reliability, validity, and sensitivity to change. It has also proved easy to use and administer.

Keywords: allergic rhinitis, health-related quality of life, questionnaire, Spain.

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Introduction

Allergic rhinitis (AR) is a common condition affecting approximately 10% to 25% of the population worldwide, and its prevalence is increasing [1,2]. The costs of the illness are high, both in terms of direct and indirect cost [3], and AR has a substantial impact on patients' quality of life [4–6].

Health-related quality of life (HRQOL) is usually defined as a multidimensional concept encompassing the physical, mental, and social components associated with an illness or its treatment [7]. When assessing HRQOL, the aim is usually "to measure not only the actual functional capability, but also the individual's perceptions of the impact of these abilities or disabilities on his or her life" [7].

Both generic [8,9] and disease-specific [10–13] instruments have been used to evaluate the impact of AR and its treatment on patients' HRQOL. Such instruments are useful for assessing treatment efficacy in clinical trials, for measuring the burden of disease in epidemiological studies, or as monitoring tools in clinical practice [14]. Nevertheless, none of the instruments used or developed to date have explicitly taken into account the concerns and views of Spanish-speaking AR patients, nor have they explored the structure of the HRQOL concept in AR patients in Spain. In fact, only one disease-specific instrument—the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ)—has been adapted and validated for use in Spain [15].

As the relevance and structure of the HRQOL concept may differ across countries and cultures [16], there is no guarantee that HRQOL-related issues which are important to AR patients in Canada or the United States, for example, will be equally relevant to patients in Spain. It has been suggested that, as a minimum, further study of the HRQOL construct across countries and cultures is warranted, and that development of locally relevant instruments may be advisable [17]. In the case of AR, differences in behavior patterns, geographic and climatic conditions, and risk factors may influence the relevance of questionnaire content. Cultural aspects may also influence the way a person lives with a disease and the way patients react to a disease psychologically and emotionally. For example, a recent study has shown that fatalism was associated with lower social functioning in Hispanic women with coronary heart disease [18] while another recent study has shown that the degree to which psychosocial aspects impact on HRQOL scores varied substantially between breast cancer patients from Germany, Japan, and Korea [19]. Likewise, one of the most widely used HRQOL measures in AR, the RQLQ, was developed almost 15 years ago, and patients' views on what is important about the disease and its treatment may have changed since its development. Finally, the techniques for the development of HRQOL measures have also improved over time, and it may be possible to improve on the psychometric performance of existing instruments.

The aim of the present study was therefore to develop an instrument to measure HRQOL in patients with AR, which would take into account issues of importance to Spanish patients with AR, which would be suitable for use in clinical studies, and which might improve on the psychometric performance of existing instruments.

Patients and Methods

The study consisted of three main phases: item generation, item reduction and questionnaire formatting, and validation of the final version of the questionnaire. An outline of the study is provided in Figure 1.

Item Generation

Questionnaire content was developed from a literature review, consultations with clinical experts and experts in the development and use of patient-reported outcomes (PRO) measures, and focus groups with AR patients. The literature review, which was extensive but nonsystematic, was performed to identify instruments already developed to measure the HRQOL of AR patients and to identify issues of relevance in the construction of the new instrument. Databases reviewed included MEDLINE and the Índice Médico Español. The consultation with experts was in the form of a structured brainstorming technique, and was designed to obtain expert views on potential content, uses, and characteristics (such as length, mode of administration, and scoring) of the questionnaire. Experts attending the meeting included allergy and ear, nose and throat (ENT) specialists and experts in the development of PRO measures.

Four focus groups with AR patients were performed in Barcelona, Madrid, Bilbao, and Seville. A semistructured script, developed from the literature review and consultations with experts, was used to guide discussions. Focus groups included five to seven patients, with a wide range of sociodemographic and clinical characteristics. All focus group discussions were tape-recorded and transcribed. Content analysis of the transcribed texts was performed by two of the study group investigators (EB, MH) and a consensus reached on which items should go forward to the next stage. Potential items for inclusion in the questionnaire were reviewed by three of the study group members (AV, EB, MH), who rejected items that were ambiguous, difficult to understand, redundant or irrelevant.

Item Reduction and Questionnaire Formatting

To identify items for inclusion in the final version of the questionnaire, the 58 items in the item pool were administered to a sample of 400 patients with inter-

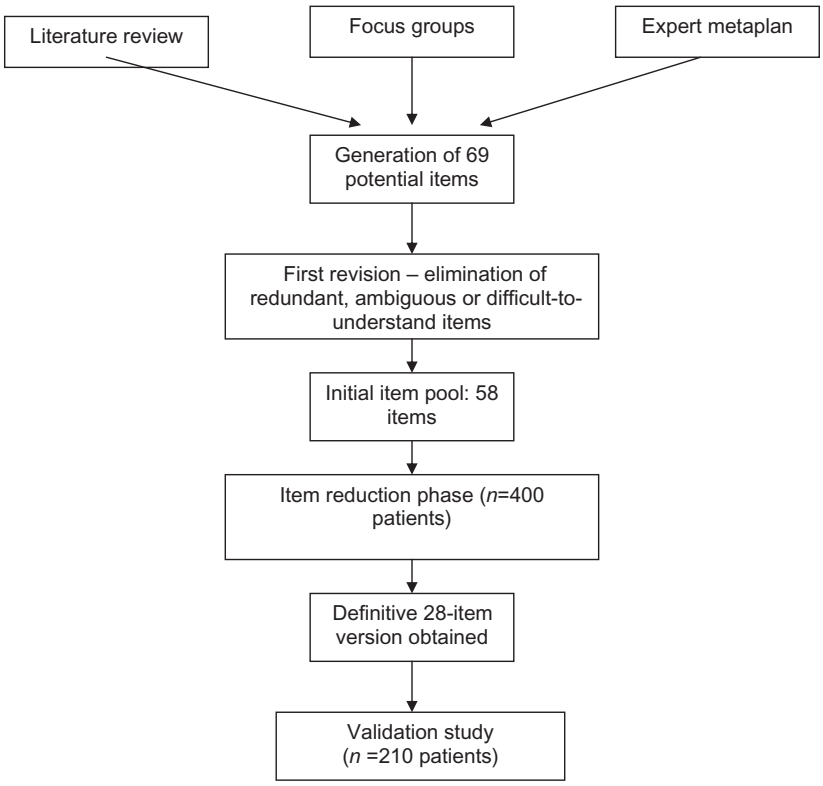

Figure 1 Development and validation process for the ESPRINT questionnaire.

mittent AR (IAR) or persistent AR (PAR) in an observational, cross-sectional, multicenter study. For all items in the pool, patients rated both the frequency and importance of each item on 5-point scales ranging from "Never" to "Always" and "Not at all important" to "Very important." The time period referred to was the last 2 weeks. Other variables measured in this phase of the study included age, sex, level of education, type of AR, time since diagnosis, symptom severity, and type of treatment for AR. AR was defined as intermittent when symptoms occurred less than 4 days per week or less than 4 weeks, and as persistent when symptoms occurred more than 4 days per week or more than 4 weeks [1].

Psychometric analyses to reduce the number of items included: 1) analysis of missing responses (exclusion of items with more than 10% of missing responses); and 2) response distribution (items in which more than 60% of respondents checked the same response category were excluded). Clinimetric analysis was based on analysis of frequency and importance scores with the product of the mean frequency and importance scores being obtained, and items ranked according to this product. Only the 30 top ranked items were retained for further analysis. In addition, Rasch analysis, a form of Item Response Theory analysis [20], was used to eliminate any remaining items that performed poorly in terms of infit and outfit values. The final phase of item selection was a meeting of the expert committee to review the item selection process, and determine whether further reduction was required or whether items eliminated in the preceding analysis should be retained on clinical or other grounds.

When item selection was complete, exploratory factor analysis was performed and internal consistency coefficients (Cronbach's alpha) were obtained for the dimensions identified as well as for the overall scale.

Validation Study

In order to determine the new questionnaire's reliability, validity, and sensitivity to change, a prospective, observational study was performed between March and August 2004 in the allergy and ENT departments of 27 Spanish hospitals. Each center consecutively included patients with the following characteristics: 1) ambulatory patients aged more than 18 years; 2) with a diagnosis of IAR or PAR; and 3) who were symptomatic at the time of inclusion in the study. The study aimed to include a total of 210 patients; approximately 33% of patients completed the questionnaire on one occasion and the remainder completed the questionnaire on two occasions, 2 to 4 weeks apart, to assess test–retest reliability and sensitivity to change. All patients provided informed consent to participate in the study and the study was approved by the Ethics Committee of the Hospital Clínic i Provincial in Barcelona.

Patient assessments were performed on inclusion in the study, and again after 2 to 4 weeks. Data were collected on sociodemographic (sex, age, and educational level) and clinical characteristics (time since diagnosis, type and severity of AR according to the Allergic Rhinitis and its Impact on Asthma Initiative [ARIA] guidelines [1], presence and type of comorbidities, treatments for AR, and symptom intensity). AR symptom intensity was measured using the Total Symptom Score (TSS4), a widely used instrument in clinical trials in AR which is defined as the sum of nasal symptoms of obstruction, rhinorrhea, itch, and sneeze. Each of these is scored on a scale from 0 to 3 resulting in a TSS4 score ranging from 0 (no symptoms) to 12 (maximum symptom intensity [21,22]. To be included, patients had to score at least three points on the TSS4.

The new questionnaire was self-administered alongside the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) [10,15] and the Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12) [23]. The RQLQ consists of 28 items in seven dimensions: Sleep (3 items), Non–hay fever symptoms (7 items), Practical problems (3 items), Nasal symptoms (4 items), Eye symptoms (4 items), Activities (3 items), and Emotions (4 items). The items in the "Activities" dimension are individualized, which means that the patient should choose the three dimensions which are most affected by AR. Responses to the individual items are on a 7-point ordinal scale, and scores are provided by dimension and overall, on a 0–6 scale where 0 represents good HRQOL and 6 represents poor HRQOL. The instrument has been adapted and validated for use in Spain [15].

The SF-12 [23] is a shortened version of the 36-item health survey, which has been adapted and validated for use in Spain [24]. The SF-12 provides a measure of physical (physical component summary [PCS]) and mental health (mental component summary [MCS]), with lower scores indicating worse health status. All scores were calculated using standard scoring algorithms for the Spanish population, which yield a mean score of 50 and a SD of 10 in the general population [23].

A health status transition item was self-administered at the second visit to assess changes in health status perception from the first visit. Patients answered on a Likert-type ordinal scale with 13 response options ranging from "have greatly improved" to "have greatly worsened." The results were used in the analysis of test–retest reliability and sensitivity to change.

Patients were also asked to rate the new questionnaire's ease of use on a scale ranging from "Very difficult to complete" to "Very easy to complete," and the time taken to complete the questionnaire was recorded. Other variables measured included age, sex, level of education, time from diagnosis, presence and type of comorbidities (particularly asthma and conjunctivitis) and whether the patient was currently receiving treatment for AR.

Statistical Analysis

The questionnaire's feasibility was assessed by examining responses to the ease of use question, and the time taken to complete the questionnaire. The number and percentage of missing responses was also taken into account by estimating the number and proportion of patients with at least one missing response, and maximum number of missing responses per item.

The distribution of the overall and dimension scores was analyzed by calculating mean scores, standard deviations, observed score ranges, and floor and ceiling effects (the proportion of patients with the worst and best possible scores, respectively) for the overall score and for each dimension of the new questionnaire.

The instrument's internal consistency was assessed by estimating Cronbach's alpha coefficients for individual dimensions and the overall score at baseline. The 2- to 4-week test–retest reliability was assessed by calculating the intraclass correlation coefficient (ICC) between visits in patients who did not report any significant change on the health status transition item.

Known groups validity was tested by determining whether the instrument was able to discriminate between patient groups likely to differ in HRQOL: different degrees of AR severity, with and without comorbidities, groups with IAR and PAR. AR severity was classified empirically as mild if patients scored 3 to 6 points on the TSS4, moderate if they scored 7 to 9 points, and severe if they scored 10 to 12 points. Patients with PAR were also expected to report worse HRQOL than patients with IAR [25].

Convergent validity was tested by estimating Spearman correlations between scores on the SF-12 PCS and MCS, scores on the RQLQ and scores on the individual dimensions and overall score of the new questionnaire. Correlations were expected to be higher between the new questionnaire and the RQLQ, as both are disease-specific, than between the new questionnaire and the SF-12. Similarly, correlations between dimensions measuring similar content in the two disease-specific questionnaires (e.g., dimensions measuring psychological and emotional impact) were expected to be higher than those between dimensions measuring dissimilar content (e.g., the "Practical problems" dimension on the RQLQ and the "Sleep" dimension on the new questionnaire). A series of hypotheses were developed regarding where the highest correlations were likely to be seen between dimensions on the two questionnaires.

Sensitivity to change was assessed by calculating the effect size (i.e., the standardized mean score change) and standardized response mean (SRM), in the sub-

group of patients who reported a "small improvement" or greater on the health status transition item. Effect size values of about 0.2 were considered to represent a small change, values of about 0.5 a moderate change, and values of about 0.8 or higher a large change in the attribute of interest [26]. The SRM was calculated by dividing the mean change in score by the standard deviation of the change scores between the two study visits [27].

Results

Item Generation

The literature review identified 11 instruments which had previously been designed to measure AR or related illnesses, ranging from 14 to 31 items in length. Recommendations from the expert consensus meeting concerning the characteristics of the HRQoL questionnaire included that it should be self-administered, easy to score, and include basic symptoms. The focus group sessions included 27 AR patients and generated 69 potential items. After elimination of items that were ambiguous, difficult to understand, redundant or irrelevant, an initial pool of 58 items was produced. This was the version administered to 400 patients for further item reduction using psychometric and clinimetric methods.

Item Reduction and Questionnaire Formatting

After administration of the 58 remaining items to respondents, a further four items were removed because more than 60% of respondents used the same response option, 24 items were eliminated because they scored lowest on the impact score, and four items were removed because they had infit or outfit values more than 1.30 in the Rasch analysis. On the basis of clinical recommendations, however, one of these items was retained, giving a total of 27 items distributed in seven dimensions (Nasal symptoms, Non-nasal symptoms, Energy/vitality, Activities of daily living [ADL], Environmental aspects, Sleep, and Psychological impact) as well as an additional question on overall health related to AR. Responses are on a 5-point Likert scale and the questionnaire produces both an overall score and a score for each dimension, which are calculated from the mean of all items in the scale, or in each dimension, respectively. Lower scores indicate better health status and higher scores indicate worse health status. The questionnaire was called the ESPRINT-28 (Cuestionario ESPañol de Calidad de Vida en RINiTis). Item frequency and importance scores in the item reduction stage of the study are shown in Table 1.

Validation Study

In the validation study, evaluable responses were available for a total of 206 patients at the first visit. Patient characteristics are shown in Table 2. The study sample was relatively young (mean age 32.3 years, SD 9.7 years), 62% were women, and the educational level was generally high (69% had completed secondary or university level education). Of the total sample, 65.5% of patients were receiving treatment for AR at the baseline visit, and 49% had PAR. Using the ARIA classification, AR was classified as moderate/severe in 96.6% of cases.

In terms of feasibility, only one patient had a missing response on the ESPRINT-28 at the baseline visit, and mean (SD) time to complete the questionnaire was 7.1 (5.4) minutes. The questionnaire was considered easy or very easy to answer by 89.3% of patients.

Table 3 shows the score distributions, floor and ceiling effects, internal consistency, and test–retest reliability coefficients for the questionnaire. Floor and ceiling effects were negligible (<15%) in all dimensions and for the overall score. The highest floor or ceiling effect was seen on the "Energy/vitality" dimension, which had a ceiling effect of 14.1%. Cronbach's alpha and ICC values were more than 0.70 for the overall score and for all dimensions, except for the dimension of "Nasal symptoms" which had an ICC value of 0.63.

Table 4 shows the results of testing the known groups' validity of the ESPRINT-28. Patients with more severe AR symptoms had statistically significant ($P < 0.01$) worse (higher) scores on all ESPRINT-28 dimensions and the global score. Score differences between patients with mild AR and those with severe AR were in the region of two points on the 6-point scale in all dimensions. Patients with PAR also had statistically significant ($P < 0.01$) worse scores than IAR patients on all dimensions and on the overall score, with a difference between the groups of approximately 0.5 to 1.0 points. Patients with comorbidities reported slightly worse HRQOL on the "Non-nasal symptoms" and "Energy/vitality" dimensions than patients without reported comorbidities (mean scores of 2.77 vs. 1.90 and 2.55 vs. 1.84, respectively), but there were no statistically significant differences between these two groups on the other dimensions.

Table 5 shows the results of testing the convergent validity of the ESPRINT-28 by estimating correlations between ESPRINT-28 dimension and overall scores, and the RQLQ and SF-12 mental and physical health summary scores. As predicted, correlations between the disease-specific ESPRINT-28 and the SF-12 PCS and MCS scores were lower than those between the overall scores of the two disease-specific instruments, with the correlations between the MCS and the ESPRINT-28 overall score being particularly low. In the case of the ESPRINT-28 and RQLQ dimension scores, the pattern of correlations was generally as expected, with dimensions that measure similar

Table I Mean frequency and importance scores for 58 items included for item reduction

Ranking	Item content	Mean score: frequency	Mean score: importance	Mean impact score
1	Annoyed by rhinitis symptoms	1.87	1.79	4.13
2	Nasal itching and/or repeated sneezing	2.31	2.05	5.45
3	Blocked or stuffy nose	2.42	2.09	5.78
4	Liquid or watery nasal mucus	2.36	2.08	5.78
5	Constantly thinking about nasal symptoms	2.56	2.35	7.23
6	Itchy eyes or having to rub eyes	2.78	2.38	7.93
7	Angry at having to constantly interrupt activities	2.81	2.42	8.12
8	Worried by rhinitis symptoms	2.69	2.57	8.12
9	Slept badly because of rhinitis	3.00	2.50	8.82
10	Woken with a dry mouth or because of dry mouth	2.90	2.66	9.13
11	Felt bitter or weighed down by rhinitis symptoms	2.94	2.62	9.17
12	Worried about not having a handkerchief to hand	2.93	2.61	9.27
13	Had a bad time in closed, airless places	3.01	2.67	9.36
14	Bothered by sunlight or wind	2.95	2.71	9.56
15	Problems at work or uncomfortable at work	3.04	2.70	9.71
16	Watery eyes	3.07	2.81	9.92
17	Bothered by sudden changes of temperature	2.98	2.85	9.93
18	Problems sleeping or getting to sleep	3.27	2.78	10.48
19	Nose red or irritated	3.21	2.92	10.58
20	Woken up or got up at night because of rhinitis	3.31	2.85	10.91
21	Woken up feeling tired or fatigued	3.27	2.98	10.98
22	Bothered by symptoms dining out	3.29	2.94	11.03
23	Red or puffy eyes	3.28	2.96	11.01
24	Tickle in throat or roof of mouth	3.23	3.00	11.30
25	Irritable or bad-tempered because of rhinitis	3.39	2.97	11.43
26	Difficulties concentrating	3.38	2.97	11.50
27	Difficulty breathing, breathlessness	3.45	2.92	11.52
28	Lack of desire to do anything	3.41	3.02	11.54
29	Bothered by eyes or sensitive to sunlight	3.32	3.15	12.06
30	So tired felt like you would not recover all day	3.47	3.11	12.62
31	Low in spirits	3.52	3.18	12.77
32	Problems doing work around house	3.50	3.23	12.82
33	Poor performance at work	3.66	3.15	12.81
34	Conditions at work make rhinitis worse	3.49	3.27	13.22
35	Worried symptoms will bother or irritate others	3.54	3.26	13.30
36	Make noises in throat to relieve itching	3.48	3.32	13.35
37	Headache	3.72	3.33	13.62
38	Loss of smell or taste	3.55	3.49	13.64
39	Distressed by not having rhinitis medication to hand	3.63	3.37	13.67
40	Avoided heated or air-conditioned places	3.67	3.48	14.20
41	Nasal voice or hoarseness	3.63	3.55	14.23
42	Snored because of rhinitis	3.54	3.57	14.25
43	Embarrassed by constantly blowing nose or sneezing	3.78	3.44	14.59
44	Uncomfortable or embarrassed around others	3.74	3.44	14.61
45	Sleepy during the day because of symptoms	3.78	3.52	14.63
46	Chest tightness or coughing that wakes you at night	3.90	3.41	14.79
47	Rhinitis limits you in doing things you want to do	3.86	3.53	15.21
48	Worried about side effects of rhinitis medication	3.71	3.69	15.31
49	Worried more liable to catch other illnesses	3.92	3.79	16.24
50	Itching in ear	3.96	3.81	16.50
51	No energy to do anything because of rhinitis	4.22	3.85	17.45
52	Embarrassed by physical appearance due to rhinitis	4.15	3.96	17.75
53	Stopped doing daily activities and tasks	4.40	3.81	17.75
54	Bothered by having to explain the problem	4.17	4.16	18.12
55	Missed work or left early because of rhinitis	4.52	3.96	18.75
56	Sexual life affected	4.42	4.15	19.22
57	Slept during day because of rhinitis	4.50	4.33	20.27
58	Don't like taking rhinitis medication in front of others	4.64	4.58	21.87

content on the two instruments showing stronger correlations than those between dimensions with more dissimilar content. Eight of the 11 initial hypotheses made regarding where the highest correlations would be found, were met. The three exceptions were observed in the correlation between the ADL dimensions on the two questionnaires, the correlation between the ESPRINT-28 "Non-nasal symptoms" dimension and the RQLQ "Other symptoms" dimension, where a very slightly higher correlation was seen with the RQLQ "Practical problems" dimension (correlations of 0.48 and 0.50, respectively), and the correlation between the ESPRINT-28 "Environment" dimension and the RQLQ "Eye symptoms"

Table 2 Baseline characteristics of the validation study sample (N = 206)

Sex (n, %)	
Female	133 (64.6)
Age (mean, SD)	33.7 (10.5)
Educational level (n, %)	
Primary education	64 (31.1)
Secondary education	81 (39.3)
University education	60 (29.7)
Time from diagnosis (mean, SD)	8.4 (6.5)
Comorbidities (n, %)	
Asthma	87 (42.2)
Conjunctivitis	108 (52.4)
In treatment for AR* (n, %)	135 (65.5)
Type of AR† (n, %)	
Persistent	101 (49)
Intermittent	105 (51)
Severity of AR† (n, %)	
Mild	7 (3.4)
Moderate/severe	199 (96.6)
Total symptom score‡ (mean, SD)	7.4 (2.5)
RQLQ§ (mean, SD)	
Global score	2.61 (1.10)
Activity limitations	3.35 (1.36)
Practical problems	3.78 (1.46)
Nose symptoms	3.54 (1.33)
Eye symptoms	2.33 (1.69)
Emotional problems	1.63 (1.34)
Sleep problems	2.01 (1.66)
Other symptoms	2.28 (1.45)
ESPRINT-28‖ (mean, SD)	
Global score	2.72 (1.17)
Nasal symptoms	3.38 (1.21)
Non-nasal symptoms	2.53 (1.37)
Activities of daily living	2.57 (1.52)
Environmental impact	3.13 (1.47)
Energy/vitality	2.36 (1.71)
Sleep	2.50 (1.72)
Psychological impact	2.56 (1.66)
SF-12¶ (mean, SD)	
PCS	47.57 (8.8)
MCS	46.65 (10.7)

*At inclusion.
†According to ARIA guidelines.
‡Scores range from 3 (mild symptoms) to 12 (severe symptoms).
§Global and dimension scores range from 0 (no impairment) to 6 (greatest impairment).
‖Overall scores range from 0 (minimum impact in HRQOL) to 5.8 (maximum impact in HRQOL); dimension scores range from 0 (minimum impact in HRQOL) to 6 (maximum impact in HRQOL).
¶Global and dimension score range from 0 (worse health status) to 100 (better health status).
AR, allergic rhinitis; MCS, mental component summary; PCS, physical component summary; RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire.

dimension, which was lower than that between the "Environment" and "Practical problems" dimensions.

Finally, Table 6 shows the results of testing the sensitivity to change of the ESPRINT-28 questionnaire, among patients reporting an improvement in health status (n = 74). Effect sizes for all dimensions and the global score were all close to or greater than 1, with the largest effect size (1.76) being seen on the "Nasal symptoms" dimension and the smallest (0.97) on the dimension of "Energy/vitality." The SRMs were all lower than the effect sizes, though the pattern of results was the same, with the "Non-nasal symptoms" and "Energy/vitality" dimensions being the least responsive and the "Environment" and "Nasal symptoms" dimensions and the overall score being the most responsive.

Discussion

The present study has described the development of a new questionnaire to measure the impact of AR and its treatment on patients' HRQOL with a particular emphasis on issues and concerns which are relevant to AR patients in Spain. Data presented demonstrate that the questionnaire is reliable, valid, and sensitive to change. The instrument has also proven quick and easy to complete and generates a negligible level of missing responses.

The development of the ESPRINT-28 followed recommended guidelines for the construction and validation of this type of instrument [27,28]. Considerable effort was made to include the point of view, at various stages of the process, of the principal parties interested in the development and use of this type of instrument, particularly clinicians and patients. In addition to being easy to complete, the instrument only requires a relatively short time to administer (7.1 minutes). In a recent study to validate a Spanish version of the RQLQ, the authors reported an administration time for that instrument of 9.67 (SD 6.25) minutes, though the version used was the original version of the RQLQ

Table 3 Score distributions, floor and ceiling effects, internal consistency, and test–retest reliability of the ESPRINT-28 questionnaire

ESPRINT-28 dimensions	Nasal symptoms	Non-nasal symptoms	Energy/ vitality	ADL	Environment	Sleep	Psychological impact	Global score*
Items (n)	4	5	3	4	3	4	4	28
Mean	3.35	2.44	2.31	2.75	3.24	2.60	2.35	2.73
SD	1.36	1.40	2.08	1.83	1.83	2.07	1.85	1.50
Theoretical range	0–6	0–6	0–6	0–6	0–6	0–6	0–6	0–5.8
Observed range	0.25–6	0–6	0–6	0–6	0–6	0–6	0–6	0.07–5.64
Floor† (%)	1.5	0.5	2.4	1.0	1.9	3.4	2.9	0
Ceiling‡ (%)	0	1.9	14.1	5.3	1.5	7.3	7.3	0
Cronbach's alpha	0.78	0.79	0.94	0.91	0.79	0.92	0.93	0.95
ICC§	0.63	0.83	0.89	0.81	0.81	0.89	0.86	0.86

*Includes a general item: "In general, thinking only of your rhinitis and no other illness, how would you say your health is?".
†Percentage of patients with the worst possible score.
‡Percentage of patients with the best possible score.
§Intraclass correlation coefficient (stability assessed by patient; subgroup of stable patients n = 35).
ADL, activities of daily living; ICC, intraclass correlation coefficient.

Table 4 Known groups validity based on symptom severity, type of AR and presence of comorbidity

ESPRINT-28 dimensions	Nasal symptoms	Non-nasal symptoms	Energy/ vitality	ADL	Environment	Sleep	Psychological impact	Global score
AR symptom intensity*: mean (SD)								
Mild (n = 79)	2.53 (0.99)	1.83 (1.16)	1.60 (1.50)[a]	1.78 (1.38)	2.22 (1.28)	1.78 (1.44)[b]	1.81 (1.43)[a]	1.97 (0.99)
Moderate (n = 80)	3.52 (0.93)	2.63 (1.25)	2.43 (1.52)[a]	2.64 (1.29)	3.27 (1.21)	2.42 (1.50)[b]	2.58 (1.60)[a]	2.78 (0.88)
Severe (n = 47)	4.55 (0.86)	3.53 (1.21)	3.53 (1.70)	3.77 (1.30)	4.42 (1.10)	3.85 (1.73)	3.79 (1.38)	3.89 (0.87)
P-value	All comparisons (mild–moderate, moderate–severe, mild–severe) were significant at $P < 0.001$, except those marked [a] and [b] which were significant at $P < 0.01$ and $P < 0.05$, respectively							
Type of AR: mean (SD)								
Intermittent (n = 101)	3.12 (1.24)	2.26 (1.32)	1.91 (1.70)	2.19 (1.54)	2.66 (1.46)	1.95 (1.62)	2.09 (1.62)	2.34 (1.18)
Persistent (n = 105)	3.64 (1.13)	2.79 (1.37)	2.80 (1.63)	2.94 (1.42)	3.59 (1.34)	3.04 (1.65)	3.03 (1.58)	3.11 (1.05)
P-value	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Presence of comorbidities†: mean (SD)								
Without (n = 55)	3.40 (1.37)	1.90 (1.29)	1.84 (1.58)	2.76 (1.64)	2.93 (1.60)	2.16 (1.71)	2.50 (1.71)	2.49 (1.21)
With (n = 150)	3.38 (1.16)	2.77 (1.33)	2.55 (1.73)	2.51 (1.49)	3.21 (1.43)	2.64 (1.72)	2.60 (1.65)	2.82 (1.16)
P-value	NS	<0.01	<0.01	NS	NS	NS	NS	NS

*For this analysis, patients' symptom intensity was classified using their TSS4 scores: mild AR = 3–6 points on the TSS4; moderate AR = 7–9 points; severe AR = 10–12 points.
†Asthma or conjunctivitis.
ADL, activities of daily living; AR, allergic rhinitis; NS, not significant.

which uses individualized items in the "Activity limitations" dimension, and therefore will be longer to administer [15]. The authors also reported that 16.9% of participants had a missing response on at least one of the questionnaire items, which is higher than the level of missing responses found in the present study for the ESPRINT-28.

The ESPRINT-28 also shows good psychometric characteristics, and meets accepted criteria for use in clinical studies [27–29]. Floor and ceiling effects, which can be taken as an indication of whether a measure will be at least theoretically capable of reflecting changes for better or worse, were within acceptable limits on all dimensions, with fewer than 15% of

Table 5 Convergent validity of ESPRINT-28 with the RQLQ and SF-12 mental and physical health summary scores

ESPRINT-28 dimensions	Nasal symptoms	Non-nasal symptoms	Energy/ vitality	ADL	Environment	Sleep	Psychological impact	Global score
SF-12								
MCS	–0.04	–0.01	–0.26	–0.12	–0.12	–0.08	–0.23	–0.12
PCS	–0.36	–0.39	–0.49	–0.50	–0.37	–0.45	–0.40	–0.54
RQLQ								
Overall score	0.63	0.64	0.74	0.72	0.71	0.63	0.70	0.86
ADL	0.43	0.36	0.48	**0.45***	0.50	0.41	0.46	0.55
Sleep	0.42	0.32	0.51	0.48	0.44	0.86*	0.50	0.64
Other symptoms	0.42	**0.48***	0.78*	0.64	0.60*	0.55	0.63	0.74
Practical problems	0.63*	0.50	0.42	0.59	0.59	0.38	0.55	0.66
Nose symptoms	0.76*	0.44	0.48	0.58	0.62*	0.50	0.50	0.69
Eye symptoms	0.31	0.80*	0.40	0.36	**0.48***	0.23	0.27	0.50
Emotional impact	0.44	0.41	0.57	0.58	0.49	0.34	0.68*	0.63

*Indicates where the strongest correlations were expected to occur between dimensions. Cells in bold indicate cases in which initial hypotheses were not met.
All correlations were statistically significant at $P < 0.01$.
ADL, activities of daily living; MCS, mental component summary; PCS, physical component summary; RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire.

Table 6 Sensitivity to change of ESPRINT-28 questionnaire, among patients reporting at least a small improvement in health status (N = 74)

	Nasal symptoms	Non-nasal symptoms	Energy/ vitality	ADL	Environment	Sleep	Psychological impact	Global score
Mean score (SD), visit 1	3.47 (1.16)	2.56 (1.39)	2.29 (1.44)	2.61 (1.47)	3.11 (1.29)	2.34 (1.54)	2.65 (1.54)	2.72 (0.98)
95% CI, visit 1	2.68–4.26	1.98–3.14	1.77–2.81	2.02–3.20	2.40–3.82	1.81–2.87	2.05–3.25	2.10–3.34
Mean score (SD), visit 2	1.43 (1.14)	1.19 (1.12)	0.90 (1.12)	0.91 (1.08)	1.53 (1.13)	0.76 (0.97)	0.77 (1.08)	1.12 (0.90)
95% CI	1.10–1.76	0.92–1.46	0.69–1.11	0.70–1.12	1.18–1.88	0.59–0.93	0.59–0.95	0.86–1.38
Effect size	1.76	0.99	0.97	1.16	1.22	1.03	1.22	1.63
SRM	0.73	0.5	0.5	0.61	0.74	0.61	0.63	0.73

ADL, activities of daily living; CI, confidence interval; SRM, standardized response mean.

patients at either the maximum or the minimum score on any of the dimensions or the overall score [30]. The instrument also shows good internal consistency on all dimensions and for the overall score and meets the recommended level of 0.7 for use at group level [27–29]. The Cronbach's alpha values obtained for the overall score and four of the dimensions (Energy/vitality, ADL, Sleep, Psychological impact) on the new questionnaire (>0.90) are sufficient to permit their use at individual level [31]. In terms of test–retest reliability, the results were also positive, with only one dimension (Nasal symptoms) falling below the recommended threshold of 0.70. This might be expected in this type of dimension, as nasal symptoms are likely to change quite substantially in a relatively short period of time, and we did not adjust for this fact.

The instrument's content validity was ensured by the process used in the development of the questionnaire, and particularly by the inclusion of focus groups of patients with the condition, which included a wide spread of patient characteristics, in terms of age, sex, educational level, and clinical characteristics. An effort was also made to include patients from different parts of Spain to ensure that the sample was also reasonably geographically representative. This also probably helped to broaden the range of opinions collected, which is important in this type of sampling. It is interesting to note that there are a number of differences with the RQLQ in terms of content. Specifically, there were some differences at dimension level; for instance, the ESPRINT-28 does not contain any items relating to practical problems associated with AR, as in the RQLQ, but does contain items on environmental aspects, an issue which is not covered in the RQLQ. It also includes a specific dimension on "Energy/vitality," an aspect which is only covered in the RQLQ within the "Non–hay fever symptoms" dimension. Likewise, there were differences at item level, such as the inclusion in the ESPRINT-28 of an item relating to the impact of AR on eating and dining out, which is an important aspect of Spanish life.

The analysis of known groups' validity showed that the questionnaire discriminated well between groups with different levels of symptoms, as well as between patients with PAR and IAR. This is, in fact, one of the first studies to examine differences in quality of life between patients classified as having IAR or PAR according to the new ARIA classification scheme [1], and it appears to confirm the results of an earlier study which showed that AR symptoms were more severe in patients with PAR [25]. The fact that most of the dimensions did not discriminate between patients with and without comorbidities may also be taken as positive as the instrument is intended to focus on the problems of AR patients, not patients with other types of illness.

The pattern of correlations between the ESPRINT-28 and the SF-12 PCS and MCS and the RQLQ were also generally as expected, thereby confirming the instrument's convergent validity. Correlations were generally higher with the SF-12 PCS than with the MCS, suggesting that the main impact of the illness is on physical rather than on mental domains. The majority of correlations between dimensions on the ESPRINT-28 and the RQLQ also met a priori expectations, with eight of the 11 initial hypotheses regarding likely correlations being met. This signifies a strong confirmation of the new questionnaire's convergent validity. The least expected result was the low correlation between the ADL dimension on the two questionnaires. This may be due to the fact that, in the present study, the nonstandardized version of the RQLQ was used, whereby patients had to choose the three activities which were most important to them, whereas ESPRINT-28 uses closed questions which focus on the impact on work or study, eating and dining out, and on whether the condition has obliged patients to interrupt their daily activities. The type of activities referred to in the two questionnaires could therefore be substantially different. The high correlation between the ESPRINT-28 dimension of "Energy/vitality" and the RQLQ dimension of "Other symptoms" is likely due to the fact that approximately half of the items in the RQLQ "Other symptoms" dimension refer to aspects related to energy and vitality.

Finally, the instrument appears to be sensitive to changes in patients' health status, with changes on all of the dimensions represented by effect sizes close to or greater than 1, which would represent a large effect size, according to Cohen's classification [26]. In testing the questionnaire, the same approach as that employed by Juniper and colleagues was used to test sensitivity to change, in that patients were asked at the second study visit whether they had noted any changes in their health status related with their AR [10]. The changes are not, therefore, necessarily related to the effects of any given treatment, and improvements could be due to the natural progression of the illness. The effect sizes by dimension for the RQLQ in the recent validation of the Spanish version were slightly lower than those observed in the present study, from 0.76 for the general symptoms dimension to 1.46 for the "Nasal symptoms" dimension and the overall score [15]. It would be helpful to test the new instrument's ability to detect changes associated with a particular treatment for AR to determine its potential usefulness in clinical trials.

One of the limitations of the present study was the relatively small sample size used in the validation stage of the study. Although the sample size was sufficient to test the new instrument's reliability, validity, and sensitivity to change, it was too small to be able to reliably generalize the results to a larger population, and studies in larger samples are needed to confirm the

instrument's external validity. Likewise, the sample was too small to be able to examine the instrument's responsiveness in patients according to the amount of positive or negative change they reported on the health state transition item, which can be useful in determining the instrument's longitudinal validity.

In conclusion, this new instrument, which has been designed primarily to measure the HRQOL of Spanish and Spanish-speaking respondents, has shown good reliability, validity, and sensitivity to change. It has also proved easy to use and administer and has arguably improved on some aspects of psychometric performance when compared with the RQLQ, which can be considered the gold standard in the field. There are also differences in content between the new instrument and the RQLQ which justify the development of this new instrument. Further studies should concentrate on obtaining additional information such as the Minimum Clinically Important Difference, which will aid in the interpretation of scores.

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Appendix A. Validated version of the ESPRINT-28 questionnaire

Below you will find some questions about bother caused by rhinitis. Please circle the number which corresponds to your choice of answer. It is important that you answer all of the questions.

Over the last 2 weeks, how much have you been bothered by each of the following symptoms or situations?

Nasal symptoms	Not at all	Hardly at all	A little	Moderately	Quite a lot	A lot	Extremely
1. The sensation of a blocked or stuffy nose	0	1	2	3	4	5	6
2. Runny nasal mucus, like water	0	1	2	3	4	5	6
3. Itchy nose or constant sneezing	0	1	2	3	4	5	6
4. Red or irritated nose	0	1	2	3	4	5	6
Other symptoms	Not at all	Hardly at all	A little	Moderately	Quite a lot	A lot	Extremely
5. Watery eyes	0	1	2	3	4	5	6
6. Itchy eyes, or need to rub eyes	0	1	2	3	4	5	6
7. Red or swollen eyes	0	1	2	3	4	5	6
8. Difficulty breathing, breathlessness or shortness of breath	0	1	2	3	4	5	6
9. Tickle in the throat or roof of the mouth	0	1	2	3	4	5	6
Activities of daily living	Not at all	Hardly at all	A little	Moderately	Quite a lot	A lot	Extremely
10. Have you felt uncomfortable at work or have you had difficulties at work because of your rhinitis	0	1	2	3	4	5	6
11. Have you been bothered by rhinitis symptoms when you've been out to eat or for a drink	0	1	2	3	4	5	6
12. Have you had problems concentrating on your work, studies, etc. because of your rhinitis	0	1	2	3	4	5	6
13. Have you had to constantly interrupt what you were doing because of your rhinitis	0	1	2	3	4	5	6
Environmental aspects	Not at all	Hardly at all	A little	Moderately	Quite a lot	A lot	Extremely
14. Have you had a bad time in closed, airless places, because of your rhinitis	0	1	2	3	4	5	6
15. Have you been bothered by sudden changes of temperature, because of your rhinitis	0	1	2	3	4	5	6
16. Have you been bothered by sunlight or the wind, because of your rhinitis	0	1	2	3	4	5	6
Energy	Not at all	Hardly at all	A little	Moderately	Quite a lot	A lot	Extremely
17. Have you woken up tired or fatigued, because of your rhinitis	0	1	2	3	4	5	6
18. Have you been so tired because of your rhinitis that it seemed like you would not recover at all during the day	0	1	2	3	4	5	6

Appendix A. continued

Over the last 2 weeks, how much have you been bothered by each of the following symptoms or situations?

19. Could you not be bothered to do anything, because of your rhinitis	0	1	2	3	4	5	6
Sleep	Not at all	Hardly at all	A little	Moderately	Quite a lot	A lot	Extremely
20. Have you had trouble sleeping or falling asleep, because of your rhinitis	0	1	2	3	4	5	6
21. Have you woken up with a dry mouth or have you woken up because of a dry mouth, due to your rhinitis	0	1	2	3	4	5	6
22. Have you woken up or gotten up in the night, because of your rhinitis	0	1	2	3	4	5	6
23. Have you slept poorly, because of your rhinitis	0	1	2	3	4	5	6
Mood	Not at all	Hardly at all	A little	Moderately	Quite a lot	A lot	Extremely
24. Have you felt bitter or fed up due to your rhinitis symptoms	0	1	2	3	4	5	6
25. Have you found yourself always thinking about nasal symptoms	0	1	2	3	4	5	6
26. Have you been more irritable or in a bad mood because of your rhinitis	0	1	2	3	4	5	6
27. Have you had a bad time or felt poorly, because of your rhinitis	0	1	2	3	4	5	6

28. In general, taking into account only your rhinitis and no other illness, how would you rate you health?

Excellent Very good Good Fair Bad

This version in English of the ESPRINT-28 questionnaire is provided only to give readers an idea of questionnaire content. It is not an official adapted version, and should not be used in any type of study or in clinical practice. Anyone wishing to use the ESPRINT-28 questionnaire should contact the corresponding author.