Adaptation to Spanish and validation of the Rhinitis Control Assessment Test (RCAT) questionnaire

Running title: Adaptation of the RCAT to Spanish

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Abstract

Background: The Rhinitis Control Assessment Test (RCAT) is a widely used patient-based questionnaire developed to evaluate control of rhinitis.

Objective: To develop and validate a Spanish version of the RCAT ($RCAT_e$).

Methods: After translation and cultural adaptation of the original RCAT, this multicentric observational, prospective study evaluated the properties/attributes of the $RCAT_e$ assessing its validity, reliability, responsiveness, size effect, minimal important difference and cut point score.

Results: A total of 252 allergic rhinitis (AR) patients from 27 allergy and otolaryngology departments from hospitals throughout Spain were included. Significant and strong correlations were found between the $RCAT_e$ and the total nasal symptom score and the visual analogue scale (-0.79 and -0.77, respectively; $p<0.0001$). The $RCAT_e$ significantly distinguished between patients grouped in different severity or duration AR categories ($p<0.001$). The internal consistency (Cronbach alpha) was good (0.84) and the test-retest reliability was moderate (0.54 by the physician and 0.49 by the patient). The $RCAT_e$ responsiveness to change was high and significant ($p<0.0001$), and linearly correlated with the improvement of AR. The overall size effect was 1.62. The cut-off point to identify patients with adequate AR control was >20 (ROC curve area= 0.746; sensitivity= 58.3%; specificity= 90.9%).

Conclusion: The psychometric evaluation and validation of $RCAT_e$ indicated good reliability, validity, and responsiveness suggesting it can be effectively used to measure control of AR symptoms by Spanish-speaking patients.

Key words: Allergic rhinitis. Patient-reported outcome. Rhinitis control. Psychometric evaluation. Rhinitis Control Assessment Test

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Resumen

Antecedentes: El cuestionario de control de la rinitis RCAT (*Rhinitis Control Assessment Test*) es un cuestionario auto administrado para evaluar el control de la rinitis, de uso muy extendido.

Objetivo: Desarrollar y validar una versión traducida del cuestionario RCAT para pacientes hispanohablantes ($RCAT_e$).

Métodos: Tras la traducción y adaptación cultural del cuestionario original, se realizó un estudio multicéntrico prospectivo para evaluar los atributos y propiedades del $RCAT_e$ analizando su validez, fiabilidad, capacidad de respuesta, tamaño del efecto, diferencias mínimas relevantes y puntos de corte.

Resultados: Se incluyeron 252 pacientes con rinitis alérgica (AR) de 27 unidades de Alergia y Otorrinolaringología de hospitales de toda España. El $RCAT_e$, la puntuación total de síntomas y la escala visual analógica se correlacionaron de forma robusta y significativa (-0.79 and -0.77, respectivamente; $p<0.0001$). El $RCAT_e$ diferenció de forma significativa pacientes clasificados en diferentes categorías de gravedad o duración de la AR ($p<0.001$). La consistencia interna (alfa de Cronbach) resultó buena (0.84) y la fiabilidad test-retest moderada (0.54 evaluada por el especialista y 0.49 por el paciente). La sensibilidad al cambio del $RCAT_e$ fue elevada significativamente ($p<0.0001$), y se correlacionó linealmente con la mejoría de la AR. El tamaño del efecto global fue 1.62. El punto de corte para identificar pacientes con un adecuado control de la AR fue >20 (área de la curva ROC= 0.746; sensibilidad= 58.3%; especificidad= 90.9%).

Conclusiones: La evaluación psicométrica y la validación del $RCAT_e$ indicaron una buena fiabilidad, validez y capacidad de respuesta, sugiriendo que puede usarse eficazmente para evaluar el control de los síntomas de AR en pacientes hispanohablantes.

Palabras Clave: Rinitis alérgica, variables informadas por pacientes, control de la rinitis, evaluación psicométrica, cuestionario de control de la rinitis.

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Introduction

Allergic rhinitis (AR) is the non-communicable chronic disease with the highest prevalence, affecting approximately one fourth of the world population [1]. AR has a major impact on patient quality of life [2], assessed using standardized questionnaires [3, 4], that is related to the severity of the disease [5]. It has been shown that disease-related indirect and direct costs represent a major burden for health systems [6].

The concept of control of chronic diseases has been introduced in recent decades given the difficulties to reach full remission in affected patients and the need for a new individualized medical care approach, known as precision medicine [7]. Control defines a status in which the treatment objectives are reached, and symptoms are minimized [8]. Disease control comprises various dimensions of the disease such as effects on daily or nocturnal symptoms, on social life, work, academic education or leisure activities. Similarly, it includes the influence on these aspects of the medication and its adverse effects, the impact on respiratory function, the degree of response to treatments, the impact of exacerbations and the prognosis of the disease. In contrast, the concept of disease severity refers to the intensity of the loss of function of the organ/s affected by the disease. Severity is an intrinsic feature of the disease that can change in time.

The evaluation of disease control in AR is challenging due to the difficulty of including all the above dimensions in a single measurement tool. The evaluation of AR control can be performed using standardized questionnaires, in a similar way to the evaluation of control proposed for the management of asthma. These questionnaires are relatively simple and practical tools which allow a fast assessment of disease control by interrogating the patient with a few questions [9]. The Rhinitis Assessment

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Control Test (RCAT) is a patient reported outcome composed of 6 Likert-type questions with 5 response options, scoring from 1 to 5, with a total score from 6 to 30 (the higher the score, the better the control) [10]. It was originally validated in American English and then widely validated and translated to some languages [11]. The RCAT is likely the patient-based questionnaire most widely used to assess AR control, especially in clinical research, and it has been positively evaluated with respect to its psychometric qualities and its capacity to evaluate control [9].

The objective of this study was to translate and adapt the RCAT questionnaire for its use by Spanish-speaking patients, as well as to evaluate the psychometric attributes of this translated version, following the recommendations of the international consensus-based standards for the selection of health measurement instruments (COSMIN) [12].

Methods

RCATe translation and cultural adaptation

It was carried out following established procedures through a forward and back translation process [13]. Qualitative assessment was performed by pilot interviews using translated versions of the questionnaire with 11 AR patients from the *Hospital Clínico de Zaragoza* and the *Hospital Clínic de Barcelona*, to test readability and comprehensibility.

AR patients

To validate psychometrically the $RCAT_{e,}$ a multicentric, observational prospective study in real-life conditions was designed. Allergologists and otolaryngologists from referral hospitals throughout Spain participated in the study. To avoid possible biases, each

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physician did not include more than 4 patients per month, up to a total of 15 patients per investigator. Patient inclusion criteria were ≥18 years old diagnosed with moderate to severe AR following the criteria of the modified ARIA Guidelines (mARIA) [14], and with a reflective total nasal symptom score (rTNSS: the sum of a bilateral scoring symptom of nasal congestion/obstruction, nasal itching, rhinorrhea and sneezing, scoring from 0 -no symptom- to 3 -highest intensity-) ≥ 8 (from 0 to 12). Patients excluded were those participating in clinical trials or patients diagnosed with obstructive septal deviation, chronic rhinosinusitis or nasal polyps. All patients signed a written informed consent to participate in the study. The study was approved by the Ethics Committee for Clinical Research of the *Hospital Clínic de Barcelona*. The study was carried out from November 2015 to October 2016.

Study design

The patients were interviewed twice within a month (baseline visit and second visit). Data was collected on demography, concomitant diseases and medication use, etiology of allergic sensitization, severity of rhinitis depending on a symptom score, on the affectation of quality of life (ESPRINT Questionnaire) [15] and through visual analogical scales (VAS, 0-10 cm) for global and symptoms severity. Additionally, patients were given the Spanish version of the RCAT questionnaire ($RCAT_e$) (Figure 1).

The psychometric validation of the $RCAT_e$ questionnaire was performed according to the following parameters:

- Feasibility: Percentage of patients able to respond to all questions of the $RCAT_e$ questionnaire.
- Floor and ceiling effect: Percentage of patients with the maximum and minimum score.

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- Convergent validity: Estimated by computing the Spearman rank-order correlations between the score from the $RCAT_e$ questionnaire and the rTNSS, and between the $RCAT_e$ and a global AR severity score assessed by the patient on a VAS.
- Discriminant validity: Assessment of the differences in the $RCAT_e$ score among patients classified in different categories of the classification of AR according to the modified ARIA Guidelines [14].
- Reliability: Internal consistency was measured using the Cronbach's alpha coefficient and test-retest reliability was measured by the intraclass correlation coefficient (ICC) between the $RCAT_e$ score at initial and final visits in patients who reported a similar state of health with respect to AR in a specific likert scale question called “change in health status”, asked in the final visit.
- Responsiveness: Relationship between changes in the $RCAT_e$ score, in initial and final visits, with the degree of improvement in the AR symptoms evaluated by a specific question asked to the patient (“change in health status”) and to the physician, as with the changes in the rTNSS between the initial and final visits.
- Size effect: was calculated as the difference between the means of the $RCAT_e$ scores of the two visits divided by the standard deviation of the score at the baseline visit.
- Minimally important differences (MID): To calculate the MDI two approaches were used, one based on the distribution of the values and one based on evaluating the relationship between the scores of the instrument and an independent measure (anchor-based) [16]. In the distribution-based approach, the score equivalent to half a standard deviation and a standard error of the

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mean (SEM) was considered. The SEM was obtained by multiplying the standard deviation of the scale at the baseline visit by the square root of one minus the reliability coefficient of that scale (Cronbach's α). To calculate the MID according to the anchor-based approach, the means of the $RCAT_e$ score at baseline and final visit were determined, as well as the difference between the two visits, obtained by patients stratified according to the variable 'change in health status'. The mean change was considered for patients who reported a 'somewhat better' change as MID.

- Cut-off point to discriminate between poorly controlled and well-controlled patients (a second cut-off point for partially controlled): The degree of control according to the physician was used as reference, considering the patient well-controlled when the physician considered that he/she had improved much, while the rest of the categories (somewhat better, same, somewhat worse or much worse) was considered uncontrolled. To evaluate the ability of the $RCAT_e$ questionnaire to classify patients according to the level of control, in the full spectrum of cut-off points (poor control vs. good control), the area under the receiver operating characteristic (ROC) curve was calculated. For each cut-off point, the sensitivity, specificity, positive predictive value, negative predictive value and the percentage of patients correctly classified together with 95% confidence intervals (CI) were calculated. In addition, the percentages of false positives and false negatives were analyzed. The point that allowed maximizing sensitivity, specificity, and positive and negative predictive values was chosen as the cut-off point, using the Youden Index (sensitivity + specificity - 1). In addition, a second cut-off point was calculated to discriminate between

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partially controlled patients and not-controlled patients, excluding controlled patients, with the same methodology. Partially controlled patients were defined as those who had 'somewhat improved' and not-controlled patients where those who were the 'equal', 'somewhat worse' or 'much worse'.

Statistical Analysis

We used the SAS software package version 9.2 for Windows for the statistical analysis of the data. We used the mean, standard deviation, minimum and maximum, median (percentile 50^{th}), percentiles 25^{th} and 75^{th}, and the number of valid cases, for the description of continuous variables. For the description of categorical variables, we used the number and percentage of patients by response category. Prior to performing parametric tests, we applied statistical techniques to ensure compliance with the assumptions. In case the established assumptions were not met, non-parametric tests were employed. We used a statistical significance level of p-value <0.05 for all tests.

Results

AR patients included in this study (N=252) were selected by 27 allergologists or otorhinolaryngologists working in major hospitals throughout Spain. The age (mean±SD) of the patients was 35±12 years and 71% were women. The time (mean±SD) elapsed between the date of diagnosis and the study was 6.3±9.7 years. Most of the patients presented persistent AR (60%) while the other had intermittent AR. Regarding disease severity, 29.4% presented mild AR, 60.1% moderate, and 10.4% severe. Additionally, 35.7% of the patients had concomitant asthma (34.4% mild, 65.6% moderate) and 60% presented concomitant ocular symptoms.

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Feasibility. 99.2% of patients answered 100% of the $RCAT_e$ questions, indicating that the test is viable and easy to understand. The percentage of patients with the minimum and the maximum score was 0 and 1.8%, respectively, suggesting no significant floor or ceiling effects.

Convergent validity was high as suggested by high Spearman correlation coefficients of -0.79 ($p < 0.0001$) between the $RCAT_e$ and the rTNSS, and of -0.77 ($p < 0.0001$) between the $RCAT_e$ and the AR severity assessed using a VAS.

Discriminant validity. Significant differences ($p<0.001$, Tukey's range test) were found in the $RCAT_e$ score among patients grouped in different categories of the AR classification according to the ARIA Guidelines (Figure 2).

The **internal consistency** of the $RCAT_e$ was robust, as shown by a Cronbach's alpha coefficient of 0.84. The ICC was 0.49 in the case of patients who assessed their health status as the same, and 0.54 in the case that the assessment of the change in health status was made by the physician.

The **responsiveness** of the $RCAT_e$ was high, being significantly higher the changes in the $RCAT_e$ for the patients who consider that their health status was much better or much worse compared to those that consider that their health status was equal or somewhat worse or improved ($p < 0.0001$, Tukey's range test). The same if the evaluation of the changes in the health status was made by the physician (Figure 3). The $RCAT_e$ scores (mean ± SD) increased by 9.2±5.1 for the patients for whom AR symptoms were strongly improved, 4.6±4.6 for those who were somewhat improved, 2.6±3.7 for those who were the same, and 2.7±3.5 for those who had somewhat worse, when the evaluation was made by the physician. When this evaluation was made by the patient, the scores on the $RCAT_e$ questionnaire increased by 9.8±5.1

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points for those who declared that their state of health at the final visit was strongly improved from the baseline visit, 7.3±5.0 for those that it was somewhat improved, 3.8±3.1 for those that it was slightly improved, 2.9±4.0 for those that it was the same, and -1.6±3.2 points for those that it was somewhat worse. A linear association was observed between the changes in the $RCAT_e$ and the improvement of AR ($p < 0.001$, Tukey's range test). A strong correlation was observed between changes in $RCAT_e$ score and changes in rTNSS, with a correlation coefficient of -0.71 ($p < 0.0001$).

The **overall size effect** was 1.62. Higher values of effect size were observed in patients with a greater change reported in health status.

The **MID** calculated by the method of distribution of values was 2.0 points and calculated according to the anchor-based approach was 3.8 points.

Cut off point to discriminate levels of control. The area under the ROC curve was used to assess the capacity of the questionnaire $RCAT_e$ to classify patients according to the level of control, using as reference the degree of control according to the physician (poor control vs. good control). The area under the ROC curve was 0.8106, suggesting good accuracy. The optimal cut-off point obtained to differentiate the controlled patients from the rest was 20 (area under the ROC curve= 0.746; sensitivity= 58.3%; specificity= 90.9%). In addition, a second point was calculated to discriminate between partially controlled patients and uncontrolled patients (excluding controlled patients), which resulted in cut-off of 18 (area under the ROC curve= 0.6646; sensitivity= 69.7%, and specificity= 36.8%).

The correlation between RCATe and the **quality of life** questionnaire (ESPRINT-15) scores was high and significant (Pearson coefficient=0.85; $p<0.0001$)

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Discussion

This study shows that the psychometric validation of the Spanish version of the Rhinitis Control Assessment test ($RCAT_e$) was satisfactory and fulfilled all the requirements established in the COSMIN [12]. The COSMIN brings together the common properties of patient-reported outcome measures (PROs), grouping the nine properties that are considered relevant in any PRO in 3 domains: reliability (which also includes internal consistency and precision), validity (which encompasses the validity of content, criteria and construction, and cultural adaptation), and sensitivity. Here we present favorable results for each of these properties, which show that the $RCAT_e$ questionnaire has good or very good levels of reliability and sensitivity.

The first psychometric evaluation of the original RCAT questionnaire, although performed on a larger sample, included patients of an age and sex distribution similar to our study [17]. While the Cronbach's alpha coefficient in the Meltzer study and ours was similar (0.84), the test-retest reliability was lower in our study (0.78 versus 0.54 if evaluation was done by the physician or 0.49 if it was done by the patient). It is possible that the difference was due to the inclusion of patients with more types of rhinitis than AR in the first, compared with ours, that included AR exclusively. Additionally, most of the patients in our study improved significantly, being only few the patients who remained unchanged and were available to assess the test-retest reliability.

Regarding convergent validity, the study by Meltzer assessed the correlation of the questionnaire with the rTNSS, the patient's overall assessment of the severity of his rhinitis, and the physician's assessment of the severity and control of the rhinitis. They obtained correlations between -0.3 and -0.6 when the assessment was done by the

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patient, but of 0.24 in the case it was done by the physician. In our case, the convergent validity was evaluated against the rTNSS and the overall evaluation of the patient's severity of AR, obtaining in both cases significant correlation values above 0.70.

With respect to discriminant validity, which is evaluated against known groups, in the study by Meltzer the stratification of severity was performed in mild, moderate and severe, based on the rTNSS, following non-validated criteria. The degree of control was obtained evaluated according to the physician. Questionnaire scores were significantly different among all these groups of patients. In our case, the known groups were established according to the standardized and validated criteria of severity and duration in the modified ARIA guidelines [14]. This resulted in significant and relevant differences in the $RCAT_e$ score obtained by patients with intermittent or persistent AR, and by patients with mild, moderate, or severe AR.

Longitudinal validity and responsiveness were evaluated in the study by Meltzer by comparing the changes in the questionnaire and changes in the TNSS, in the evaluation of the control by the physician and in the patient's self-assessment of the change in the disease. A significant improvement was obtained in the RCAT score in patients who improved both according to the physician and according to the patient, but with greater correlation when the evaluation was made by the patient. In our study, a good correlation (>0.70) was obtained between the changes in the $RCAT_e$ and the change in the rTNSS. We also observed a linear association between the change in the $RCAT_e$ score and the subjective evaluation of the patient's change, but this linear association was smaller if the evaluation of the change in AR was performed by the physician. This

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aspect coincides in a recurrent way in the two studies, highlighting the character as PRO of all RCAT idiomatic versions.

In the Meltzer study, the optimal cutoff point was established to differentiate between controlled and uncontrolled at the physician's criterion, obtaining the value of 21 from the questionnaire as the one that best discriminates (area under the ROC curve= 0.689, sensitivity= 83%, specificity= 55%). In our case, the optimal value was obtained in 20 (area under the ROC curve= 0.746, sensitivity= 58.3%, specificity= 90.9%), and we calculated a second value for partially controlled patients that resulted in 18. In the original study they obtained a value of 17 for this group of poorly controlled patients.

Finally, the clinical MID in the Meltzer study resulted in 2.2 and 2.4, depending on the approach (based on the distribution or "anchor based"), and in our study the values were similar (2.0 and 3.8, respectively).

Comparing both analyses, the Meltzer study and ours, we can conclude that the psychometric evaluation results were similar and satisfactory. The Spanish version of the questionnaire obtained in our study is suitable according to the quality standards suggested in the COSMIN consensus. In our case we also evaluated some additional features such as the effect size, which turned out to be satisfactory, and the floor and ceiling effects, also reasonable.

The RCAT questionnaire has been translated, adapted and validated psychometrically to other languages, such as Portuguese [18]. Table 1 shows a comparison of the main parameters derived from the original study by Meltzer, the validation of Portuguese version, and our study. The Portuguese adaptation included an objective measurement of nasal function (peak nasal inspiratory flow or PNIF)

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which presented a moderate correlation with the RCAT questionnaire (0.52), thus relating control with a measurement of nasal permeability. Strong correlations were also obtained between the Portuguese version of the RCAT and rTNSS, both nasal and extra nasal, as well as a good discriminant validity, with data similar to those obtained in our work. Unfortunately, the Portuguese version of the RCAT did not evaluate sensitivity to change or longitudinal validity.

Control and quality of life are different but related dimensions in the evaluation of the impact of the disease. In our study $RCAT_e$ and quality of life questionnaire scores (ESPRINT-15) were linearly correlated meaning that a better control of AR is related to a better specific health related quality of life. Both questionnaires can be used in a complementary way when assessing patients with AR.

In conclusion, our study shows that the translated and culturally-adapted version of the RCAT in Spanish ($RCAT_e$) shows good psychometric properties, similar to the original and to other versions of the questionnaire, which result in a useful version to evaluate the control of AR in Spanish-speaking patients.

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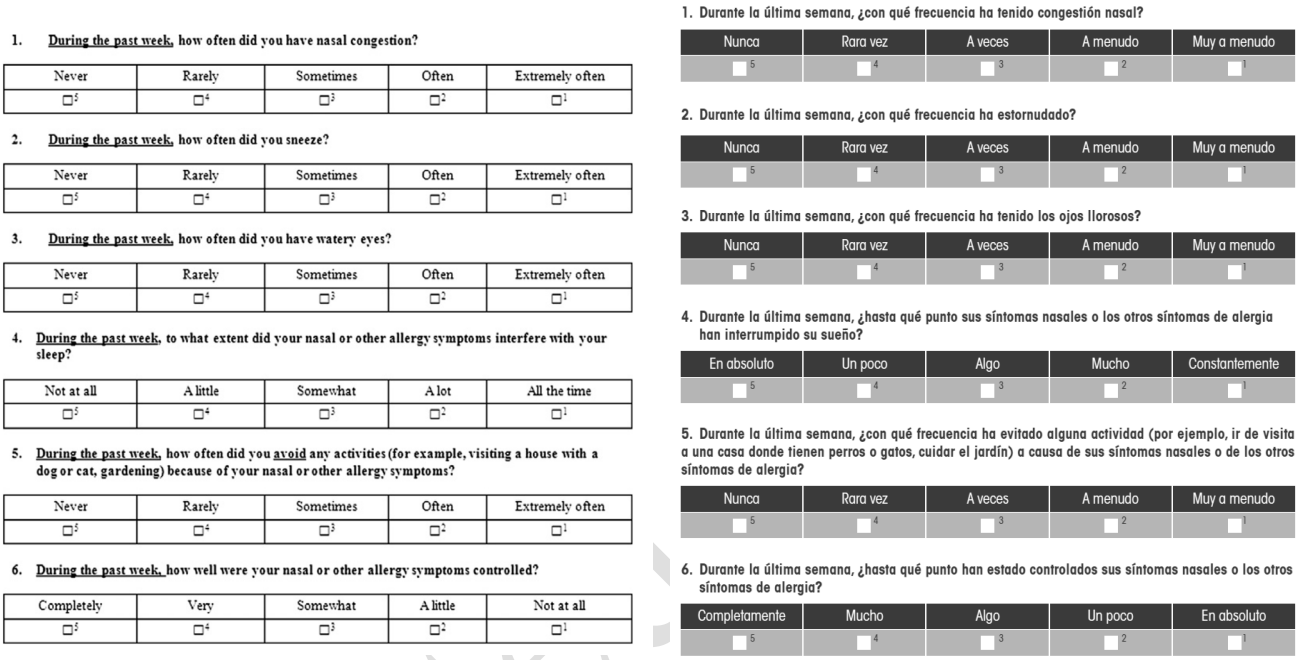
Table 1. Main parameters obtained in the psychometric validations of the US, Portuguese, and Spanish versions of the RCAT.

	Meltzer (2012)	Fernandes (2016)	Current study
Patients, N	402[1]	141[2]	252
Internal consistency (Cronbach's α)	0.85/0.83[3]	0.73	0.84
Test-retest reliability	0.78/0.84[3]	-	0.54/0.49[4]
Convergent validity (rTNSS)	-0.53/-0.59[3]	-0.73	-0.79
ROC cut-off point	<21	22	20
MID	2.2/2.4[5]	-	2.0/3.8[5]

[1] *Patients >12 years old with allergic or non-allergic rhinitis.*
[2] *Adolescent patients (12-18 years old) with allergic rhinitis.*
[3] *Perennial or seasonal AR, respectively.*
[4] *Physician or patient evaluations, respectively.*
[5] *distribution and anchor-based approaches, respectively.*
Abbreviations: N=number of patients; MID=minimally important differences; ROC= receiver operating characteristic; rTNSS=reflective total nasal symptom score.

Figure 1. Rhinitis control assessment test (RCAT) questionnaire in its original English (left) and Spanish (right) versions.



1. **During the past week, how often did you have nasal congestion?**

Never	Rarely	Sometimes	Often	Extremely often
☐5	☐4	☐3	☐2	☐1

2. **During the past week, how often did you sneeze?**

Never	Rarely	Sometimes	Often	Extremely often
☐5	☐4	☐3	☐2	☐1

3. **During the past week, how often did you have watery eyes?**

Never	Rarely	Sometimes	Often	Extremely often
☐5	☐4	☐3	☐2	☐1

4. **During the past week, to what extent did your nasal or other allergy symptoms interfere with your sleep?**

Not at all	A little	Somewhat	A lot	All the time
☐5	☐4	☐3	☐2	☐1

5. **During the past week, how often did you avoid any activities (for example, visiting a house with a dog or cat, gardening) because of your nasal or other allergy symptoms?**

Never	Rarely	Sometimes	Often	Extremely often
☐5	☐4	☐3	☐2	☐1

6. **During the past week, how well were your nasal or other allergy symptoms controlled?**

Completely	Very	Somewhat	A little	Not at all
☐5	☐4	☐3	☐2	☐1

1. **Durante la última semana, ¿con qué frecuencia ha tenido congestión nasal?**

Nunca	Rara vez	A veces	A menudo	Muy a menudo
☐5	☐4	☐3	☐2	☐1

2. **Durante la última semana, ¿con qué frecuencia ha estornudado?**

Nunca	Rara vez	A veces	A menudo	Muy a menudo
☐5	☐4	☐3	☐2	☐1

3. **Durante la última semana, ¿con qué frecuencia ha tenido los ojos llorosos?**

Nunca	Rara vez	A veces	A menudo	Muy a menudo
☐5	☐4	☐3	☐2	☐1

4. **Durante la última semana, ¿hasta qué punto sus síntomas nasales o los otros síntomas de alergia han interrumpido su sueño?**

En absoluto	Un poco	Algo	Mucho	Constantemente
☐5	☐4	☐3	☐2	☐1

5. **Durante la última semana, ¿con qué frecuencia ha evitado alguna actividad (por ejemplo, ir de visita a una casa donde tienen perros o gatos, cuidar el jardín) a causa de sus síntomas nasales o de los otros síntomas de alergia?**

Nunca	Rara vez	A veces	A menudo	Muy a menudo
☐5	☐4	☐3	☐2	☐1

6. **Durante la última semana, ¿hasta qué punto han estado controlados sus síntomas nasales o los otros síntomas de alergia?**

Completamente	Mucho	Algo	Un poco	En absoluto
☐5	☐4	☐3	☐2	☐1

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Figure 2. Boxplots showing the RCAT questionnaire scores (median, 1st and 3rd interquartil values) according to allergic rhinitis duration (A) and severity (B). The differences are statistically significant (p<0.0001, Tukey test) for both comparisons.

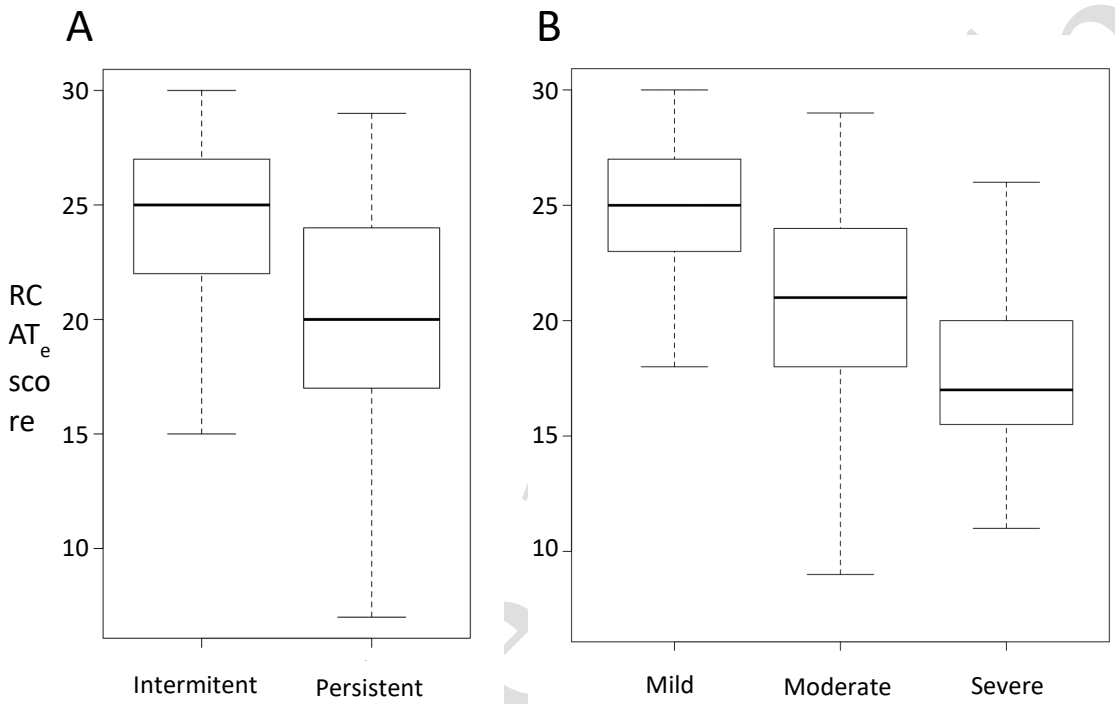
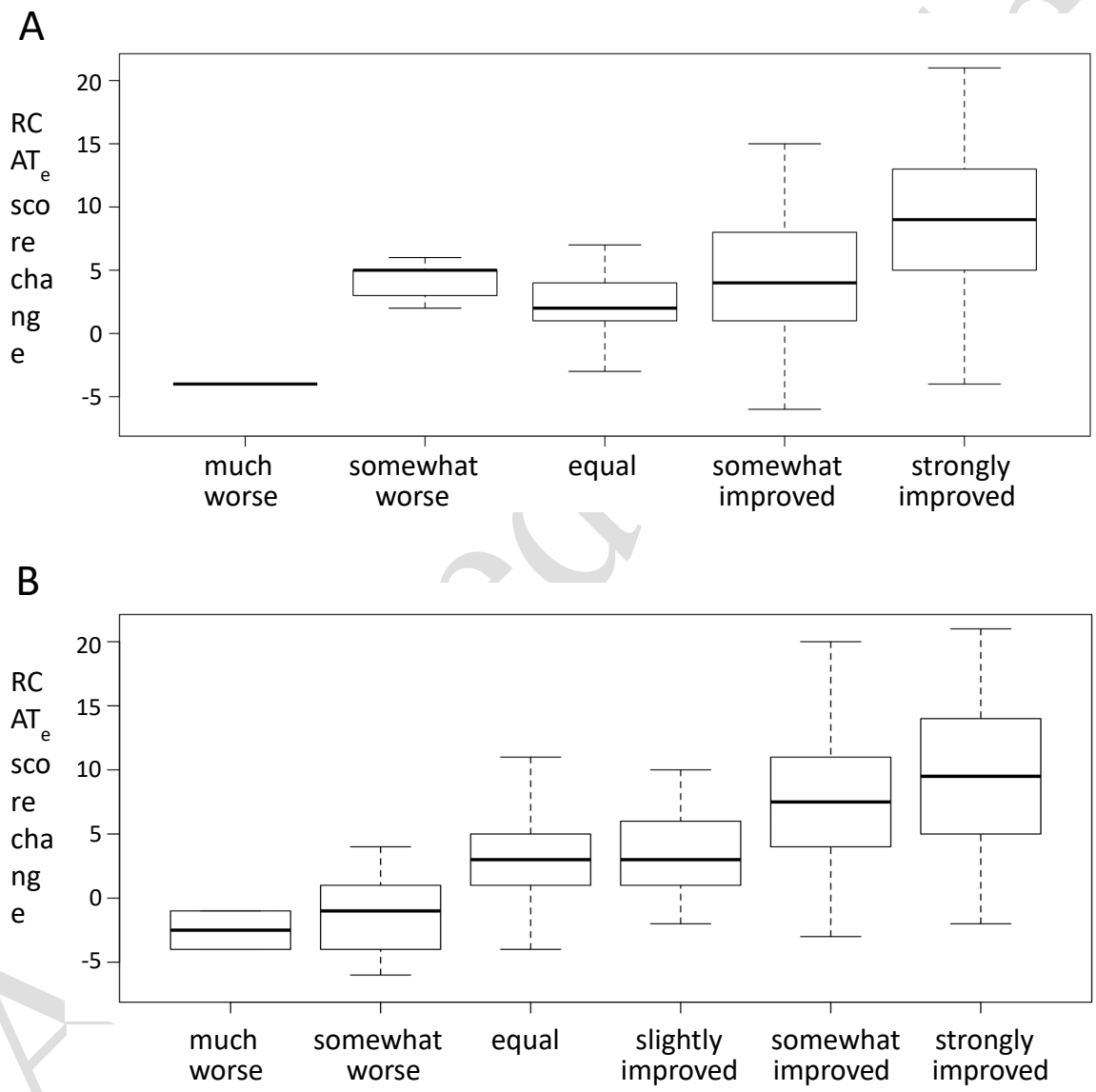


Figure 3. Boxplots showing RCAT questionnaire score changes (median, 1st and 3rd interquartile values) between first and second visit for AR patients, according to the improvement evaluated by the physician (A) or the patient (B). The differences are statistically significant (p<0.0001, Tukey test) for both comparisons.



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