Expert Review of Gastroenterology & Hepatology

ISSN: 1747-4124 (Print) 1747-4132 (Online) Journal homepage: http://www.tandfonline.com/loi/ierh20

Quality assessment of clinical practice guidelines for eosinophilic esophagitis using the AGREE II instrument

Alfredo J. Lucendo, Ángel Arias, Olga Redondo-González & Javier Molina-Infante

To cite this article: Alfredo J. Lucendo, Ángel Arias, Olga Redondo-González & Javier Molina-Infante (2017) Quality assessment of clinical practice guidelines for eosinophilic esophagitis using the AGREE II instrument, Expert Review of Gastroenterology & Hepatology, 11:4, 383-390, DOI: 10.1080/17474124.2017.1285696

To link to this article: https://doi.org/10.1080/17474124.2017.1285696

EXPERT REVIEW OF GASTROENTEROLOGY & HEPATOLOGY, 2017
VOL. 11, NO. 4, 383–390
http://dx.doi.org/10.1080/17474124.2017.1285696

Taylor & Francis
Taylor & Francis Group

ORIGINAL RESEARCH

Quality assessment of clinical practice guidelines for eosinophilic esophagitis using the AGREE II instrument

Alfredo J. Lucendo [a,b], Ángel Arias [b,c], Olga Redondo-González [c] and Javier Molina-Infante[b,d]

[a]Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso, Spain; [b]Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain; [c]Research Support Unit, Hospital General La Mancha-Centro, Alcázar de San Juan, Spain; [d]Department of Gastroenterology, Hospital San Pedro de Alcántara, Cáceres, Spain

ABSTRACT

Background: High-quality evidence-based clinical practice guidelines can guide diagnosis and treatment to optimize outcomes. We aimed to systematically review the quality of international guidelines on eosinophilic esophagitis (EoE).

Methods: MEDLINE and Scopus databases were searched for appropriate guidelines up to 2016. Two gastroenterologists and two methodologists independently evaluated the documents using the Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument.

Results: Amongst the 25 records initially retrieved, four guidelines developed by recognized scientific organizations met inclusion criteria. AGREE II results varied widely across domains, but none achieved an overall assessment score of over 60%. Scope and purpose (61.82 ± 19.24%), clarity of presentation (57.13 ± 40.56%) and editorial independence (93.75 ± 1.69%) showed the highest mean rating, whereas stakeholder involvement (28.82 ± 11.19%), rigor of development (32.29 ± 12.02%) and applicability (21.62 ± 7.14%) did not reach quality thresholds. Intraclass correlation coefficients for agreement was excellent among appraisers (0.903), between gastroenterologists and methodologists (0.878) and for each individual guideline (0.838 to 0.955).

Conclusion: Clinical practice guidelines for EoE vary significantly in quality, are invariably limited and currently, none can be 'strongly recommended'.

ARTICLE HISTORY
Received 30 September 2016
Accepted 19 January 2017

KEYWORDS
Eosinophilic esophagitis; food allergy; quality; recommendation; guidelines

1. Introduction

Eosinophilic esophagitis (EoE) represents a chronic inflammatory esophageal disease, characterized clinically by a variety of symptoms related to esophageal dysfunction and histologically by an eosinophil-predominant infiltration of the esophageal mucosa [1,2]. From the initial description of the disease in the early 1990s by two independent groups of researchers [3,4], the incidence and prevalence of EoE have risen sharply, currently affecting up to 1 in 2000 inhabitants in Europe and North America [5]. As a result, EoE represents the most common cause of dysphagia and food impaction among children and young adults, and the second leading cause of chronic esophagitis after gastroesophageal reflux disease (GERD) [6]. Despite not been associated to mortality or malignancy risk, the chronicity of the disease and its progressive behavior [7] negatively impact on patients' quality of life [8].

The adequate management of EoE is challenging because of its only recent recognition, the variable presentation of symptoms in children and adults [6,9], its conflicting relationship with GERD [10], the relative lack of evidence-based approaches to therapy [11], and uncertainties about its long-term effects. Considering the aforementioned issues, a number of organizations have addressed the problem by developing and publishing relevant consensus documents and clinical practice guidelines (CPGs) [1,12–14]. CPGs are defined as 'statements that include recommendations, intended to optimize patient care, that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options' [15]. CPGs are thus disseminated to promote excellence delivered by health-care providers, helping practitioners and sometimes also patients to make decisions about appropriate health care for specific clinical circumstances. For this reason, CPG should involve all the relevant stakeholders who participate in the management of a disease, in order to design documents able to provide specific recommendations for clinical practice, reduce inadequate variations, optimize results, minimize risk, and promote cost-effective practice [16].

The potential for CPG to improve the use of resources and patient care largely depends on the rigor of their development, dissemination, and implementation strategies [17]. Several studies have demonstrated the modest quality and wide heterogeneity that exists between different guidelines [18–20], which mainly derives from the lack of rigorous methods applied in guideline development. Therefore, a highly methodological quality development process for CPG is encouraged in order to provide relevant and appropriate recommendations.

CONTACT Alfredo J. Lucendo ajlucendo@hotmail.com Department of Gastroenterology, Hospital General de Tomelloso, Servicio de Salud de Castilla-La Mancha, Vereda de Socuéllamos, s/n, Tomelloso 13700, Spain

Supplemental data for this article can be accessed here

To ensure their quality, tools to assess the process of guideline development and reporting have been proposed [21], the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument being the most widely used of these. Initially developed by an international group of researchers from 13 countries in 2003 [22], it was updated in 2009 to AGREE II [23]. These criteria mainly concern methods used for developing CPG and reporting quality [24].

The aim of the present study was to assess the quality, methodological rigor, and transparency of CPG for the management (including diagnosis and treatment) of EoE up to August 2016, using the AGREE II instrument. This review was initiated as a part of the development of the pending European Guidelines for the diagnosis and management of EoE in children and adults, within the United European Gastroenterology Link Award program 'Harmonizing diagnosis and therapy of EoE across Europe.'

2. Methods

2.1. Search strategy

A search in PubMed and Scopus electronic databases was independently performed by AJL and AA, searched from inception to 5 August 2016 using the combination of MeSH terms 'eosinophilic esophagitis' or 'eosinophilic oesophagitis' with 'guideline' or 'recommendation*' or 'guideline' or 'practice guideline*' or 'guidance' or 'consensus development conference.' In addition, reference lists for all relevant guidelines were manually scanned.

2.2. Inclusion and exclusion criteria

CPG guidelines that provided clinical practice recommendations for EoE patients were eligible for inclusion. Single-author documents and any publications such as summaries developed from CPGs as well as their translations were excluded.

2.3. Data extraction and quality assessment

The full texts of all of the retrieved documents were critically reviewed according to the predefined criteria. From each guide, the title, first author name, publication year, developer society, methods (evidence-based, literature review, or expert consensus), health question, target population, definition of EoE, number of references, conflict of interest, and funding were extracted. Following the recommendations of the AGREE II consortium, which recommends that for each guideline appraisal at least 2 and preferably 4 appraisers are involved, all the authors independently assessed the methodology of each guideline using the AGREE II instrument, after undergoing training from the online AGREE II tutorial and practice exercise, available at www.agreetrust.org. Two of the reviewers were gastroenterologists largely experienced in EoE, and the two other methodologists skilled in critical appraisal of the literature.

The AGREE II instrument is comprised of 23 key items organized into six domains: (1) scope and purpose, (2) stakeholder involvement, (3) rigor of development, (4) clarity and presentation, (5) applicability, and (6) editorial independence. Each item is rated on a 7-point Likert scale ranging from 'strongly agree' to 'strongly disagree' (Supplemental Table 1). There are two additional assessment items (overall guideline assessment) pertaining to an overall judgment of the guideline: one is, again, rated using a 7-point Likert scale, and the other is a question as to whether the guideline should be used, with or without modifications, or should not be used at all.

For each domain, the scores were added up and calculated as a percentage of the maximum possible score for that domain using the formula provided by the AGREE II consortium: [(score obtained – minimum possible score)/(maximum possible score – minimum possible score)] × 100. The possible standardized scores range from 0% to 100%.

Although AGREE II does not provide a minimum or maximum range for domain score quality to differentiate high- and low-quality CPG, the following method used in previous studies was applied: a guideline was 'strongly recommended' if five to six domain scores were ≥50%; 'recommended' if three to four main domain scores were ≥50%; 'weakly recommended' if one to two domain scores were ≥50%; 'not recommended' if all item scores were <50% [25,26].

2.4. Statistical analysis

Descriptive statistics were used to describe the basic features of the data in each study. Unless otherwise specified, continuous nonparametric data were presented as a median followed by range, and parametric data were presented as a mean ± standard deviation (SD). To assess inter-rater reliability within each domain, the intraclass correlation coefficient (ICC) was calculated, the values of it were interpreted according to the Landis and Koch criteria [27,28]. SPSS v18.0 (SPSS Inc., Chicago, IL, USA) statistical software was used for all calculations.

3. Results

A total of 25 records were identified through an electronic search, of which 4 were single-authored documents, and 6 additional ones were CGP not dealing with EoE. Six were original papers or case reports; three review papers and a systematic review were also excluded, as well as two survey-based papers. Finally, four CPGs were included in the systematic analysis using the AGREE II instrument [1,12–14].

3.1. Characteristics of eligible guidelines

The characteristics of the included CPGs are summarized in Table 1. All four guidelines, published between 2007 and 2014 (after the publication of the AGREE instruments from 2003), were developed using specialized associations or scientific societies; three of them under the support of North American organizations and intended for both children and adult patients, and the remaining sponsored by the European Pediatric Gastroenterological Society. Expert consensus was used as a method to provide recommendations in all cases; a systematic literature search was specifically used in two guides [1,12] (Table 1).

Table 1. Characteristics of eligible clinical practice guidelines for eosinophilic esophagitis.

Authors	Publication time	Region	Developer	Publication type	Development methods	Health question	Intended population	Definition of EoE considered	Number of references
Furuta et al.	2007	USA	AGA, NASPGHAN	Consensus	Systematic review and expert consensus	Diagnosis and treatment	Children and adults	Primary clinicopathologic esophageal disorder, characterized by esophageal and/or upper gastrointestinal tract symptoms in association with esophageal mucosal biopsy specimens containing ≥15 intraepithelial eosinophils/high power field in one or more biopsy specimens, plus absence of pathologic GERD as evidenced by a normal pH monitoring study of the distal esophagus or lack of response to high-dose PPI medication	121
Liacouras et al.	2011	USA	AAAI, AGA, NASPGHAN	Consensus	Systematic review and expert consensus	Diagnosis and treatment	Children and adults	A chronic, immune/antigen-mediated esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil predominant inflammation	171
Dellon et al.	2013	USA	ACG	Consensus	Exper t consensus	Diagnosis, and treatment	Children and adults	A clinicopathologic disorder diagnosed by clinicians taking into consideration both clinical and pathologic information, and defined by: symptoms related to esophageal dysfunction, eosinophil-predominant inflammation on esophageal biopsy, mucosal eosinophilia is isolated to the esophagus and persists after a PPI trial. Secondary causes of esophageal eosinophilia excluded	121
Papadopoulo et al	2014	Europe	ESPGHAN	Guidelines	Expert consensus	Diagnosis and treatment	Children	Not provided	100

EoE: eosinophilic esophagitis; AGA: American Gastroenterology Association; NASPGHAN: North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition; GERD: gastroesophageal reflux disease; AAAAI: American Academy of Allergy, Asthma & Immunology; ACG: American College of Gastroenterology; ESPGHAN: European Society of Pediatric Gastroenterology, Hepatology and Nutrition; PPI: proton pump inhibitor.

3.2. Domain scores

a. Domain 1: Scope and purpose. Aspects related to the overall objective(s) of the guideline and a detailed description of the health questions covered by the guideline should be described in detail. The overall mean ± SD score for the scope and purpose domain was 61.82 ± 19.24% (median 65.97%; range: 36.11%–79.17%). One guide received a score below 50% [13], due to a lack of proper reporting. The overall inter-rater agreement for Domain 1 as determined by the ICC was 0.814 (excellent).
b. Domain 2: Stakeholder involvement item refers to the professionals who were involved at some stage of the development process, excluding external reviewers. The target users should be clearly defined; experiences and expectations of health care from target population should inform the development of a guide. For this domain, the mean ± SD score was 28.82 ± 11.19% (median 30.56; range: 13.89%–40.28%). None of the guides achieved a score over 50% due to the absence of patients' involvement in the development process and under-representativeness of some relevant health professionals [13, 14]. Inter-reviewer agreement (as determined by an ICC of 0.908) concluded excellent.
c. Domain 3: Rigor of development includes the use of systematic methods to search the evidence, explicitly described criteria and reasons for including and excluding evidence, strengths and limitations of the evidence provided, information on methods used to formulate the recommendations and how final decisions were arrived at, considering health benefits, side effects, and risks when formulating the recommendations, explicit links between recommendations given and the supporting evidence, the external review of the guide, as well as providing a procedure to update the guide. As for 'rigor of development,' no clinical practice guide on EoE achieved a score ≥50%, the overall score in this domain being poor, with a mean ± SD of 32.29 ± 12.02% (median 34.64; range 15.63–44.27%). Specifically, only two guides described systematic methods for searching and selecting evidence [1,12], and no guides were externally reviewed. Only one guide referred to the Grading of Recommendations Assessment, Development and Evaluation system to assess the strength of recommendations and the level of evidence [13]. Reviewers' agreement similarly concluded excellent (ICC being 0.862).
d. Domain 4: Clarity of presentation assesses whether recommendations are specific and unambiguous, a clear presentation of all the possible options to manage the disease, and key recommendation easily identifiable. In this domain, all the four guidelines on EoE scored ≥50%. The mean ± SD for the overall quality score for this domain was 57.13 ± 40.56% (median 65.28; range 62.50–97.22%). A moderate-to-good ICC of 0.693 was found.
e. Domain 5: Applicability assessment includes the description of existing facilitators and barriers that will impact on the application of guideline recommendations, advise, and/or tools on how the recommendation can be put into practice, plans to disseminate and implement the guide with additional materials, the identification of additional resources in order to be applied, and the description of guide monitoring or auditing criteria. No current guide scored over 50% in this domain, the mean ± SD for the overall quality score being 21.62 ± 7.14% (median 23.44; range 11.46–28.13%). The inter-rater agreement was only moderate, with an ICC of 0.507.
f. Domain 6: Editorial independence is evaluated by assessing explicit statements that the views or interests of the funding body have not influenced the final recommendations. Competing interests of guideline development group members have to be recorded and addressed. The overall score for this domain was high, with a mean ± SD of 93.75 ± 1.69% (median 93.75; range 91.67–95.83%). A moderate-to-good inter-rater agreement was found from an ICC of 0.686.

3.3. AGREE II overall quality scores

Of the four included guidelines, one was considered of suboptimal quality by reviewers [14]; none of the currently available guides on EoE achieved 60% of the overall quality, according to the AGREE II criteria (Table 2). Three CPGs were considered as 'recommended' [1,12,14], because the result of

Table 2. The AGREE II results for each clinical practice guideline on eosinophilic esophagitis, and overall inter-rater agreement, expressed by intraclass correlation coefficients (ICCs).

	Domain scores (%)							
	1	2	3	4	5	6	7	8
Guidelines	Scope and purpose	Stakeholder involvement	Rigor of development	Clarity and presentation	Applicability	Editorial independence	Overall quality	Overall assessment
Furuta et al. [12]	58.33%	33.33%	44.27%	68.06%	28.13%	93.75%	58.33%	Recommended with modifications
Liacouras et al. [1]	79.17%	40.28%	33.85%	62.50%	22.92%	95.83%	50%	Recommended with modifications
Dellon et al. [13]	36.11%	13.89%	35.42%	97.22%	23.96%	93.75%	50%	Recommended with modifications
Papadopoulo et al. [14]	73.61%	27.78%	15.63%	75%	11.46%	91.67%	25%	Not recommended
Overall inter-rater reliability (ICC values)	0.814	0.908	0.862	0.693	0.507	0.686	NA	NA

NA: Not applicable.

Table 3. The AGREE II results for each sub-domain in all available clinical practice guideline on eosinophilic esophagitis, and overall inter-rater agreement, expressed by intraclass correlation coefficients.

Guidelines	Furuta et al. [12]			Liacouras et al [1]			Dellon et al. [13]			Papadopoulo et al. [14]		
Scope and purpose	58.33%	*Item 1*	45.8%	79.17%	*Item 1*	91.7%	36.11%	*Item 1*	29.2%	73.61%	*Item 1*	75%
		Item 2	54.2%		*Item 2*	79.2%		*Item 2*	45.8%		*Item 2*	62.5%
		Item 3	75%		*Item 3*	66.7%		*Item 3*	33.3%		*Item 3*	83.3%
Stakeholder involvement	33.3%	*Item 4*	70.8%	40.28%	*Item 4*	91.7%	13.89%	*Item 4*	16.7%	27.78%	*Item 4*	29.2%
		Item 5	4.2%		*Item 5*	0%		*Item 5*	0%		*Item 5*	16.7%
		Item 6	25%		*Item 6*	29.2%		*Item 6*	25%		*Item 6*	37.5%
Rigor of development	44.27%	*Item 7*	54.2%	33.85%	*Item 7*	58.3%	35.42%	*Item 7*	0%	15.63%	*Item 7*	4.2%
		Item 8	75%		*Item 8*	25%		*Item 8*	4.2%		*Item 8*	0%
		Item 9	58.3%		*Item 9*	25%		*Item 9*	79.2%		*Item 9*	12.5%
		Item 10	33.3%		*Item 10*	33.3%		*Item 10*	29.2%		*Item 10*	20.8%
		Item 11	75%		*Item 11*	66.7%		*Item11*	87.5%		*Item 11*	50%
		Item 12	37.5%		*Item 12*	37.5%		*Item 12*	79.2%		*Item 12*	33.3%
		Item 13	0%		*Item 13*	4.2%		*Item 13*	0%		*Item 13*	0%
		Item 14	20.8%		*Item 14*	20.8%		*Item 14*	4.2%		*Item 14*	4.2%
Clarity and presentation	68.06%	*Item 15*	62.5%	62.5%	*Item 15*	58.3%	97.22%	*Item 15*	95.8%	75%	*Item 15*	54.2%
		Item 16	83.3%		*Item 16*	66.7%		*Item 16*	95.8%		*Item 16*	79.2%
		Item 17	58.3%		*Item 17*	62.5%		*Item 17*	100%		*Item 17*	91.7%
Applicability	28.13%	*Item 18*	25%	22.92%	*Item 18*	37.5%	23.96%	*Item 18*	29.2%	11.46%	*Item 18*	16.7%
		Item 19	20.8%		*Item 19*	20.8%		*Item 19*	37.5%		*Item 19*	25%
		Item 20	33.3%		*Item 20*	4.2%		*Item 20*	4.2%		*Item 20*	4.2%
		Item 21	33.3%		*Item 21*	29.2%		*Item 21*	25%		*Item 21*	0%
Editorial independence	93.75%	*Item 22*	87.5%	95.83%	*Item 22*	95.8%	93.75%	*Item 22*	91.7%	91.67%	*Item 22*	87.5%
		Item 23	100%		*Item 23*	95.8%		*Item 23*	95.8%		*Item 23*	95.8%

Table 4. Inter-appraiser agreement of clinical practice guidelines on eosinophilic esophagitis, expressed as intraclass correlation coefficients (ICC) of the scores provided by a four-reviewer team (two methodologists and two gastroenterologists).

Authors and publication year	Overall ICC	ICC (methodologist/ gastroenterologist)
Furuta et al. [12]	0.838	0.848
Liacouras et al. [1]	0.869	0.858
Dellon et al. [13]	0.930	0.873
Papadopoulo et al. [14]	0.955	0.927
All guidelines	0.903	0.878

the three items assessed were ≥50%. The remaining CPG was 'weakly recommended' [13] with only two items ≥50%. In contrast, reviewers' scores for the overall assessment did not recommend one CPG [14]; however, the other three were recommended after modifications (Table 2). Detailed scores for each sub-domain assessed in the AGREE II instrument, as well as inter-rater agreement, are shown in Table 3.

3.4. Inter-appraiser agreement analyses

Inter-appraiser agreement between the four reviewers was excellent (with an ICC value of 0.903, which represents an extremely high level of agreement) and remained excellent for each of the individual guides assessed (ICC ranging from 0.838 to 0.955). The same level of agreement (excellent) was maintained when gastroenterologists' scores were compared with those provided by methodologists, both overall (ICC being 0.878) and independently for each CPG (with ICC ranging from 0.848 to 0.927) (Table 4).

4. Discussion

In this study, we used the AGREE II tool to review the methodological quality of the CPG available for the diagnosis and treatment of patients with EoE. Based on our results, the overall quality of these guidelines, all of which were developed on behalf of well-recognized scientific societies, is limited. None of them reached an overall quality score of 60%, as assessed by a panel of expert reviewers comprising of gastroenterologists and methodologists using the AGREE II instrument. Thereby, three of the four guides were 'recommended,' and the remaining one only 'weakly recommended' following the criteria used in this evaluation [25,26]. The fact that no guide was considered as 'strongly recommended' suggests an analysis of the way the different CPGs are managed in the 6 domains and 23 items that the AGREE II tool includes as quality standards is required.

The independent assessment by four reviewers showed that the quality scores for each domain varied widely. Of all of the domains, Domain 2 (stakeholder involvement), Domain 3 (rigor of development), and Domain 5 (applicability) had the lowest mean scores, none of them reaching the 50% threshold for quality. Notably, inter-reviewer agreement was excellent for the first two domains (at ICC 0.908 and 0.862, respectively) and moderate for the last (ICC value 0.507). On the other hand, clarity and presentation and, especially editorial independence, provided the highest mean scores.

Our study was able to identify several areas where certain CPGs could be improved. First, some CPGs had insufficient information regarding Domain 1 (purpose and health questions to be answered) [13], overall failing to follow a PICO (patient, intervention, comparator, and outcome) structure when explicitly presenting the CPG goals. Second, some CPGs lacked multidisciplinary development teams (in fact, some guides were exclusively developed by gastroenterologists [13] or pediatricians [14], with no participation from pathologists, allergists, or dietitians), and no CPG considered the preferences and experiences of patients. This is noteworthy since EoE is a complex condition that can appear in childhood and persist throughout adulthood [29,30]; EoE is an allergic disorder which may benefit from elimination diets [31], but should be diagnosed and monitored based on endoscopic and bioptic assessments [32]; EoE treatment includes a range of dietary modifications [33] that are facilitated with dietary and nutritional advice [34]; and some patients may present

with symptoms which should also be referred to the otolaryngologist [35]. The emergent increase of EoE incidence in recent years [5] requires the full awareness of primary care practitioners in order to facilitate diagnosis and avoid commonly reported diagnostic delay [7,36,37]. EoE significantly affects the health-related quality of life of suffering patients [8], with the disease greatly impacting on eating, social, and emotional development [38]. For this reason, patient's preferences and values need to be integrated into CPGs' developing teams to increase the potential to achieve more solid goals in EoE. Restrictive participation in CPGs development has been recognized as potentially harmful or limiting for physicians, patients, and other users [17].

Interestingly, of all the domains, Domain 3 (rigor of development) was recognized as a sub-optimally developed aspect in every EoE guide assessed, according to the AGREE II criteria. The use of evidence-based methods to provide clinical recommendations at the highest level needs to begin with a systematic review of the literature, a task that only two guidelines undertook [1,12]; a systematic literature review provides evidence in relation to those specific diagnostic and/or therapeutic circumstances a CPG intends to cover. Evidence should then be critically appraised, summarized, graded, and presented. The four guides showed a variable low-to-moderate adherence to most of these items, with statement writing generally lacking details of the strengths and limitations of the evidence retrieved and methods to elaborate recommendations superficially presented and mostly based on expert opinions. It must be noted that none of the guides were submitted for multidisciplinary external reviewing, and despite the fact that the 2007 guide [12] was updated in 2011 [1], no explicit criteria to do so were mentioned.

Our research represents the first evaluation of CPG on EoE in the literature using a scientific instrument such as AGREE II and adds to the mounting body of evidence on the use of this methodology to appraise and improve the development and utility of CGP to harmonize and improve clinical practice. Obtaining the overall high rates of agreement among the methodologists and gastroenterologists who undertook this task provides proof on the reliability of the AGREE II tool. However, Domain 5 (applicability) obtained only a moderate agreement according to ICC values, with the last guide only having an ICC of 0.507. The applicability domain includes considering facilitators and barriers to applying guidelines' recommendation and on how to put them into practice, including the potential resources required, and audits on how they are working. No specific mention of these is included in any CPGs on EoE, despite the technology needed to properly manage patient with EoE being fully available at every hospital, as organizational aspects and improving staff knowledge on EoE are the keys to succeed.

The main strengths of our study include conducting a systematic search to find all CPG focused on EoE that have been published to date and evaluation undertaken using a scientific instrument such as AGREE II for assessing the methodological quality of each guide. The four independent appraisers who conducted this assessment completed AGREE II online training prior to the review. The reviewer team included gastroenterologists and methodologists, who provided consistent scoring for the different domains assessed, despite the differential background of their components. In fact, the applicability domain (which is integral for the methodological quality of a CPG) has been recently shown to be unsatisfactorily low in those guides published up to 2014 despite the steady improvement found in CPG quality after 2010 [39].

Still, this study also has a number of limitations, mainly due to the fact that AGREE evaluates the methods for developing a CPG, but not its scientific content, including whether it provides updated, state-of-the-art recommendations. The overall score we used to recommend a specific CPG based on the number of domains that matched or exceeded the 50% quality threshold is a system that provides a similar value for all domains. It seems obvious that 'rigor of development' impacts more strongly on clinical practice patterns and patients' health results than 'editorial independence,' but the aforementioned criteria assessed both domains equally. Additionally, the four reviewers/appraisers were not blinded to the authors/organization that developed the guidelines, which may have been a potential source of bias. As most of the guidelines were well known to the authors, true blinding would not have been feasible. Finally, the AGREE II tool has its own limitation, despite being a valid, reliable, and strongly recommended tool [40,41], it allows for some subjectivity in the reviewer's interpretation of the scores for every item, and there is a lack of clear criteria for applying scores.

Our present findings show that the quality of most CPGs is not yet satisfactory for the management of EoE. An updated CPG with the involvement of all stakeholders, including healthcare professionals, patients, and their relatives, more rigorous methodological development, and a focus on the practical applicability of the recommendations should be a major goal for the future, probably using the AGREE II instrument.

Key issues

- The incidence of eosinophilic esophagitis has increased significantly to become the leading cause of dysphagia and food impaction in children and young adults.
- The practical management of EoE patients is frequently challenging because of the complex clinical picture and several controversies related to disease diagnosis and therapy.
- Up to four clinical practice guidelines have been published to date, but their methodological quality has not as yet been assessed with standardized criteria.
- Currently available clinical practice guidelines on EoE show a variable and limited quality according to the AGREE II appraisal instrument, with none of them being 'strongly recommended'.
- Of all of the domains, stakeholder involvement, rigor of development, and applicability had the lowest mean scores, with none of them reaching the 50% threshold for quality, and therefore being the major areas for improvement.
- Upcoming guidelines on EoE should benefit from the use of the AGREE II instrument in order to optimize their potential impact in clinical settings and the advantages for patients.

Funding

This paper was not funded.

Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

ORCID

Alfredo J. Lucendo http://orcid.org/0000-0003-1183-1072
Ángel Arias http://orcid.org/0000-0003-1006-0958
Olga Redondo-González http://orcid.org/0000-0003-0964-5668

References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. J Allergy Clin Immunol. 2011;128(1):3–20.
2. Molina-Infante J, Bredenoord AJ, Cheng E, et al. Proton pump inhibitor-responsive oesophageal eosinophilia: an entity challenging current diagnostic criteria for eosinophilic oesophagitis. Gut. 2016;65(3):524–531.
   •• **Consensus report made by a multidisciplinary panel of international experts in EoE summarizing the mounting evidence that supports the concept that PPI-responsive esophageal eosinophilia represents a continuum of the same immunological mechanisms that underlie EoE.**
3. Attwood SE, Smyrk TC, Demeester TRJJ. Esophageal eosinophilia with dysphagia. A distinct clinicopathologic syndrome. Dig Dis Sci. 1993;38(1):109–116.
4. Straumann A, Spichtin HP, Bernoulli R, et al. Idiopathic eosinophilic esophagitis: a frequently overlooked disease with typical clinical aspects and discrete endoscopic findings. Schweiz Med Wochenschr. 1994;124(33):1419–1429.
5. Arias A, Perez-Martinez I, Tenias JM, et al. Systematic review with meta-analysis: the incidence and prevalence of eosinophilic oesophagitis in children and adults in population-based studies. Aliment Pharmacol Ther. 2016;43(1):3–15.
   •• **The most recently published research on the epidemiology of EoE. Current prevalence and incidence rates from every population-based study are summarized to show the magnitude of the disease and evolving trends.**
6. Lucendo AJ, Sánchez-Cazalilla M. Adult versus pediatric eosinophilic esophagitis: important differences and similarities for the clinician to understand. Expert Rev Clin Immunol. 2012;8(8):733–745.
7. Schoepfer AM, Safroneeva E, Bussmann C, et al. Delay in diagnosis of eosinophilic esophagitis increases risk for stricture formation in a time-dependent manner. Gastroenterology. 2013;145(6):1230–1236.
8. Safroneeva E, Coslovsky M, Kuehni CE, et al. Eosinophilic oesophagitis: relationship of quality of life with clinical, endoscopic and histological activity. Aliment Pharmacol Ther. 2015;42(8):1000–1010.
9. Straumann A, Aceves SS, Blanchard C, et al. Pediatric and adult eosinophilic esophagitis: similarities and differences. Allergy. 2012;67(4):477–490.
10. Cheng E, Souza RF, Spechler SJ. Eosinophilic esophagitis: interactions with gastroesophageal reflux disease. Gastroenterol Clin North Am. 2014;43(2):243–256.
11. González-Cervera J, Lucendo AJ. Eosinophilic esophagitis: an evidence-based approach to therapy. J Investig Allergol Clin Immunol. 2016;26(1):8–18.
12. Furuta GT, Liacouras CA, Collins MH, et al. Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. Gastroenterology. 2007;133(4):1342–1363.
   • **These systematic review-based expert committee-consensual guidelines were the first ones provided for the management of EoE in children and adults. The available body of knowledge accumulated to that moment was incorporated in the reference document, which also provided recommendation for further research.**
13. Dellon ES, Gonsalves N, Hirano I, et al. ACG clinical guideline: evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE). Am J Gastroenterol. 2013;108(5):679–692.
14. Papadopoulou A, Koletzko S, Heuschkel R, et al. Management guidelines of eosinophilic esophagitis in childhood. J Pediatr Gastroenterol Nutr. 2014;58(1):107–118.
15. Graham R, Mancher M, Wolman DM, et al. Clinical practice guidelines we can trust. Washington (DC): National Academies Press; 2011.
16. Boluyt N, Lincke CR, Offringa M. Quality of evidence-based pediatric guidelines. Pediatrics. 2005;115(5):1378–1391.
17. Woolf SH, Grol R, Hutchinson A, et al. Clinical guidelines: potential benefits, limitations, and harms of clinical guidelines. Brit Med J. 1999;318(7182):527–530.
18. Ward JE, Grieco V. Why we need guidelines for guidelines: a study of the quality of clinical practice guidelines in Australia. Med J Aust. 1996;165(10):574–576.
19. Graham ID, Beardall S, Carter AO, et al. What is the quality of drug therapy clinical practice guidelines in Canada? Can Med Assoc J. 2001;165(2):157–163.
20. Grilli R, Magrini N, Penna A, et al. Practice guidelines developed by specialty societies: the need for a critical appraisal. Lancet. 2000;355(9198):103–106.
   •• **This seminal paper showed that most clinical practice guidelines developed by scientific societies did not reach the minimum thresholds of methodological quality. The authors proposed the need to develop and promote quality standards with the participation of all stakeholders involved in improving clinical results.**
21. Vlayen J, Aertgeerts B, Hannes K, et al. A systematic review of appraisal tools for clinical practice guidelines: multiple similarities and one common deficit. Int J Qual Heal. 2005;17(3):235–242.
22. AGREE Collaboration. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. Qual Saf Heal Care. 2003;12(1):18–23.
   •• **This is the first appraisal instrument for clinical practice guidelines that was developed and tested internationally. The AGREE tool provided a sensitive and easy-to-use instrument to improve the consistency and quality of the reporting of guideline development and provided a framework to encourage international comparison of clinical practice guidelines.**
23. Brouwers MC, Kho ME, Browman GP, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. J Clin Epidemiol. 2010;63(12):1308–1311.
   •• **The AGREE II incorporated key changes from the original version including a new seven-point response scale, with modifications to half of the items, and a new user's manual. As a result, the new development improved its measurement properties, usefulness to a range of stakeholders and ease of implementation.**
24. AGREE Next Steps Consortium (2009). The AGREE II instrument [electronic version]. 2016 [cited 2016 May.09]. Available from: http://www.agreetrust.org
25. Zhang Z, Guo J, Su G, et al. Evaluation of the quality of guidelines for myasthenia gravis with the AGREE II instrument. Plos One. 2014;9(11):e111796.
26. Zhang X, Zhao K, Bai Z, et al. Clinical practice guidelines for hypertension: evaluation of quality using the AGREE II instrument. Am J Cardiovasc Drugs. 2016;16:439–451. DOI:10.1007/s40256-016-0183-2

27. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159–174.
28. Kramer MS, Feinstein AR. Clinical biostatistics: LIV. The biostatistics of concordance. Clin Pharmacol Ther. 1981;29(1):111–123.
29. DeBrosse CW, Franciosi JP, King EC, et al. Long-term outcomes in pediatric-onset esophageal eosinophilia. J Allergy Clin Immunol. 2011;128(1):132–138.
30. Eluri S, Book WM, Kodroff E, et al. Lack of knowledge and low readiness for healthcare transition in eosinophilic esophagitis and eosinophilic gastroenteritis. J Pediatr Gastroenterol Hepatol. 2016. DOI:10.1097/MPG.0000000000001415
31. Kelly KJ, Lazenby AJ, Rowe PC, et al. Eosinophilic esophagitis attributed to gastroesophageal reflux: improvement with an amino acid-based formula. Gastroenterology. 1995;109(5):1503–1512.
32. González-Castillo S, Arias Á, Lucendo AJ. Treatment of eosinophilic esophagitis: how should we manage the disease? J Clin Gastroenterol. 2010;44(10):663–671.
33. Arias Á, González-Cervera J, Tenias JM, et al. Efficacy of dietary interventions for inducing histologic remission in patients with eosinophilic esophagitis: a systematic review and meta-analysis. Gastroenterology. 2014;146(7):1639–1648.
34. Venter C, Fleischer DM. Diets for diagnosis and management of food allergy: the role of the dietitian in eosinophilic esophagitis in adults and children. Ann Allergy Asthma Immunol. 2016;117:468–471. DOI:10.1016/j.anai.2016.08.003
35. Górriz-Gil C, Villarreal IM, Álvarez-Montero Ó, et al. Eosinophilic esophagitis: a relevant entity for the otolaryngologist. Acta Otorrinolaringol Esp. 2016;67(3):167–178.
36. Lucendo AJ, Arias T, Molina-Infante J, et al. Diagnostic and therapeutic management of eosinophilic oesophagitis in children and adults: results from a Spanish registry of clinical practice. Dig Liver Dis. 2013;45(7):562–568.
• **This survey-based research revealed a wide variability in the management of patients with EoE throughout Spain and analyzed reasons behind the heterogeneity in the diagnosis and treatment of patients.**
37. Lipka S, Kumar A, Richter JE. Impact of diagnostic delay and other risk factors on eosinophilic esophagitis phenotype and esophageal diameter. J Clin Gastroenterol. 2016;50(2):134–140.
38. Lucendo AJ, Sánchez-Cazalilla M, Molina-Infante J, et al. Transcultural adaptation and validation of the "Adult Eosinophilic Esophagitis Quality of Life Questionnaire" into Spanish. Rev Esp Enfermedades Dig. 2014;106(6):386–394.
39. Armstrong JJ, Goldfarb AM, Instrum RS, et al. Improvement evident but still necessary in clinical practice guideline quality: a systematic review. J Clin Epidemiol. 2016. doi:10.1016/j.jclinepi.2016.08.005
•• **This review of the quality of clinical practice guidelines from a wide range of health-care topics found a steady improvement in their quality over time. This was particularly evident in guidelines published after releasing the AGREE instruments in 2010. However, certain domains that are integral to the methodological quality of guidelines remained unsatisfactorily low.**
40. Lee GY, Yamada J, Kyololo O, et al. Pediatric clinical practice guidelines for acute procedural pain: a systematic review. Pediatrics. 2014;133(3):500–515.
41. Polus S, Lerberg P, Vogel J, et al. Appraisal of WHO guidelines in maternal health using the AGREE II assessment tool. Plos One. 2012;7(8):e38891.