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POINT OF VIEW

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PedEoEvolution: optimizing pediatric and adolescent eosinophilic esophagitis management in Italy

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ABSTRACT

This review addresses the unique challenges of pediatric eosinophilic esophagitis (EoE) management, aiming to develop a comprehensive knowledge base, standardize therapeutic approaches, and explore new targeted biological treatments. A non-systematic literature review was conducted, complemented by two surveys: one for clinicians to validate current practices and another for the President of the Italian Association of Families Against Eosinophilic Esophagitis to assess disease burden. An expert panel discussed and validated the results. The study identified a prevalence of 32.9 per 100,000 in pediatric EoE in Italy, with only half of the cases accurately diagnosed and an average diagnostic delay of 18 months. Current treatments show limitations in long-term management, with 27.8% of patients proving ineligible, intolerant, or inadequately controlled. The Impact Score and SCOPE (Symptoms, Comprehensive Observation, Pathological Evaluation) approach were recommended for early diagnosis and treatment efficacy evaluation. Dupilumab emerged as a promising therapy for patients unresponsive to conventional treatments, demonstrating significantly higher rates of histological remission in children aged 1-11 years compared to placebo in clinical trials. This study provides a standardized approach to pediatric EoE management, emphasizing early diagnosis, multidisciplinary care, and targeted biological treatments. The findings highlight the need for increased awareness, standardized care pathways, and further research to address ongoing challenges in pediatric EoE management.

Keywords: Disease management, Eosinophilic esophagitis, IMPACT score, Pediatric gastroenterology, Treatment algorithm

Introduction

Eosinophilic esophagitis (EoE) is a chronic, progressive, relapsing, type 2 inflammatory disorder of the esophagus, characterized by an abnormal accumulation of eosinophils in the esophageal epithelium (1,2). This condition, increasingly recognized in recent years, presents unique challenges in pediatric populations, where its management differs significantly from adult cases (3).

The etiology of EoE is multifactorial, involving a complex interplay of genetic predisposition, environmental factors, and immunological responses to antigenic stimuli (4). In young patients, the clinical presentation is often diverse and age-dependent, including symptoms such as dysphagia, food impaction, retrosternal pain, and manifestations mimicking gastroesophageal reflux (GERD). This broad spectrum of symptoms can make diagnosis challenging, particularly in younger children who may present with abdominal pain, vomiting, or failure to thrive (4-6).

EoE has gained increasing importance in the field of pediatric gastroenterology, necessitating greater awareness among healthcare professionals. Globally, the prevalence of EoE in the pediatric population is 32.9 cases per 100,000

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inhabitants, with an incidence rate of 4.9 cases per 100,000 person-years (7).

Diagnosis of EoE requires a comprehensive approach, integrating clinical history, endoscopic evaluation, and histological examination. The management of pediatric EoE necessitates a multidisciplinary strategy involving gastroenterologists, allergists, and pediatric specialists. Current therapeutic modalities include empiric food elimination diets, proton pump inhibitors (PPIs), topical corticosteroids (TCS), esophageal dilation in case of refractoriness (in the presence of strictures) and dupilumab, a monoclonal antibody targeting the shared receptor subunit of IL-4/IL-13, two interleukins central for type 2 inflammation. The latter is EMA-approved for patients aged 1 year and older with a body weight of at least 15 kg who are inadequately controlled by, intolerant to, or not candidates for conventional pharmacological therapy, and is currently reimbursed in Italy for adults and adolescents aged 12 years and older with a body weight of at least 40 kg meeting the same clinical criteria.

The management of EoE in children presents additional complexities related to long-term safety considerations, adherence challenges, and potential impacts on growth and development (5). These factors underscore the urgent need for standardized care pathways that ensure equitable access to appropriate treatments across different regions.

In light of these challenges and the evolving landscape of EoE management, there is a pressing need for comprehensive research to guide clinical practice in pediatric EoE. To address this need, our research aims to develop a comprehensive knowledge base on the management of pediatric patients with EoE. This research seeks to address existing knowledge gaps, standardize therapeutic approaches, and gather insights for positioning the new targeted biological treatment approved for EoE.

Our research aims to investigate the epidemiology of EoE in young patients (<12 years old) and to identify pediatric patients with EoE who are inadequately controlled by, intolerant to, or not candidates for conventional pharmacological therapy. These patients represent the target population for dupilumab treatment. Additionally, we examine patient management from diagnosis through treatment strategies to follow-up, identifying related gaps and critical issues. Importantly, we also explore the disease burden on patients' quality of life, recognizing the significant impact EoE has beyond its physical symptoms.

At last, this analysis aims to define an ideal therapeutic algorithm to standardize the treatment approach for pediatric and adolescent (up to 18 years old) EoE patients in Italy in order to contribute to more equitable and effective care for this patient population, addressing the unmet needs highlighted in the current landscape of EoE management.

Methods

A multi-faceted approach was employed to comprehensively assess the current landscape of EoE management in pediatric and adolescent patients. Initially, an in-depth literature review was conducted to map the patient journey and identify existing knowledge gaps. Based on these findings, two distinct questionnaires were developed: the first targeted clinicians to validate the literature review results, verify current clinical practices, and integrate additional aspects of EoE management. The second questionnaire, administered to the President of the Italian Association of Families Against Eosinophilic Esophagitis (ESEO Italia), was designed to gather the perspectives on EoE burden and quality of life from both patients and their families/caregivers. Subsequently, all interview results were shared and validated through a discussion panel composed of the same experts involved in the previous phases. This interdisciplinary approach facilitated a comprehensive overview of EoE management strategies, encompassing both clinical perspectives and patient experiences provided by the President of ESEO Italia, thus providing a more complete understanding of the challenges and needs in EoE care.

The research steps are illustrated in Table 1 and detailed below.

TABLE 1 – Research steps

Step	Activity	Detail
1	Expert Selection	An expert panel of 7 clinicians and the President of the patients association
2	Desk Research	A literature review was conducted to identify high-level information on EoE management.
3	Survey Drafting	The survey covered the topics of EoE management gaps and the patient journey.
4	Expert Interviews	The survey was administered to the expert panel through one-to-one sessions.
5	Results Analysis	Survey results were collected, analyzed and summarized.
6	Algorithm, Key Concepts and Final Meeting	An algorithm for disease management was developed, and key concepts were extrapolated and validated in a meeting.

Expert selection

For the purpose of evaluating the current management of EoE in the pediatric population and drawing key concepts to standardize patient care across the country, a panel of seven experts was selected. These experts were chosen based on their demonstrated experience in treating pediatric and adolescent patients with EoE. The selection process ensured that the affiliated institutions of the involved experts provided a representative geographical distribution across the national territory (Fig. 1). To incorporate a comprehensive perspective on the disease burden, the President of the patient association ESEO Italia was also included in the panel.

Desk research

A non-systematic literature review was conducted by the authors, following shared research objectives, with the purpose of constructing an essential knowledge framework concerning the epidemiology of the pediatric population, as well as the diagnostic and therapeutic strategies for pediatric/adolescent patients with EoE. The results were subsequently presented to the expert panel for validation and integration with real-world clinical insights.

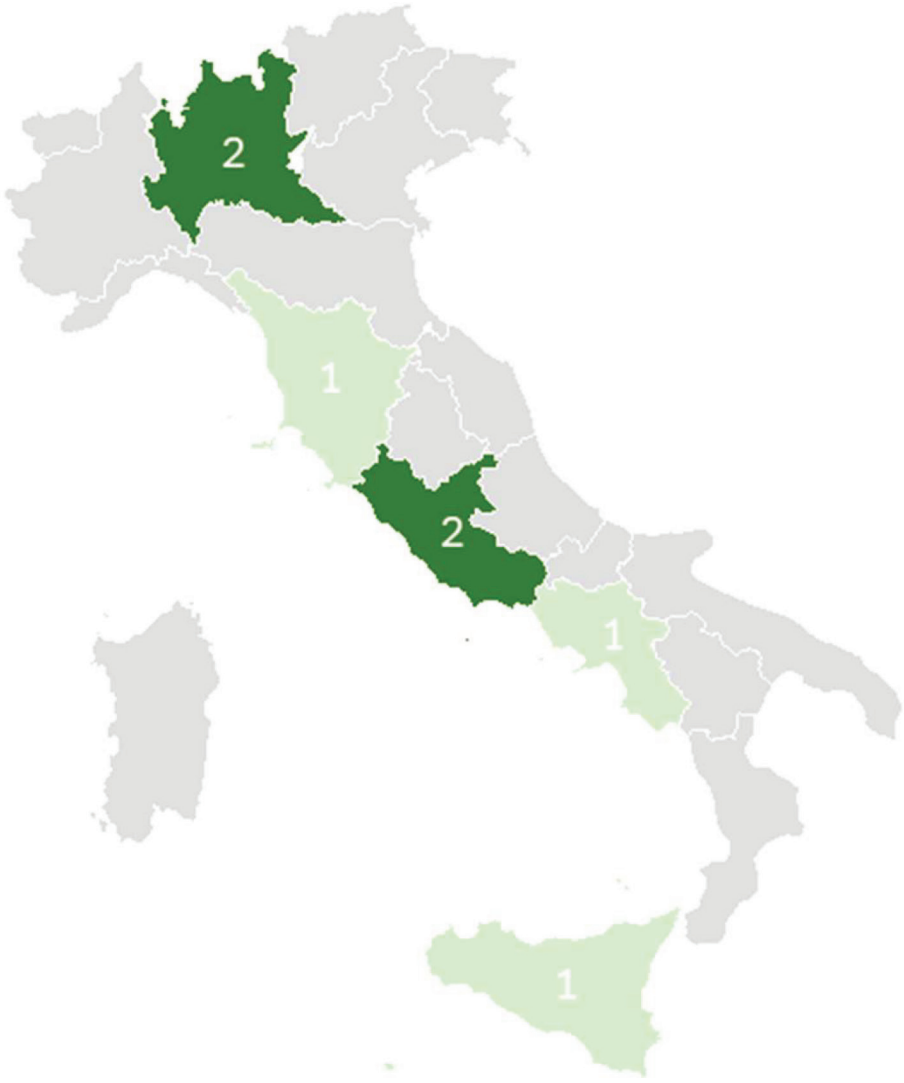

FIGURE 1 - Geographic distribution of centers with selected expert panel members.

Survey drafting

Following the desk research, two distinct surveys were developed to address specific aspects of EoE management. The first survey, directed at clinicians, comprised 28 questions divided into six main themes: (i) epidemiology, (ii) diagnostic pathway, (iii) therapeutic approaches, (iv) follow-up, (v) unmet needs, (vi) potential role of new targeted biological therapies in the condition under consideration (Supplementary Material 1). This survey aimed to bridge gaps in understanding the patient's diagnostic and therapeutic pathway, verify the most prevalent therapeutic approaches, and validate the epidemiological funnel.

The second survey, designed for the President of ESEO Italia, consisted of 33 questions (Supplementary Material 2). These were categorized into four areas: (i) daily management and quality of life, (ii) diagnosis and symptomatology, (iii) costs and services, (iv) therapeutic needs.

The primary objectives of this survey were to delineate the disease burden and assess the impact of EoE on patients and their families or caregivers.

Both surveys were constructed based on the findings from the literature review, ensuring that they addressed key areas of interest and potential knowledge gaps identified in the literature review.

Expert interviews

The surveys were administered to the involved experts through private, web-based, one-on-one sessions in an interview format. This approach allowed for a more dynamic and interactive data collection process, enabling the experts to provide in-depth responses and additional comments beyond the structured questions. The one-on-one nature of these sessions ensured confidentiality and allowed each expert to express their views freely without influence from peers. This methodology maximized the quality and depth of the

information gathered, providing a rich dataset for subsequent analysis and consensus-building efforts in standardizing EoE management across the national context.

Results analysis

Following the interviews, results were collated and compared through a qualitative analysis, highlighting areas of consensus and divergence among experts. Points of agreement formed the basis for preliminary recommendations, while areas of disagreement were identified for further discussion. This process ensured that the final outputs would reflect both established practices and address current uncertainties in EoE management.

Algorithm, key concepts drafting and final meeting

The analysis of results allowed the validation of the patient funnel, identifying the burden of pediatric patients (under 12 years old) with EoE who are inadequately controlled, intolerant, or ineligible for current treatments. Additionally, key messages were formulated regarding patient management throughout the diagnostic, therapeutic, and follow-up pathway, and a management algorithm was developed synthesizing the key steps of the care process. These elements were subsequently shared and further validated in the context of a final meeting involving all the experts interviewed in the previous phases of the project. Although the experts who participated in the final discussion also completed the initial questionnaires, their individual responses were collected independently and anonymously prior to the meeting. The final discussion aimed to synthesize collective insights and address areas of divergence, rather than to retrospectively validate or modify individual answers. During this session, the proposed key messages were discussed, and participants expressed their agreement with the aim of standardizing the approach to care and management of pediatric and adolescent patients with EoE.

Results

This section presents aggregated results that integrate findings from the literature review with clinical practice insights gathered through surveys and discussed collectively during a dedicated expert meeting.

Epidemiology

The first objective of the survey was to identify pediatric patients with EoE who are ineligible, intolerant, or inadequately controlled by current treatments.

The analysis started from pediatric EoE global prevalence reported by Hahn et al. (2023) of 32.9 patients per 100,000 and a European rate of 20.5 per 100,000 (7). Despite the lower European average, experts suggest that in the national context, particularly in Italy, the prevalence is more likely to align with the global rate of 32.9 per 100,000, similar to the situation observed in Spain (7).

The survey explored the percentage of patients correctly diagnosed, given that EoE presents similar symptoms and can often be confused with related conditions (such as GERD and dyspepsia) (8). On average, experts estimate that only 50% of prevalent cases receive an accurate diagnosis. However, once diagnosed, 100% of patients receive treatment, either pharmacological or dietary. Among these treated patients, literature evidence indicates that between 27.3% and 30.3% prove to be ineligible, intolerant, or inadequately controlled by currently available treatments, despite proper management (9). Finally, considering the population under 12 years old residing in Italy as of January 1, 2024 (10), it is estimated that approximately 260 patients with EoE are ineligible, intolerant, or inadequately controlled by current treatments (Table 2). This number identifies patients potentially eligible for treatment with a new biological drug (once authorized).

TABLE 2 - Epidemiology of pediatric EoE patients

People resident in Italy as of 1 January 2024 (<12 years)		**5,498,128 (10)**
Patients with EoE (prevalence)	32.9 per 100,000 (0.0329%) (7)	**1,809**
Correctly diagnosed patients	50%*	**904**
Patients diagnosed with EoE receiving treatment	100%*	**904**
Ineligible, intolerant, inadequately controlled patients	28.8% (9)	**260**

*Experts' opinion

Algorithm and key concepts for disease management

Diagnostic pathway and challenges in pediatric/adolescent EoE

The experts report a notable difference in diagnostic delay between pediatric/adolescent and adult populations with EoE. For the pediatric and adolescent group, the average diagnostic delay is approximately 18 months, substantially lower than the 3-year delay observed in adults (8). This reduced delay is attributed to heightened attention to pediatric and adolescent health concerns. Moreover, according to the experts, the presence of comorbidities may further shorten this delay.

Based on survey results, the experts identified several factors that contribute to the diagnostic delay:

- Adaptive behaviors: Patients often develop instinctive adaptive behaviors that mask the disorder, potentially delaying suspicion of EoE until symptoms reach a critical point.
- Limited disease awareness: There is a general lack of widespread, comprehensive knowledge about EoE among healthcare providers.
- Challenging sophisticated differential diagnosis: EoE is frequently misdiagnosed as other diseases, particularly GERD.

Concerning adaptive behaviors, to facilitate early diagnosis and assess treatment efficacy in EoE, experts suggest the implementation of the **IMPACT Score**. This tool consists of 10 targeted questions designed to uncover adaptive behaviors that may obscure the underlying condition (Table 3) (11-13).

TABLE 3 - Impact Score (11,12)

I	M	P	A	C	T
Imbibe fluids with meals	Modify food	Prolong mealtime	Avoid textured food	Chew excessively	Turn away tablets/ pills

10 possible questions to ask the patient to identify adaptive behaviors masking the manifestation of EoE symptoms			
Question	**YES**	**NO**	**Assign a score from 1 to 10 to express frequency or intensity**
1. Do you get food stuck while swallowing it?	□	□	
2. Do you feel you have to chew more or longer to swallow your food without difficulty?	□	□	
3. Does it take you longer than others to finish your meal?	□	□	
4. Are you typically the last one to finish eating?	□	□	
5. Do you need to cut food into small pieces?	□	□	
6. Do you need to soften certain foods that you find harder?	□	□	
7. Do you drink a lot of water during meals to facilitate swallowing?	□	□	
8. Do you often avoid going out to eat?	□	□	
9. Have you ever had to resort to excuses to avoid eating in public?	□	□	
10. Are there any foods you avoid? If yes, please indicate which ones.	□	□	

The IMPACT Score's application extends beyond patients with overt eating-related symptoms. Experts advocate its use in patients presenting with other immune-inflammatory conditions such as asthma, rhinitis, and food allergies, as these individuals may harbor subclinical EoE symptoms.

Each question in the IMPACT Score is rated on a scale of 1-10. This approach facilitates accurate diagnosis by revealing the subtle impacts of EoE that might otherwise go unnoticed.

The IMPACT score thus emerges as a valuable asset in the diagnostic toolkit for EoE, offering a structured method to quantify and interpret the subtle behavioral adaptations characteristic of this condition.

Furthermore, to address these challenges and improve diagnostic accuracy and timeliness, the involved experts formulated a set of suggestions, as illustrated in Figure 2. This figure outlines the 'red flags' to be vigilant for at clinical, endoscopic, and histological evaluation levels, along with corresponding best practice guidelines for effective and prompt diagnosis.

This strategy highlights the critical need for a comprehensive diagnostic assessment in EoE, integrating clinical evaluations, endoscopic investigations, and histopathological studies to guarantee a thorough and prompt diagnosis in young patients. Given that EoE is a chronic, progressive, and type 2 immune-mediated inflammatory disease, experts emphasize the critical importance of considering the potential coexistence of other type 2 inflammation-mediated conditions. This consideration is crucial for a holistic understanding of the patient's health status and for tailoring appropriate treatment strategies.

Finally, to guarantee an accurate and complete evaluation, a multidisciplinary approach is strongly recommended. This approach should involve key specialists, including a gastroenterologist, allergist, pathologist and possibly a psychologist. This collaborative, multidisciplinary strategy ensures that all aspects of the patient's condition are thoroughly examined and addressed, leading to more effective diagnosis, management, and long-term care of pediatric and adolescent EoE patients.

Current therapeutic approaches and follow-up

The therapeutic approach for EoE encompasses a range of options, including pharmacological interventions, dietary modifications, and esophageal dilation. Budesonide orodispersible tablets have been approved for marketing and granted reimbursement for the treatment of adult patients in most European countries (Italy included), and dupilumab is approved by both FDA and EMA for patients aged 12 and above and by FDA for patients aged ≥1 year and weighting ≥15 kg (6), and it has been reimbursed in Italy for patients ≥12 years weighting ≥40 kg. However, it is crucial to note that, as of now, there are no treatments specifically approved for the pediatric population in Italy below 12 years of age at the time of this manuscript's drafting. Consequently, in pediatric practice, experts rely on the off-label use of PPIs and TCSs, whereas dupilumab is the newly approved treatment in the adolescent age (12-17 years) in Italy.

The therapeutic choice should be thoroughly discussed with the patient and their family or caregivers (6). This collaborative approach ensures that all parties are informed about the off-label nature of the treatments currently employed in pediatric EoE management and can make informed decisions about the care plan.

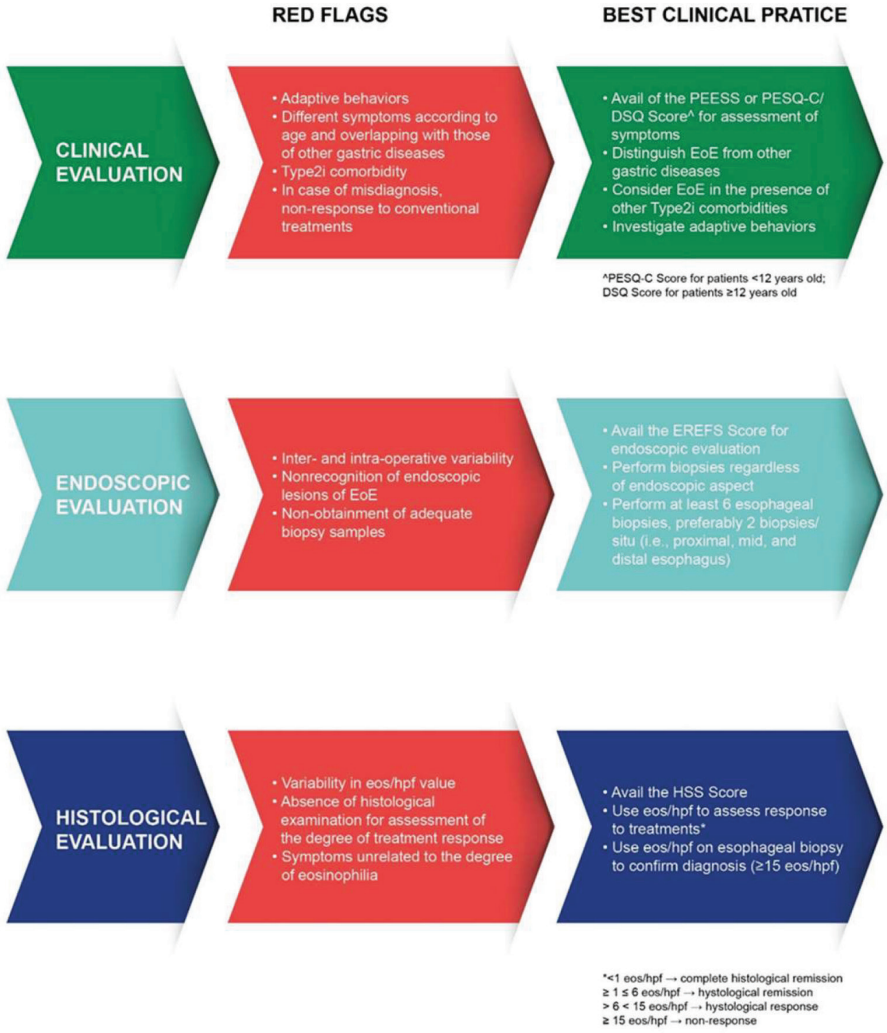

FIGURE 2 - Key red flags and best practices in clinical, endoscopic, and histologic assessment.
Acronyms: **DSQ:** Dysphagia Symptom Questionnaire; **EoE:** Eosinophilic Esophagitis; **eos/hpf:** Eosinophils per High-Power Field; **EREFS:** Endoscopic Reference Score; **HSS:** Histology Scoring System; **PEESS:** Pediatric Eosinophilic Esophagitis Symptom Severity; **PESQ-C:** Pediatric Eosinophilic Esophagitis Sign/Symptom Questionnaire – Caregiver; **Type 2i:** Type 2 Immune-mediated inflammatory disease.

Treatment typically begins with conventional off-label therapies such as PPI (especially when GERD is present) and TCS. The primary objectives of EoE treatment are to control symptoms, reduce esophageal inflammation, and prevent complications (6, 11). In cases of severe esophageal narrowing, dilation may be strongly suggested (6). Although elimination diets offer a non-pharmacological alternative, adherence can be challenging due to their restrictive nature.

The efficacy of the induction therapy is evaluated 8-12 weeks after initiation (5). If remission is achieved, the same treatment is continued long-term. However, if the patient is not adequately controlled, it is crucial to verify treatment adherence and consider switching to biological therapy, once available.

For patients on biological therapy, efficacy is assessed after 12-16 weeks. If the disease is in remission, long-term treatment is maintained. Long-term management is crucial even if clinical symptoms are absent (14): the experts involved recommend an endoscopy within 9 months of the initial evaluation and, after the first year, in the absence of symptoms, alternating clinical and endoscopic evaluations (with biopsy) are recommended at 6-month or 1-year intervals. The complete treatment and follow-up management algorithm for pediatric/adolescent EoE patients is available in the supplementary materials (Figure S2).

In the evaluation of treatment efficacy, experts emphasize the importance of a multidimensional assessment that simultaneously considers clinical, histological, and endoscopic evaluations. They further stress that this comprehensive approach is crucial to reveal hidden progression and uncover patients who are not fully controlled, ensuring a more accurate assessment of the disease state.

To support this multidimensional evaluation, the SCOPE (Symptoms, Comprehensive Observation, Pathological Evaluation) approach has been recommended. SCOPE is an all-encompassing method that guides the assessment of symptoms (evaluating severity and frequency), comprehensive observation of adaptive behaviors (using the IMPACT Score), diet/weight-related issues, and completed therapy cycles, and pathological evaluation through endoscopy with biopsy, detecting visible changes in the esophagus, calculating EREFS (Endoscopic Reference Score), eosinophil count and HSS (Histology Scoring System) Score.

This holistic SCOPE approach aids in determining whether there is a response to therapy and if a treatment switch is necessary. By integrating symptomatic, adaptive-behavioral

(assessed by IMPACT), and pathological (assessed by endoscopic and histologic scores and eosinophil count) aspects, SCOPE provides a more nuanced and accurate picture of the patient's condition and treatment progress.

This structured follow-up protocol ensures continuous monitoring of disease activity and treatment efficacy, allowing for timely adjustments in the therapeutic approach and maintaining optimal control of EoE in pediatric and adolescent patients.

Finally, regardless of the pharmacological choice, the chronic and progressive nature of EoE requires ongoing continuous treatment. Indeed, failure to maintain prolonged symptom control increases the likelihood of recurrence, and patients who do not have continuous and sustained histological control are at increased risk of developing fibrosis (15). Some clinicians report using cyclic therapy to reduce the risk of long-term side effects. This is due to concerns about the safety of prolonged treatment and poor compliance.

However, as mentioned above, literature data show greater efficacy with continuous therapy (16).

Limitations of current therapies and the potential role of new biological anti-IL-4 and IL-13 drugs in pediatric and adolescent EoE

The management of EoE in pediatric and adolescent patients presents significant challenges due to the limitations of currently available therapies.

While TCS are effective in inducing EoE remission and can provide clinical and histological improvement, their long-term use is associated with substantial side effects (6), making them unsuitable for chronic management of EoE. To date, no TCS has been approved for children. However, for adults over 18 years old, the EMA has approved an effervescent tablet that releases budesonide in the oral cavity to be swallowed with saliva. This has shown efficacy both in inducing remission (58% at Week 6 and 87% at Week 12) and in maintenance, with a range of 73.5–75% at Week 48 (17-19), which has been confirmed by recently published long-term follow-up data (20). Recently, the FDA approved a budesonide oral suspension for the induction treatment of patients with EoE over 11 years old. Currently, the use of oral topical steroids in children younger than this age, or where the drug is not commercially available (17-19), remains off-label, although several clinical trials of new formulations for children are underway. Experts (5) report that the primary adverse events associated with long-term steroid use include alterations in the glycemic curve, suppression of the hypothalamic-pituitary-adrenal axis, and the occurrence of recurrent candidiasis. These side effects often lead to treatment discontinuation, defining a subset of patients as intolerant to TCS therapy. Additionally, patients with recurrent infections or immunosuppression are not candidates for TCS treatment, further limiting its applicability.

PPI treatment can achieve clinical and histological remission in a significant proportion of patients with EoE. However, this approach is currently off-label, and long-term maintenance data have a low level of evidence. Moreover, during extended follow-up, potential adverse effects should be considered, including an increased risk of fractures, intestinal dysbiosis, and deficiencies in certain micronutrients, although these are rare (6).

Beyond the patients who are ineligible for or intolerant to these treatments, there is a significant proportion of patients who are inadequately controlled by current therapies. These are patients who, despite adherence to prescribed treatment, continue to experience persistent or recurrent symptoms typical of active disease. This situation highlights a substantial unmet need in the pediatric and adolescent EoE population, where patients have limited therapeutic alternatives. In this context, experts suggest that a targeted biological treatment like dupilumab represents a new therapeutic approach in the management of pediatric and adolescent EoE. This drug, by targeting the underlying pathophysiology of EoE, has the potential to address this unmet need and may slow the progressive evolution of the disease, potentially transforming its course. This potential has been demonstrated in the phase 3 EoE KIDS study, showing significantly higher rates of histological remission in children aged 1-11 years compared to the placebo arm (21), as well as in the TREET study, in which adolescents have been included (22).

The introduction of an anti-IL4 and IL-13 biological treatment for pediatric and adolescent EoE patients who are unresponsive to, intolerant to, or ineligible for conventional therapies could represent a significant advancement in care. Its mechanism of action, targeting the root cause of the disease (i.e., IL-4 and IL-13, which are key and central drivers of type 2 inflammation), offers the possibility of not just managing symptoms, but potentially altering the disease trajectory. Safety profile during studies in EoE was consistent with the known dupilumab safety profile (23). Additionally, transcriptomic data from clinical studies have shown the potential for improving the signature associated with type 2 inflammation and the EoE Diagnostic Panel (EDP) (21). The experts agree that this treatment could offer an alternative for patients who are ineligible for, intolerant to, or inadequately controlled on current therapies, but also for patients who have rapidly progressing and aggressive disease with an increased tendency to develop fibrostenosis since confirmation of diagnosis.

The impact of pediatric/adolescent EoE on patients and families/carers

A comprehensive discussion with the President of ESEO Italia and the expert panel has revealed the profound impact of EoE on pediatric/adolescent patients and their families. The disease significantly affects daily life, with meal preparation and consumption becoming central to family routines. This constant focus on food and eating habits not only disrupts normal daily activities but also places a considerable psychological burden on both patients and caregivers.

EoE's influence extends beyond the physical aspects of food consumption, significantly impacting social relationships. Patients, especially children and adolescents, may experience challenges in personality development and self-esteem, leading to substantial psychological repercussions. The disease necessitates a consistently high level of vigilance from patients and families in organizing meals, administering medications, and anticipating potential challenges in everyday situations.

To address these challenges, the experts emphasized the critical need for increased awareness and education about EoE. Promoting knowledge about the disease and its early warning signs among healthcare providers and the general

public is crucial for facilitating early diagnosis. Timely identification and intervention can lead to more favorable prognoses and improved quality of life for patients.

Another key point raised was the necessity of standardizing care pathways and access to services across the country, especially during the transition of patients from pediatric to adult care, to avoid loss to follow-up and waste of healthcare resources due to disease progression and complications. Creating transitional care centers of excellence ensures continuous management for all patients, regardless of their geographical location, and is fundamental in providing consistent and high-quality care for EoE patients nationwide.

This insight into the lived experience of EoE patients and their families underscores the complex nature of the disease's impact and highlights the areas where improvements in care and support systems could significantly enhance patient outcomes and quality of life.

Discussion

This study provides a comprehensive overview of the current landscape of pediatric EoE management in Italy, highlighting several critical areas for improvement and future research.

One of the key issues identified is the significant diagnostic delay in pediatric EoE, averaging 18 months. Although the diagnostic delay is even longer in the adult population, this delay remains one of the major critical issues in pediatric/adolescent patients as well, impacting timely intervention and disease management. This delay is largely due to the diverse and often nonspecific symptoms that mimic other conditions, such as GERD. The implementation of the IMPACT Score as a diagnostic tool could potentially reduce this delay by uncovering adaptive behaviors that mask the disease, allowing for earlier and more accurate diagnosis.

The analysis also underscores the limitations of current treatments, including PPIs and TCS, which are often used off-label in pediatric patients. The lack of approved therapies for children under 12 years old in Italy highlights a significant unmet need. The emergence of a targeted biological therapy offers a potential alternative, particularly for patients unresponsive to conventional treatments.

A notable contribution of this study is the proposed SCOPE approach for evaluating treatment efficacy. By integrating clinical, histological, and endoscopic assessments, this multidimensional evaluation provides a more comprehensive understanding of the disease state and treatment response. This approach is crucial for identifying patients who are not fully controlled and for making timely adjustments to their treatment plans.

The importance of a multidisciplinary approach is also emphasized. Involving gastroenterologists, allergists, pathologists, and psychologists ensures that all aspects of the patient's condition are addressed, from diagnosis to long-term management. This collaborative strategy supports the holistic care of pediatric EoE patients, improving overall outcomes.

The analysis highlights the need for standardized transitional care pathways to ensure continuous and consistent management of EoE as patients move from pediatric to adult care. This approach is essential to prevent loss to follow-up and to maintain the quality of care throughout the patient's life.

Additionally, the discussion addresses the significant impact of EoE on the quality of life of patients and their families: the constant attention required regarding food choices and eating habits, along with the psychological burden associated with the disease, underscores the need for increased awareness and education about the disease. Promoting knowledge among healthcare providers and the general

TABLE 4 - Summary of key concepts emerging from survey and discussion

1	Implement the IMPACT Score to uncover adaptive behaviors and facilitate early EoE diagnosis, especially in patients with other immune-inflammatory conditions.
2	As EoE is a chronic, progressive, type 2 immuno-inflammatory pathology: in the diagnostic process, for a correct diagnosis, it is essential to consider the possible coexistence of other pathologies mediated by type 2 inflammation (such as atopic dermatitis, asthma, chronic rhinosinusitis with nasal polyps, allergic rhinitis, chronic spontaneous urticaria); a multidisciplinary evaluation by a gastroenterologist, an allergist and an anatomopathologist, with possible psychological support, is considered best practice. This integrated approach allows a more complete and accurate assessment of the patient.
3	In the treatment of EoE in paediatric/adolescent patients, the presence of comorbidities, type 2 inflammatory diseases, disease-associated growth problems, recurrent candidiasis/infections or immunodepressed states directs the therapeutic approach towards the use of biological drugs.
4	In order to assess therapeutic efficacy and verify disease remission, it is essential to perform a multidimensional assessment that simultaneously considers clinical, histological and endoscopic evaluations. Such an integrated approach, supported by the comprehensive SCOPE approach, provides an accurate understanding of the patient's health status and the effectiveness of the therapeutic treatment.
5	Patients with EoE require chronic continuous, rather than intermittent (cycling/stacking) therapy to achieve continuous and prolonged control of symptoms and histology and endoscopic aspects, and to prevent the development of fibrostenotic complications in the long term.
6	It is necessary to promote education about the disease and the warning signs that should raise suspicion, such as the IMPACT score, to be used in open day initiatives and public awareness campaigns, in order to achieve early diagnosis and ensure a more favorable prognosis with a better quality of life.
7	It is necessary to create standardized Transitional Care Pathways to ensure continuous and consistent treatment for patients with EoE as they transition from pediatric to adult care (6). This approach aligns with best practices and helps maintain the quality of care throughout a patient's life.

public can facilitate early diagnosis and improve patient outcomes.

Limitations of the Study

The non-systematic nature of the literature review may have led to the omission of relevant studies. The reliance on expert opinion and surveys introduces potential biases, as the findings are based on the perspectives of a limited number of specialists. Additionally, the study's focus on the Italian context may limit the generalizability of the results to other regions with different healthcare systems and patient populations. Future research should aim to include a broader range of data sources and consider longitudinal studies to validate the proposed diagnostic and therapeutic approaches.

Moreover, we acknowledge that the experts involved in the final consensus meeting were the same individuals who participated in the survey phase. While this may introduce a risk of bias, the design of the process—particularly the use of independent, one-to-one interviews—was intended to mitigate this limitation. Future studies may consider incorporating external validation panels or Delphi rounds to strengthen methodological robustness.

Conclusion

This comprehensive analysis of pediatric and adolescent EoE management has yielded valuable insights for standardizing care across Italy. The proposed diagnostic and therapeutic algorithms, along with the emphasis on multidisciplinary care, provide a solid foundation for improving patient outcomes. However, several areas require further attention and development such as the creation of a shared pathway for transitional age patients to ensure continuity during the passage from pediatric to adult care and address the unique challenges of this period; the establishment of a national disease registry which would facilitate research, improve understanding of disease patterns, and enhance patient care; the promotion of multidisciplinary care to ensure its widespread implementation across healthcare settings and the standardization of care pathways across different regions of Italy.

Addressing these open points will be crucial in further advancing the management of pediatric and adolescent EoE and improving the quality of life for affected patients and their families.

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Disclosures

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