

PROMs. Rasch analysis can be used while developing a measure or to optimize a measure.⁴ Rasch analysis methods provide greater insights into the measurement properties such as precision, unidimensionality, discrimination, fit-statistics, differential item functioning, local item dependency, and targeting.^{4,5} In addition, studies have shown that the sensitivity and precision in QOL measurement are higher when Rasch analysis is used compared with the traditional methods. In summary, PROM research in ocular allergy may benefit from advances in the field. In particular, the application of Rasch analysis may offer sound measures for evaluating the impact of ocular allergy.

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Reply to "Quality-of-life researchers in ocular allergy may benefit from the newer methods"



To the Editor:

We thank Kandel and Watson¹ for their interest in our clinical commentary review² and for taking the time to provide insightful and valuable comments concerning our article.

The reference to the Ocular Surface Disease Index (OSDI)³ and other non-allergy-specific questionnaires is noteworthy. We agree with Kandel and Watson¹ that it is important to note the "usefulness of non-allergy-specific (ophthalmic and generic) patient-reported outcome measures (PROMs)."¹ Indeed, this echoes our review conclusion, which states that there is a "dearth in the literature regarding QoL questionnaires targeting all types of" ocular allergy (OA).² This means that there is an obvious lack

of questionnaires specific to the different presentations and etiologies of OA; hence, clinicians and/or researchers currently refer to non-OA-based questionnaires.

We would, however, like to note that the key purpose of our review was to concentrate solely on identifying the gap in the literature regarding OA-related quality-of-life questionnaires.² This review was not intended to include non-OA-specific questionnaires. Furthermore, it is important to highlight that the OSDI is a questionnaire that has not been validated in OA populations. In fact, the original validation study excluded patients with OA altogether.³ Further to this, another study showed that the OSDI score was not correlated with pollen counts.⁴ Thus, we reiterate, there is an urgent need for further formation of tailor-made questionnaires on OA.

With regard to the scoring of the questionnaires, although summarizing the item scores using mean and SD and using parametric statistical methods is common in the reviewed questionnaires specifically, and in general for other Likert-based questionnaires, we would like to emphasize that, according to the central limit theorem, parametric statistics can be used with Likert data although it is a nonnormal distribution.⁵ Furthermore, parametric models can be applied to Likert-type data with small sample sizes, and/or with unequal variances.⁵

As stated by Kandel and Watson,¹ in parametric models each item does get an equal weight, and each response is equidistant. As such, the use of Item Response Theory (IRT) and Rasch Analysis (RA) is an important alternative to Classical Test Theory (CTT), although the decision about the relevant statistical method should be made on a case-by-case basis.^{6,7} It is important to note that the general differences between the CTT, IRT, and RA are minute.^{6,7} Furthermore, as we indicated in our article,² there are various psychometric measures for different questionnaire validation aspects, which vary depending on relevance. Likewise, this applies to the choice of CTT, IRT, and RA. Regarding the currently available OA questionnaires, the only OA questionnaire that used RA was the ESPRINT-15, which was the Spanish questionnaire that cannot be used until validated in other countries.² Table I summarizes the psychometric processes of the other OA-specific quality-of-life questionnaires. This shows the effectiveness of these questionnaires in the ophthalmology field, until the development of future questionnaires.

Once again, we appreciate the additional information from Kandel and Watson.¹ We would like to add that it is up to the creators of future questionnaires to be up to date with the literature regarding the most appropriate development and validation measures needed when developing a questionnaire. Furthermore, a justification for their choice of measures must be clearly established.

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TABLE I. Psychometric processes of OA questionnaires

OA questionnaire	Item selection and pretesting	Item reduction	Responsiveness	MID	Validity	Reliability
RQLQ (1991)	Items were generated through: 1. The experiences of researchers; 2. A review of generally used QOL measures; 3. Unstructured interviews with patients who had rhinoconjunctivitis. The questionnaire was pretested to identify any problems in the wording and item presentation.	Questionnaires were sent to patients who were asked to: 1. Select which items were the most troublesome as a result of their rhinoconjunctivitis—items selected for the final questionnaire were those most frequently identified as troublesome; 2. Indicate the importance of each item—items selected for the final questionnaire were the most important problems to the patients.	Responsiveness was assessed by administering the questionnaire: 1. At the beginning of the pollen season (when pollen counts were relatively low); 2. At the height of the pollen season (when pollen counts were high); 3. At the end of the pollen season (where pollen counts had decreased, and symptoms were resolving). This assessed the questionnaires' ability to detect small but important changes over time.	Patients (undergoing treatment) in the study responded to 2 sets of data (visit 1-2 and 2-3). They calculated the changes in the questionnaire score between visits and related these to the individual patient's global rating of change score. This detected the smallest change in outcome the patient regarded as important.	Validity of the questionnaire was proven through 3 points: 1. Function deteriorated as pollen counts rose and improved as pollen counts fell; 2. RQLQ dimensions showed changes in parallel with another symptom measure (nasal symptom diary and eye symptom diary); 3. Correlations between changes in RQLQ dimensions and symptom diaries were moderate and strong.	Assessed by the test-retest reliability method.
RQLQ(S) (1999)	Please note, this questionnaire changed the "patient-specific" questions in the original RQLQ to generic questions—it was not the development of a full questionnaire. The 3 generic questions were generated through: 1. Specific activities chosen by patients in previous studies using the RQLQ. These 3 questions were pretested on 10 patients to ensure there was no problem with wording.	The 3 generic questions were formed by grouping multiple answers found in previous RQLQ studies into 1 broad response (eg, social activities—this refers to activities with family and friends, playing with children and pets, sex, and hobbies).	1. The questionnaires were examined to see whether they could detect change in patients with rhinoconjunctivitis between weeks 1 and 5. Patients who had improved or deteriorated by a specific global rating were included. 2. The questionnaires were then assessed on whether they could detect change in patients who had changed and patients who had remained stable using an unpaired <i>t</i> test. 3. Responsiveness index of the questionnaires used in the study was calculated. Differences in this responsiveness index were tested with paired <i>t</i> tests.	The MID was calculated from patients who had a certain global rating of change during the 5-wk period of the study.	Cross-sectional and longitudinal construction validity were evaluated by comparing both RQLQ and RQLQ(S) with other measures of rhinoconjunctivitis severity.	Assessed by test-retest reliability and internal consistency reliability methods.

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TABLE I. (Continued)

OA questionnaire	Item selection and pretesting	Item reduction	Responsiveness	MID	Validity	Reliability
MiniRQLQ (2000)	Please note this questionnaire is a shortened version of the RQLQ. The initial RQLQ had 28 items, and the goal of this questionnaire was to reduce it to half the time and thus, half the number of items. The questionnaire eventually underwent pretesting on 10 patients to assess for wording problems.	The 28 items of the RQLQ were ranked according to the scores made by patients in a number of studies. The top 14 items were selected and examined whether any could be combined. Item-item correlations were calculated using Pearson correlation coefficient for these combinations. After combining the items, the next highest scoring items were added to the questionnaire until there was a total of 14 items. These were then split into domains.	- The questionnaires were examined to see whether they could detect change in patients with rhinoconjunctivitis between weeks 1 and 5. Patients who had improved or deteriorated by a specific global rating were included. - The questionnaires were then assessed on whether they could detect change in patients who had changed and patients who had remained stable using an unpaired <i>t</i> test. - Responsiveness index of the questionnaires used in the study was calculated. Differences in this responsiveness index were tested with paired <i>t</i> tests.	The MID was calculated from patients who had a certain global rating of change during the 5-wk period of the study.	Criterion validity was calculated by comparing the data from the MiniRQLQ with the original RQLQ. Cross-sectional and longitudinal construction validity were evaluated by comparing both RQLQ and RQLQ(S) with other measures of rhinoconjunctivitis severity.	Assessed by test-retest reliability and internal consistency reliability methods.
(N)RQLQ (2003)	Items were generated through: 1. Focus group discussions with patients; 2. A review of the literature and other QOL questionnaires; 3. Discussions with clinicians and previous experience. The questionnaire was pretested on 10 patients to assess for ease and accuracy of understanding.	Questionnaires were sent to patients who were asked to: 1. Select which items were the most troublesome as a result of their nocturnal rhinoconjunctivitis— items selected for the final questionnaire were those most frequently identified as troublesome; 2. Indicate the importance of each item —items selected for the final questionnaire were the most important problems to the patients.	- The questionnaires were examined to see whether they could detect change in patients with rhinoconjunctivitis between weeks 1 and 3. Patients who had improved or deteriorated by a specific global rating were included. - The questionnaires were then assessed on whether they could detect change in patients who had changed and patients who had remained stable using an unpaired <i>t</i> test. - Responsiveness index of the questionnaires used in the study was calculated. Differences in this responsiveness index were tested with paired <i>t</i> tests.	Reliability was determined from patients who remained in a stable clinical state between the initial visit and the end of the first week. This stability was assessed using a standardized MID value.	Cross-sectional construct validity was assessed to check for appropriate correlations between currently validated questionnaires and the (N)RQLQ. Longitudinal construct validity to check for appropriate correlations between changes in the (N) RQLQ and changes in other questionnaires. Like the cross-sectional correlations, a priori prediction was made for expected longitudinal correlations.	Assessed by test-retest reliability method.

AdolRQLQ (1994)	Items were generated through: 1. Unstructured interviews with adolescent patients; 2. A review of the literature; 3. The original RQLQ development; 4. Experience of researchers. Particular care was taken with the wording. The aim was to capture all the important aspects that affect the QOL of adolescents with rhinoconjunctivitis. The questionnaire underwent pretesting to identify problems with the questionnaire.	Questionnaires were sent to patients who were asked to select which items they experienced as a result of their rhinoconjunctivitis and by rating the importance of each item. The mean importance and overall importance were found. Items were chosen on the basis of highest overall importance and other factors.	To assess the responsiveness, a repeated-measures analysis of variance was used in which the factors examined were time, treatment, and the interaction between the 2.	Responsiveness was assessed using the MID.	Construct validity was calculated using the Pearson correlation coefficient.	NA
PRQLQ (1998)	Items were generated through: 1. Item pools from the development of the RQLQ, AdolRQLQ, and PAQLQ; 2. Discussion with children aged 6-12 y with rhinoconjunctivitis; 3. Discussion with clinicians looking after children with rhinoconjunctivitis; 4. A review of the literature on pediatric QOL. The questionnaire underwent pretesting on 10 children to ensure the questionnaire was well understood.	Questionnaires were verbally discussed with patients where they were asked to identify the items that they experienced as a result of their rhinoconjunctivitis and rate the importance of each item. The mean importance score and overall impact score were found and items with the highest impact score were included in the questionnaire.	Responsiveness was examined by assessing whether the PRQLQ could detect change in patients with rhinoconjunctivitis using a paired <i>t</i> test. Then using an unpaired <i>t</i> test, the ability of the instrument to distinguish between individuals who changed and individuals who stayed the same was assessed in terms of change from the beginning of the study to the end of the study.	NA	Cross-sectional construct validity was assessed by correlating QOL scores at second visit with scores from the symptom diary during the previous week. Longitudinal construct validity was assessed by finding appropriate correlations between the PRQLQ and changes in other questionnaires.	Assessed by test-retest reliability method.
EAPIQ (2002)	Items were generated through: 1. Modifying the DEDIQ; 2. Deriving questions from the miniRQLQ. It then underwent pretesting including focus groups to identify issues with the questionnaire.	Items were removed following the validation study, which showed items to be missing or inconsistent.	Preliminary responsiveness of the EAPIQ was assessed by comparing EAPIQ scores in patients who reported a change in their health status over the 2-wk period.	NA	Item convergent validity, item discriminant validity, concurrent validity, known-group validity, and clinical validity were all used to validate the EAPIQ.	Assessed by test-retest reliability and internal consistency reliability methods.

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TABLE 1. (Continued)

OA questionnaire	Item selection and pretesting	Item reduction	Responsiveness	MID	Validity	Reliability
QUICK (2007)	Items were generated through: 1. A review of the literature on QOL and OA; 2. A panel of ophthalmologists and immunologists to assess for VKC; 3. Ten children with VKC in the active phase; 4. Two psychologists with experience in the process of development and validation in QOL questionnaires.	Items that were redundant, ambiguous, difficult to understand, or expressed negatively were removed. Further to this, the remaining items were administered to patients who had to indicate which item they had experienced in the last 2 wk on a scale whereby the highest scoring items were used for the QUICK questionnaire.	NA	NA	Construct validity, specifically convergent validity, was assessed using the Pearson correlation coefficient to evaluate the relationship between another questionnaire and the QUICK questionnaire. Further to this, factorial analysis was performed on the preliminary QUICK questionnaire to identify potential subscales.	Assessed by internal consistency reliability method.

AdoRQLQ, Adolescent Rhinoconjunctivitis Quality of Life Questionnaire; *DEDIQ*, Dry Eye Disease Impact Questionnaire; *EAPIQ*, Eye Allergy Patient Impact Questionnaire; *MiniRQLQ*, Mini Rhinoconjunctivitis Quality of Life Questionnaire; *NA*, not applicable/not assessed; *N/RQLQ*, Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire; *PAQLQ*, Paediatric Asthma Quality of Life Questionnaire; *PROLQ*, Paediatric Rhinoconjunctivitis Quality of Life Questionnaire; *QOL*, quality of life; *QUICK*, Quality of Life in Children with Vernal Keratoconjunctivitis Questionnaire; *RQLQ*, Rhinoconjunctivitis Quality of Life Questionnaire; *RQLQ(S)*, Standardised Rhinoconjunctivitis Quality of Life Questionnaire; *VKC*, Vernal Keratoconjunctivitis.

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Type 2 chronic rhinosinusitis with nasal polyps: From phenotype to endotype



To the Editor:

I read with great interest the report by Bachert et al.¹ The authors reported current knowledge and personal opinions on the efficacy of therapeutic options, such as reboot surgery and biologics targeting type 2 (T2) cytokines in chronic rhinosinusitis with nasal polyps (CRSwNP). Another point the authors mentioned is that CRSwNP endotypes should be defined by clinical signs and/or biomarkers.¹ We thank Bachert et al for their contribution to literature with such a valuable review. We would like to share our opinions on this subject.

We share the same view as the authors. It is very important to associate T2 CRSwNP subendotypes with T2 CRSwNP phenotypes (Figure 1). This will provide cost-effective use of biologics in T2 CRSwNP phenotypes. At this point, because there are no 1-to-1 comparative studies with these biologics, “What should be the most effective biological treatment for the T2 CRSwNP phenotype?” and “Which clinical and biological markers would be useful to select the appropriate biologics for this phenotype?” are remaining questions. To answer these questions, we need to know the subendotype (the dominant pathway of the T2 endotype) of the T2 endotype underlying the T2 CRSwNP phenotype.

T2 CRSwNP endotype presents as T2-biased inflammation. T2 immune responses in CRSwNP are mediated mainly by T_H2 cells, group 2 innate lymphoid cells (ILC2s), local IgE, and profound tissue eosinophilia. ILC2s are known to produce type 2 cytokines, especially IL-5 and IL-13, and T_H2 cells secrete IL-4, IL-5, and IL-13. Both IL-4 and IL-13 induce IgE switching and IgE synthesis by B cells. Although IL-5 is the important driver of blood eosinophilia, IL-13 is strongly associated with airway eosinophilia and periostin. Periostin is a downstream molecule of IL-4 and IL-13, which potentially passes the IL-4 receptor α.²⁻⁴ IL-5 and IL-13 drive many features of the inflammation and eosinophil recruitment that is characteristic of the T2 CRSwNP.²⁻⁵ Patients with a T2 CRSwNP phenotype have higher levels of serum periostin and blood eosinophils.²⁻⁶