

Systematic review: health-related quality of life in children and adults with eosinophilic oesophagitis—struments for measurement and determinant factors

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Summary

Background: Several measures have been used to assess the health-related quality of life (HRQoL) of patients with eosinophilic oesophagitis (EoE).

Aims: To systematically review these HRQoL measures, to appraise measurement properties of specific instruments and to evaluate determinant factors influencing HRQoL in paediatric and adult EoE patients.

Methods: We searched the PubMed, Embase, Scopus, Web of Science (WOS) and PsycINFO databases for documents providing original information on the development of measurement tools and/or evaluation of HRQoL outcomes in EoE patients of all ages.

Results: Of the 596 references identified, data was collected from 34 studies (with only 16 of them being published as full papers) including a total of 1,689 individual patients. Three disease-specific HRQoL measures in EoE covering different aspects of patients' lives and developed in English, were scored positive regarding measurement properties. The PedsQL inventory (including parent and child report forms) and the Peds-QoL EoE module were the generic and specific instruments respectively used in children, while the SF-36 and EoE-QoL-A were the most used questionnaires in adults. Patients with EoE show an impaired HRQoL compared to controls, which greatly depends on symptom severity and disease duration. Severity of endoscopic features and female gender may also determine an impaired HRQoL. The effect of treatments on HRQoL requires further assessment.

Conclusions: HRQoL is a relevant outcome that should be considered in clinical practice and research of EoE. Further validation studies in several languages and populations are required to support the use of disease-specific HRQoL measures.

1 | INTRODUCTION

Eosinophilic oesophagitis (EoE) is a chronic, immune-mediated, inflammatory disorder, defined symptomatically by oesophageal dysfunction and histologically by eosinophil-predominant inflammation of the oesophagus.^{1,2} First, characterised as a distinct clinico-pathologic syndrome two decades ago,³ EoE constitutes currently the most prevalent cause of chronic dysphagia among children and young adults in the developed world, with a prevalence reported to affect up one in 2000 people in these countries.⁴ EoE is considered as a particular form of food allergy,⁵ and food avoidance by dietary exclusion constitutes a main pillar in the treatment,⁶ together with swallowed topic steroids and proton pump inhibitor drugs.²

Living with a food allergy is more difficult than is generally appreciated.⁷ Long-term avoidance of the foods that trigger EoE is able to maintain drug-free disease remission, but in turn it places a psychological burden that can result in stress and anxiety. Therefore, EoE is known to impair health-related quality of life (HRQoL) and to cause a substantial burden to both patients and their families.⁸

Measuring HRQoL provides important insights into patients' perception of their health and the effect of treatments, allowing for the estimation of the impact of the disease from a patient perspective; this is important because it is possible for two individuals with clinically similar disease severity to experience very different degrees of impairment in their everyday lives.⁹ Generic and disease-specific instruments are used to measure HRQoL: The former are aimed at measuring the overall HRQoL of patients across several conditions and are useful to compare HRQoL across different disease states as well as for the evaluation of health economic outcomes. By contrast, the latter assess domains specific to a given disease, being more sensitive to changes in the patient's health state.¹⁰

In the past few years, measurement of HRQoL has been increasingly used in patients with EoE to support both research and clinical care. Generic instruments have given way to the development of disease-specific questionnaires,^{11,12} leading to a better evaluation of patients' health. These measures are considered important outcomes to evaluate the effectiveness of new therapies in clinical trials. An up-to-date systematic review will provide a useful resource for researchers and EoE specialists to ensure they can select an appropriate HRQoL measure for patients in their practice to identify correctable factors determining an impaired perception and to improve treatment outcomes.

The aim of this study was to systematically review the current HRQoL measures for patients with EoE and to appraise their measurement properties using a robust evaluation methodology checklist. We also sought to identify disease-specific determinant factors for HRQoL in children and adults with EoE, and the effect of investigations and interventions for EoE on HRQoL.

2 | MATERIALS AND METHODS

2.1 | Protocol registration

This review has been registered with the international Prospective Register Of Systematic Reviews (PROSPERO: <http://www.crd.york.ac.uk/prosperto/>) (reference CRD42016051181). Information about searches, search strategy, type of studies reviewed, review team, and other kind of data related to the study may be consulted in our brief at PROSPERO. The reporting of this systematic review has been done in accordance with the PRISMA guidelines.¹³

2.2 | Search strategy

A highly sensitive search strategy was designed to identify and retrieve all documents dealing with the relationship between HRQoL and EoE in children and adults, with no restrictions regarding language of publication. Two researchers (AA and AJL) independently systematically screened five major bibliographic databases (PubMed, EMBASE, Scopus, PsycInfo and Web of Science) for the period up to March 2017. A predetermined protocol was used in accordance with the quality standards for reporting meta-analyses of observational studies in epidemiology.¹⁴

The thesauri for MEDLINE (MeSH) and EMBASE (EMTREE) were consulted using the following search strategy: ("eosinophilic esophagitis" OR "eosinophilic oesophagitis" OR "EoE") AND ("quality of life" OR "QoL" OR "life style" or "sickness impact profile" OR "value of life" or "health related quality of life"). As for the SCOPUS, PhycINFO and Web of Science databases, only free text searches with truncations were carried out. Reference lists from all retrieved articles we also examined for additional relevant studies.

2.3 | Inclusion and exclusion criteria

Observational prospective and retrospective case-control studies and case series reporting on the use of generic or disease-specific questionnaires in patients of all ages with EoE were retrieved. Any document relating to the description, development, and/or the validation of the above identified HRQoLs measures were also eligible for inclusion. A diagnosis of EoE was based on oesophageal symptoms plus an oesophageal eosinophilic infiltration ≥ 15 eos/HPF at baseline endoscopy, as reported in source documents.

Excluded studies included reviews, discussion papers, nonresearch letters, and editorials that did not provide original data on the HRQoL status along with clinical guidelines and consensus documents. Studies providing duplicated information (ie, repeated abstracts presented at different congresses or abstracts published later as a full paper) were also excluded. Likewise, subsets of cases or controls from previously published articles by the same authors were also excluded.

2.4 | Study selection

Titles and abstracts of retrieved documents were independently checked by two reviewers (AJL and LA-G) according to our selection criteria and categorised as: included, not included, and unsure. Full text copies of potentially relevant studies were obtained and the reviewers independently assessed each article's eligibility for

inclusion. Any discrepancies were resolved either by consensus or arbitration by a third reviewer (AA).

2.5 | Quality assessment strategy

The measure properties of each specific EoE instrument identified and their performance properties were assessed using the quality properties checklist proposed by Terwee et al.¹⁵ (Table S1). We used Cohen's criteria¹⁶ (Table S2) to determine the level of establishment of each specific HRQoL measure. The Cohen's criteria classify the measures into three levels of establishment depending on the number of publications, the extent to which the measures are described in literature, and their psychometric properties.

In addition, cohort studies, case series and case reports were evaluated for the risk of bias with the aid of the Joanna Briggs Institute (JBI) critical appraisal checklist for Case Control Studies and Case Series¹⁷ (<http://joannabriggs.org/research/critical-appraisal-tools.html>). Studies were considered to be at low risk of bias if most of the bias items could be categorised as low risk. Unclear risk of bias in two or more items increased the degree to moderate. Studies were judged to have a high risk of bias if one of the items was deemed high risk. Two researchers (AJL and LA-G) independently assessed the articles against the defined criteria, and any discrepancies were resolved by consensus and, if necessary, a third reviewer (AA) was consulted.

2.6 | Analysis, data synthesis, and reporting

Data from eligible articles were extracted independently using a pre-prepared data extraction proforma by two reviewers (AJL and LA-G); discrepancies were resolved by discussion or arbitration by a third reviewer (AA). A descriptive summary with data tables was produced to summarise the literature. Quantitative pooling of data was not meaningful in the context of this review so a narrative synthesis of the data was undertaken.

3 | RESULTS

3.1 | Literature search

The search strategy yielded 596 references after removing documents duplicated retrieved in multiple databases; 538 were excluded after examining the title and abstract because they did not fulfil the inclusion criteria. Of the remaining 58 documents retrieved for complete evaluation, 24 were excluded for the following reasons: duplicated abstracts or abstracts previous to full papers (12), lack of information regarding QoL (6) or QoL not structurally assessed (4), subsets of patients included in later papers (1) and no information related with EoE (1). In the end, 34 studies (comprising of 16 full papers^{11,12,18,19,21,22,24-31} and 18 abstracts³²⁻⁴⁹ (one of them later published in full⁵⁰) were included in our systematic review (Figure 1).

Regarding the aims of the retrieved studies, the references retrieved included five papers on specific questionnaire

developments,^{11,12,18,21,22} 1 abstract on item refinement³² and 1 trans-cultural adaptation and validation of a questionnaire.²⁶ In addition, 14 studies assessed HRQoL by generic instruments,^{19,24,25,27,29,33-36,39,49} while 11 documents employed disease-specific scales.^{28,30,31,40-42,44-48} A further study which used a non-structured telephone-based assessment⁴³ to evaluate HRQoL was not included in our systematic review.

The studies dealing with HRQoL in patients with EoE were conducted in the USA (26), Sweden (1), Spain (3), UK (1), Switzerland and USA (1), Australia (1) and The Netherlands (1). Characteristics of the studies included are summarised in Table S3. Overall, data from 1689 individual EoE patients (including 1173 adults and 514 children) were retrieved.

3.2 | Assessing the psychometric properties of EoE specific HRQoL measures

A narrative summary of the included measures and their properties assessment is presented in Table 1. The EoE-QoL-A was the specific questionnaire most widely used to assess HRQoL in EoE.^{11,32} The original paper was published in English and did not report all the psychometric properties, but subsequent translation and validation into Spanish further proved its lack of floor and ceiling effects.²⁶

The NEQoL has been recently developed as a reliable and a valid measure of HRQoL in a large cohort of adult patients with several oesophageal conditions. Half of the patients who met the inclusion criteria and completed the questionnaires during the development and refining phases presented with gastroesophageal reflux disease (GERD), EoE being the second condition in frequency with 24% suffering from it. Contrary to GERD (which mostly manifests with heartburn), most of oesophageal conditions, including EoE, have dysphagia as the clinical hallmark, with no separate analysis been developed among different diagnoses.

Regarding paediatric patients, the Peds-QoL EoE Module generated items that covered various quality of life (QoL) aspects of children with EoE, which can be child self-reported or parent proxy-reported. No version in another language or cultural environment to American English has been currently developed.

Construct validity was appropriately assessed in all measures. The HRQoL measures were compared with the other measures of QoL the respective authors used as gold standards. All scales correctly assessed the test-retest reliability and achieved the required values of the intraclass correlation coefficient, Sperman Rho or Kappa coefficients. Three of four HRQoL measures had their responsiveness assessed in the original study report. Measurement error evaluation was not assessed for most of the measures (Table 2).

According to Cohen's criteria to appraise the degree of establishment for the different HRQoL measures in EoE, only the EoE-QoL-A (refined version with 30 items) was considered to be a well-established measure, because it is the only one that has been validated in a different language to the original. The remaining were rated as promising assessments, but validated versions adapted to other languages apart from English are still not available (Table 2).

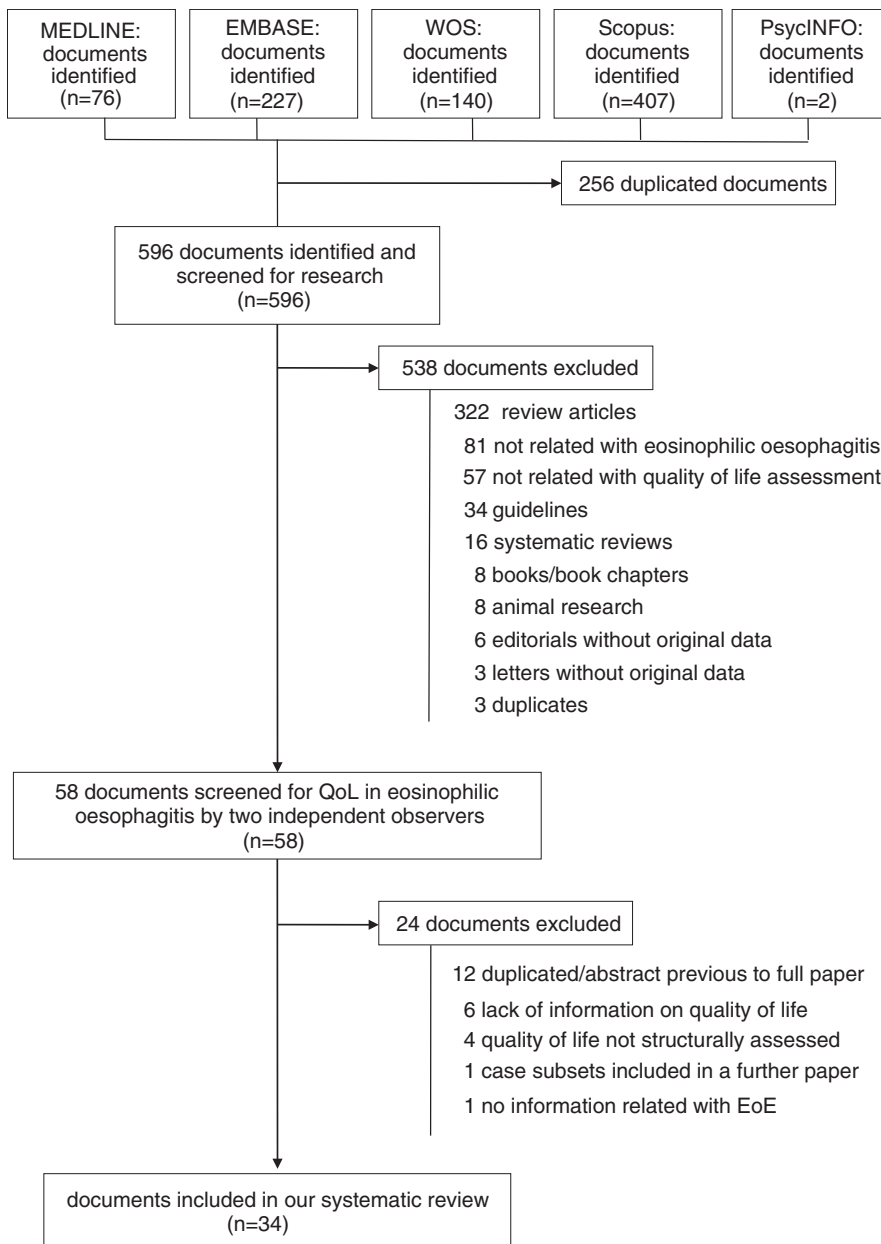


FIGURE 1 Flow chart for the process of identifying studies that were included in and excluded from the systematic review

All the 28 documents reporting observational studies on the evaluation of HRQoL in patients with EoE, the changes induced by interventions and determinant factors, and the assessment for risk of bias, are shown in Table S4.

3.3 | Assessment of HRQoL in children with EoE and determinant factors

3.3.1 | Generic HRQoL instruments for children with EoE

Five studies, overall including 154 children and adolescents with EoE,^{19,24,40,41,49} used the generic PedsQL inventory (parent and child report forms), to capture HRQoL perception. The PedQL is a brief (23 items), practical (less than 4 minutes to complete), flexible (designed for use with children in the community, school and clinic) and

appropriate for ages between 2 and 18 year old questionnaire, developed by Varni et al.⁵¹

According to available studies, EoE significantly impairs HRQoL of affected children and adolescents, which manifests in the normal development of their daily activities, their physical health and their mental status. Thus, children and adolescents with EoE (and other eosinophilic gastrointestinal disorders) missed significantly more school days in the past month (mean 4.9 vs 0.5) and year (23.2 vs 2.8) than healthy controls, and were more likely to have received mental health services (47.2% vs 14.6%) and medication for mental needs than controls (24.2% vs 7.3%).¹⁹ In addition, children with EoE sleep less hours (up to 22.2%) and have a poorer quality of sleep, so they are awake more frequently than healthy controls, with a trend towards sleep disturbance and poorer QoL.⁴¹

TABLE 1 Summary of the specific HRQoL questionnaires in EoE, their measurement properties¹⁶ and level of credibility (Cohen criteria)

HRQoL measures	References	Year	Domains covered	Items (number)
EoE-QoL-A	11	2011	Disease-specific HRQoL measure. It includes 5 domains: Eating/diet impact, Social impact, Emotional impact, Disease anxiety and Choking anxiety.	37
EoE-QoL-A (refined version)	31	2012	A shorter version of EoE-QoL -37 items. Disease-specific HRQoL measure. It includes 5 domains: Eating/diet impact, Social impact, Emotional impact, Disease anxiety and Choking anxiety.	30
NEQoL scale	18	2016	A specific HRQoL measure developed to be used across several oesophageal conditions. It includes 5 domains: Social function, Emotional distress, Eating impact, Sleep, and Financial burden	14
Peds-QoL EoE Module	21, 18	2013	A specific HRQoL measure developed to be used in children with EoE; The questionnaire, which can be child self-reported or parent proxy-reported, covers 7 domains: Symptoms I, Symptoms II, Treatment, Worry, Communication, Food and eating, and Food feelings.	33

Interestingly, mean scores given by children themselves and their parents in the specific modules of the PedsQL questionnaire do not coincide,¹⁹ with the parents generally underestimating the impact of the disease regarding children declared HRQoL³⁹ to the point that mean QoL parent form scores were not significantly different from that found in healthy controls.⁴⁹

TABLE 2 The measurement properties of the specific HRQoL questionnaires used in EoE,¹⁶ and level of credibility (Cohen criteria)

HRQoL measures	Internal consistency	Test-retest reliability	Measurement error	Content validity	Factor analysis	Construct validity	Responsiveness	Ceiling and floor effects
EoE-QoL-A	+/III	+/III	?	+/I	+/I	+/I	+/I	?
EoE-QoL-A (refined version)	+/I	+/I	?	+/I	+/I	+/I	+/I	+/II
NEQoL scale	+/II	+/II	?	+/III	+/III	+/III	?	+/III
Peds-QoL EoE Module	+/III	+/III	?	+/III	+/III	+/III	+/III	+/III

?: No information available.

Regarding determinant factors, age was not associated with HRQoL in either parent-reported or child-reported PedsQL forms. However, the "Family Impact" domain improved with patients' age.²⁴ Number and severity of symptoms negatively correlated with child-reported and Parent proxy-reported PedsQL score and family impact score. A certain "tolerance" or "adaptation" to a long-lasting disease can be recognised in paediatric EoE because PedsQL parent proxy-reported total and psychosocial functioning scores increased significantly over time, but the magnitude of the increase was small.²⁴

Apart from EoE and specific symptoms, other factors that impaired QoL perception in children, as captured with generic instruments, were prematurity, GERD symptoms, oesophageal strictures and a higher eosinophil density in oesophageal biopsies.

The effect of treatment in HRQoL in children has been limitedly assessed: Patients on active EoE treatment showed better QoL levels than those with nontreated disease in a short case series from Australia,³⁹ which contrasts with results of a large prospective American research, which found that treatment did not modify PedsQL scores at baseline, but family impact impaired with dietary restrictions.²⁴ Assessing the type of therapy prescribed, as well as its effectiveness in achieving and maintaining disease remission is, thus, essential to understand the effect of therapy in EoE. In this sense, a "good" QoL was found to be associated with increasing rates of gastrotomy, an invasive technique used to administer elemental formulas in younger children with EoE (which have been demonstrated as the most effective therapy to induce histological remission of EoE⁶) and to guarantee maintenance of nutritional status.

3.3.2 | Specific HRQoL instruments in paediatric EoE

At the present, only a single case report⁴² and a prospective series of 44 children and adolescents⁴⁰ (both documents published as abstracts, apart from those to develop the questionnaire,^{12,21,22} have used the Peds-QoL EoE module in series of children and adolescents with the disease. The first case report failed to demonstrate an impaired QoL (in both the physical and social functioning) in the patient. The second one aimed to compare HRQoL in children undergoing treatment with swallowed fluticasone propionate to those submitted to cow's milk elimination diet. After 6-8 weeks of therapy, peak eosinophil counts in oesophageal biopsies decreased below 15 eosinophils per HPF in 80% and 64% of patients treated

with fluticasone and cow's milk elimination respectively. QoL levels improved regarding the baseline in both groups of patients, in parallel to an improvement in symptoms scores.⁴⁰

3.3.3 | Generic HRQoL instruments for adults with EoE

Eight studies in literature have assessed HRQoL levels in adults with EoE using the generic measures Medical Outcome Study Sort Form (SF)-36^{25,29,30,34,35} and its abbreviated version SF-12.³⁶ Two additional studies^{27,33} used the Gastrointestinal Quality of Life Index⁵² and the Patient Assessment of Upper Gastrointestinal Disorders-Quality of Life (PAGI-QoL)⁵³ questionnaires, that were developed to assess QoL in dyspepsia, GERD and gastroparesis, among other conditions. A questionnaire validated to measure QoL in patients with oesophageal cancer⁵⁴ has been also applied to adults with EoE.²⁵

Conflicting results have been obtained when generic instruments were applied to measure HRQoL in adults with EoE. Some studies only available as abstracts found no significant differences in QoL levels in EoE compared to GERD patients and control subjects.^{33,34} In contrast, decreased levels of SF-36 vitality and general health domains of QoL were shown in EoE patients compared to the general population according to a full paper research.²⁹ Disease duration was identified as a risk factor for a low mental component summary (OR=1.064; 95%CI: 1.003-1.128; *P*=.038). An additional published research showed EoE to impact on a number of important domains including frustration, embarrassment, fear about the disease outcomes, in other research: as a result, mental health function in EoE patients was reported similar to that in patients with other chronic illnesses, while a significantly better physical health was described.³⁶

Patient gender and age has been limitedly assessed in research using SF-36 measures, with female patients showing a significantly impaired QoL in some²⁹ but not other studies,³⁵ as well as younger adults.²⁹

The effect of therapy on patients' QoL also shows conflicting results: Swedish adult patients treated with swallowed topic steroids (aerosolised mometasone furoate orally applied) showed absence of changes in SF-36 scores despite improvement in symptoms of dysphagia and choking during the period of treatment.²⁵ In contrast, a mild but nonsignificant increase in mean physical component and mental component scores were observed after a four food elimination diet-based therapy in a series of 13 American adult patients,³⁴ despite symptomatic improvement. The effect of dietary restriction of HRQoL perception of patients should be also considered, since PAGI-QoL scores were significantly lower in EoE patients on food restrictions, with no correlation found between QoL and symptoms, as measured with the MDQ-30 questionnaire.²⁷

3.3.4 | EoE disease-specific HRQoL for adults

The EoE-QoL-A specific questionnaire to measure QoL in adults with EoE has been used in 10 documents (seven of them only published as abstracts), which included patients from the USA,^{37,44-47}

Switzerland and USA,²⁸ UK³⁰ and Spain,³¹ the last document including over 170 patients and performing multivariate regression analyses to identify determinant factors.

Contrary to results found with generic instruments, measuring HRQoL with the disease-specific questionnaire demonstrates a significantly impaired perception of QoL in adult patients compared to controls; HRQoL levels may predict healthcare utilisation amongst these patients, and patients with a poorer QoL report more outpatient appointments, endoscopies and take more medication than those with a better perception.⁴⁴ A poorer QoL in adult patients with EoE was associated with perceived stigma.^{47,48}

All of the papers coincide in showing that symptom severity is a major determinant of HRQoL in adult with EoE: EoE-QoL-A scores negatively correlated with dysphagia severity^{28,30} and with disease duration.³¹ Dysphagia specifically impacted on mental health components of QoL, with a minor influence on physical health perception.³⁰

Not only the severity of symptoms overall (determined with the validated EEsAI instrument⁵⁵), but also the type of manifestation of the disease, influenced the perception of QoL, with recurrent food impaction and regurgitation identified as significant determinants.³¹ As previously shown in the strongest research with the SF-36 generic instrument,²⁹ female gender negatively influenced QoL scores when it was specifically assessed.³¹ Disease activity, as expressed by endoscopic findings, was also a significant determinant of QoL.²⁸ A higher educational level (defined as high school and university, as compared to primary school) was also found to be a strong determinant for a worse QoL.³¹

The differential effects of treatment modalities of EoE on patients' QoL has been also analysed in recent research: No significant differences in the overall mean QoL score were found in adult patients managed with dietary or pharmacological therapy,³¹ with specific treatment modalities having a negligible influence on overall EoE-specific QoL.²⁸ Dietary treatment had a limited impact on HRQoL of patients with eosinophilic gastrointestinal disorders.⁴⁵ Information regarding the effect of adherence to treatment on HRQoL has been exclusively assessed in a preliminary research that found no association with depression or anxiety in adult patients.⁴⁶

Several determinants have shown differential influences on the five dimensions that integrate the EoE-QoL-A score: Thus, symptom scores determined with the specific EEsAI instrument exerted an increased impact on swallowing anxiety and emotional impact subscales, with a minor role in disease anxiety.²⁸ Emotional impact was the only dimension with a significantly worse score in patients under dietary restrictions.³¹

4 | DISCUSSION

The present systematic review of 34 observational studies have analysed for the first time in literature HRQoL perception, measures and determinants in patients of all ages with EoE. To this end, data was retrieved from 1689 individual patients with EoE, including adults and children, who had their QoL measured for several

purposes, from assessing the impact of the disease on this relevant patient-reported outcome, for developing disease-specific questionnaires, to define the determinant factors which influence patients' perceptions.

HRQoL constitutes one of the most important primary patient reported outcome measures for assessing an individual's burden of any given chronic condition, providing valuable information for developing strategies to promote the greatest possible well-being as well as optimisation of health care resources.⁵⁶ However, the interest on how EoE impacts on QoL of sufferers has been relatively recent, with the first research focussed on assessing this topic published as an abstract only in 2009.³⁵ Most of the research carried out on HRQoL in EoE has been published in the last 3 years, in parallel to the development of disease-specific measure instruments.^{11,12}

Some important facts can be inferred from our systematic review: First, HRQoL in EoE has represented a research topic of limited interests, with a reduced scientific production compared to other topics in this disease. Thus, only 16 full papers (which represent 0.8% of the overall publications dealing with EoE indexed in PubMed) have HRQoL as the main research topic. Second, most of this research has been developed by well recognised groups from the USA, involving adults and paediatric patients, who were also responsible for developing and releasing the new disease-specific instruments to measure HRQoL in EoE,^{11,22,24} with further European groups being involved in recent years.^{25,28,30,31} However, a majority of studies in the topic are exclusively available as abstracts presented in congresses. Third, none of the multiple randomised controlled trials published until now that assessed the efficacy of therapy in EoE have considered improvements in QoL as a relevant study outcome, which contrasts with the central importance granted to HRQoL in other chronic digestive diseases.^{20,57,58} Finally, validated versions of the specific questionnaires to measure HRQoL in other languages to English have not been developed yet (except for a Spanish version of the EoE-QoL-A questionnaire²⁶), which limits the level of credibility of such instruments, according to Cohen's criteria.¹⁶

We identified three different HRQoL-specific measures used for patients with EoE.^{11,12,18,32} We assessed the internal consistency, reliability, measurement error, content validity, factor analysis, construct validity, responsiveness, and ceiling and flooring effects,¹⁵ depending on the information obtained from the literature. All the HRQoL measures had some aspects of psychometric strength, especially construct validity. However, they varied in terms of measurement error and responsiveness.

Some of the most noticeable findings of our systematic review of the literature, differences in HRQoL levels were found when measured with generic or disease-specific instruments, and when children and adult populations were considered. Thus, the generic PedsQL form concurrently demonstrated a significantly impaired HRQoL in children and adolescents,^{19,24,39,41} with a trend by parents-proxy responses to underestimate the deleterious effects of the disease on their children's HRQoL.⁴⁹ Family perceptions on QoL

impaired with dietary restrictions, but the control of symptoms increased the scores provided by children. Regarding adults the disease-specific EoE-QoL-A resulted in a more sensitive than the generic SF-36 scale in demonstrating that EoE impacts negatively on patients' QoL perceptions and also in showing female gender associated with an impaired HRQoL score.^{29,31,35} However, the previous conclusion should be taken with care due to the limited number of studies available and the high risk of bias that could not have been excluded from some of them.

However, data from literature agree in identifying severity of oesophageal symptoms,^{24,28,30,31,39} and disease duration^{24,29,31,38} as major determinants of HRQoL in patients with EoE of all ages. Food impaction was recognised as the symptom with the highest effect in impairing several dimensions of the EoE-QoL-A score in one study,³¹ which may be influenced by the biological activity of the disease as determined by the severity of endoscopic features,²⁸ including the presence of oesophageal strictures at diagnosis.³⁷ A trend towards improvement of symptoms after treatment was found in some papers with a low risk of bias,^{25,31} with others presented as abstracts failing to demonstrate such improvement.^{34,35} A cause of the underlying discrepancy is the fact that response to treatment was not assessed in such studies, so it is possible that clinico-histological improvement induced by dietary treatment could compensate for the potentially detrimental effects of food restrictions on overall patient-reported HRQoL scores. Further studies should assess this hypothesis.

Finally, our systematic review has underlined the fact that an impaired QoL in patients with EoE is also associated with a significant impact on social, psychological and physical aspects of patients with eosinophilic gastrointestinal disorders including EoE: Thus, children and adolescents missed significantly more school days than healthy controls, and were more likely to have received mental health services and medication for mental needs.¹⁹ In adults, a low QoL predicted an increased utilisation of healthcare services, more outpatient appointments and endoscopic exams, and taking more medication than controls.⁴⁴

One of the major strengths of the present study is our search strategy, which entailed an exhaustive literature search in five major databases, which also retrieved the abstract indices of the principal allergy and gastroenterology congresses, with no language restrictions. Moreover, recovered studies were critically appraised according to their methodological aspects, and different researchers independently extracted the data from the studies included. We are thus confident that the 34 documents retrieved represent all the relevant information available on this topic.

Still, several limitations should be noted for a better interpretation of our results. To begin with, the quality of the available evidence on the HRQoL expressed by patients with EoE and their determinant factors was only moderate or low in half of the documents, with a high proportion of the retrieved studies having been exclusively published as abstracts.

To our knowledge, this is the first review of HRQoL measures in EoE that systematically appraised the measurement properties and

the methodological quality of the HRQoL measures using a robust and standardised approach. Furthermore, we summarised the results of the relevant studies on this topic, after a critical appraisal using standardised tools. This review will contribute to better guidance of measuring HRQoL in various clinical and research settings. Also, it will help clinicians, researchers, and the general population to better understand the impact of EoE on the well-being perception of patients, promoting the further translation and validation of the measure instruments to other languages and socio-cultural environments and the use of changes in HRQoL as a relevant outcome in further clinical trials.

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AUTHORSHIP

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SUPPORTING INFORMATION

Additional Supporting Information will be found online in the supporting information tab for this article.

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