

SAFETY, EFFICACY, QUALITY OF LIFE AND TREATMENT DYNAMIC OF CONVENTIONAL THERAPIES FOR ADULTS AND ADOLESCENTS SUFFERING FROM EOSINOPHILIC ESOPHAGITIS, A TYPE 2 INFLAMMATORY DISEASE: QUALITATIVE AND QUANTITATIVE SYNTHESIS

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Objective

- Eosinophilic esophagitis (EoE) is an increasingly recognized condition both in children and adults characterized histologically by eosinophilic infiltration and clinically by symptoms of esophageal disfunction [1].
- Consensus guidelines have established first-line pharmacologic treatment targeted at improving patient symptoms and reducing histologic eosinophil burden [2,3]
- The aim of the present study was to review the available evidence regarding EoE in adults and adolescents associated with proton pump inhibitors (PPI) and topical steroids (TCS) treatment.

Methods

- PubMed, Embase and Cochrane Library were searched for English-language articles up to May 11, 2023 based on the PICOS criteria in Figure 1.
- Standard descriptive statistics were used to described study characteristics.
- A comprehensive inventory of outcomes and definitions was generated through qualitative review and subsequently organized into subdomains (histology, clinical, endoscopy, adverse events, PROs).
- Explorative meta-analyses (MA) were conducted on efficacy outcomes (random effect models) using STATA 15 software.

Figure 1. PICOS criteria used in the search strings

P	Population EoE patients ≥12 years
I	Intervention PPI or TCS in monotherapy or in combination
C	Comparator Any treatments
O	Outcome <ul style="list-style-type: none">efficacy: clinical, histologic and endoscopic response, symptoms reduction, relapse or response duration, esophageal dilatationsafety: any treatment related adverse event (TRAE)quality of lifechanging in treatment management dynamics.
S	Study Experimental or observational studies enrolled at least 10 patients

Results

- After screened a total of 1062 articles, 116 studies were included in the review (Figure 2). The majority were conducted before 2018 AGREE international consensus conference [4], hence PPI-responsive eosinophilic esophagitis patients were investigated in less than one third of the papers.
- Almost 80% of the selected paper are observational, 12% RCTs and 10% cross-sectional. On average, EoE patients are young (38 years), 70% male with 7+ years of symptoms history. Clinical, endoscopic and allergic presentations are reported in Figure 3.
- PPI and TCS efficacy is reported in 37 (45%) and 62 (76%) studies, respectively. The main outcome is histologic response (HR), followed by clinical (CR) and endoscopic (ER) (Figure 4).
- HR is defined as proportion of patients achieving <15 eosinophils per high-power field (eos/hpf) in almost all studies (86%); more restrictive thresholds define as <6 and <1 eos/hpf are used in 30% and 19% of studies, respectively. Based on MA results the histologic response is always higher with TCS than PPI despite the eos/hpf thresholds (Table 1).

- CR definition is heterogeneous among included papers (Figure 5): validated score (53%), symptoms assessment (33%) and non-validated score (14%). Proportion of patients experienced symptoms improvement is comparable among TCS and PPI while symptoms resolution and mean score reduction from baseline seem to be slightly higher with PPI (Table 1)
- ER is assessed using the endoscopic reference score (EREFS) mostly. Patients treated with TCS seem more severe at baseline than patients treated with PPI (4.27 vs. 3.8) while the mean reduction in the score post treatment is comparable (Table 1).
- No significant TRAE were found for PPI or esophageal dilatation while about 50% of patients treated with TCS experienced TRAE but only 1.4% leading to discontinuation (Figure 5). Most frequent events are infections (one third candidiasis)
- Finally, quality of life (QoL) was measured in 13 studies mainly using EoE-QoL-A score (N=7), only in 1 study the EQ-5D questionnaire was used. 5 studies reported an increase in QoL associated to PPI and TCS treatment and one study measured a positive significant correlation between endoscopic symptoms reduction and QoL improvement (p=0.61, p<0.001).

Figure 2. PRISMA FLOW diagram: paper included in the review

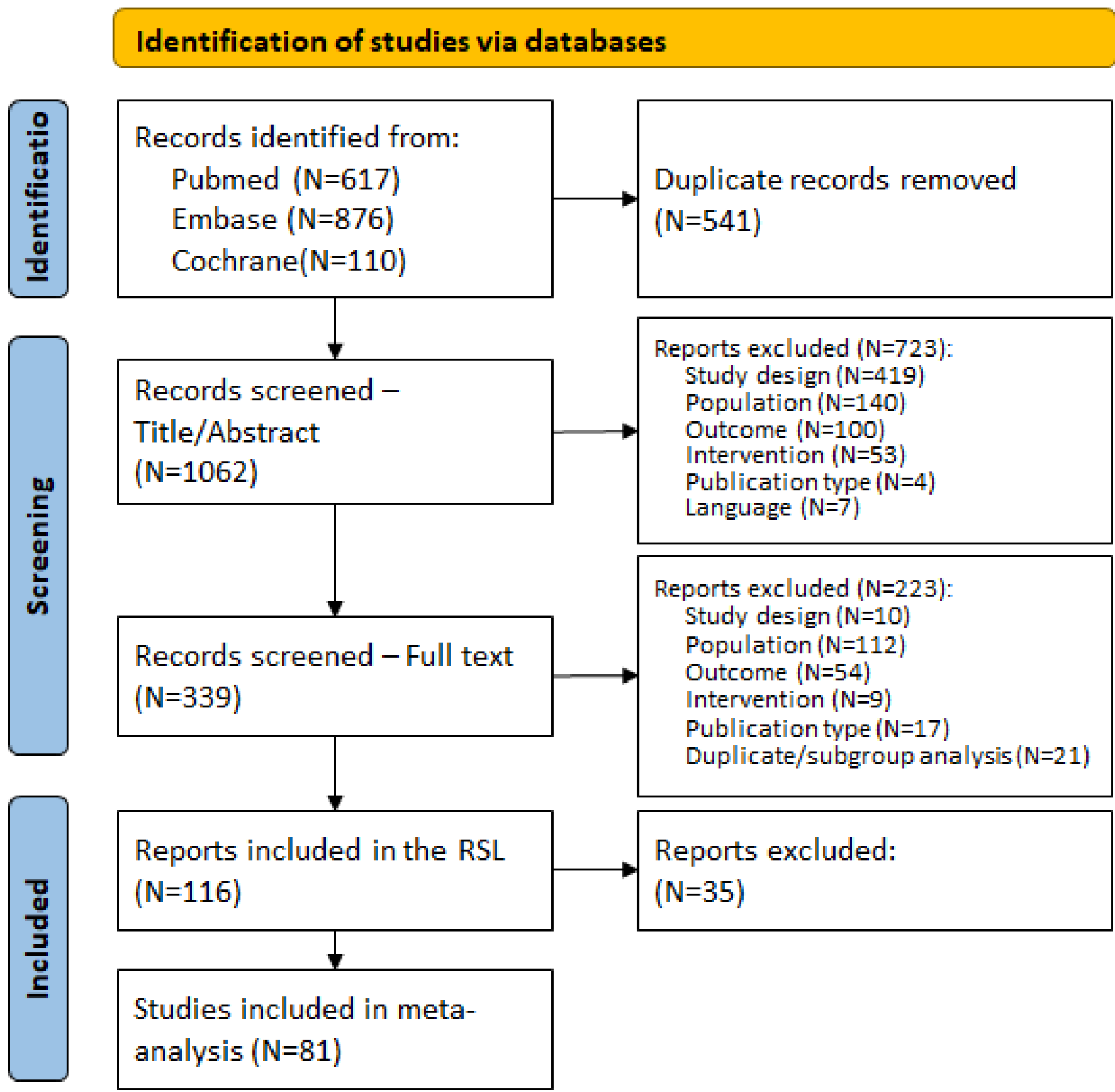


Figure 4. Number of studies investigating PPI and TCS efficacy

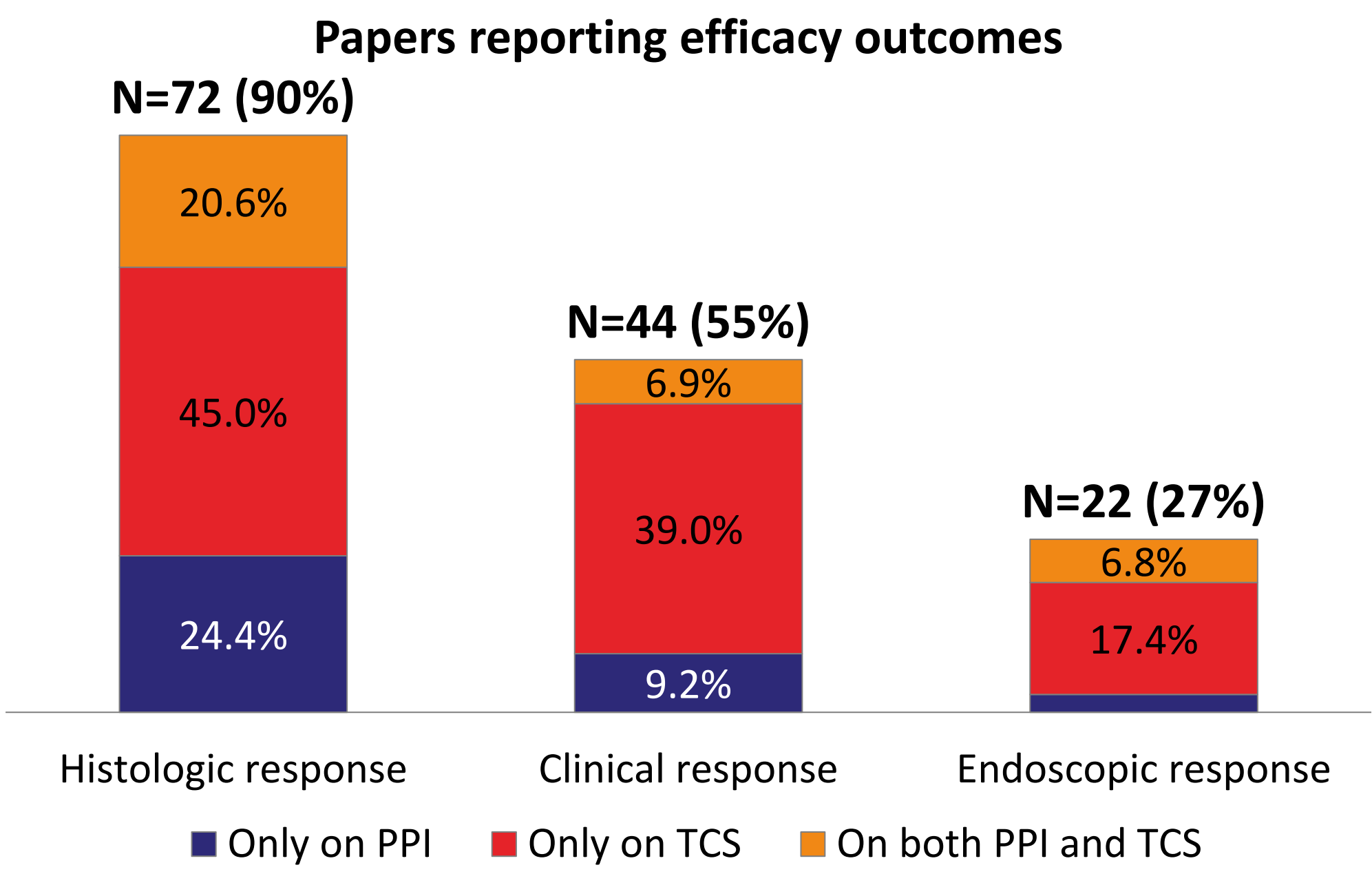


Figure 5. Instrument used to assess clinical response

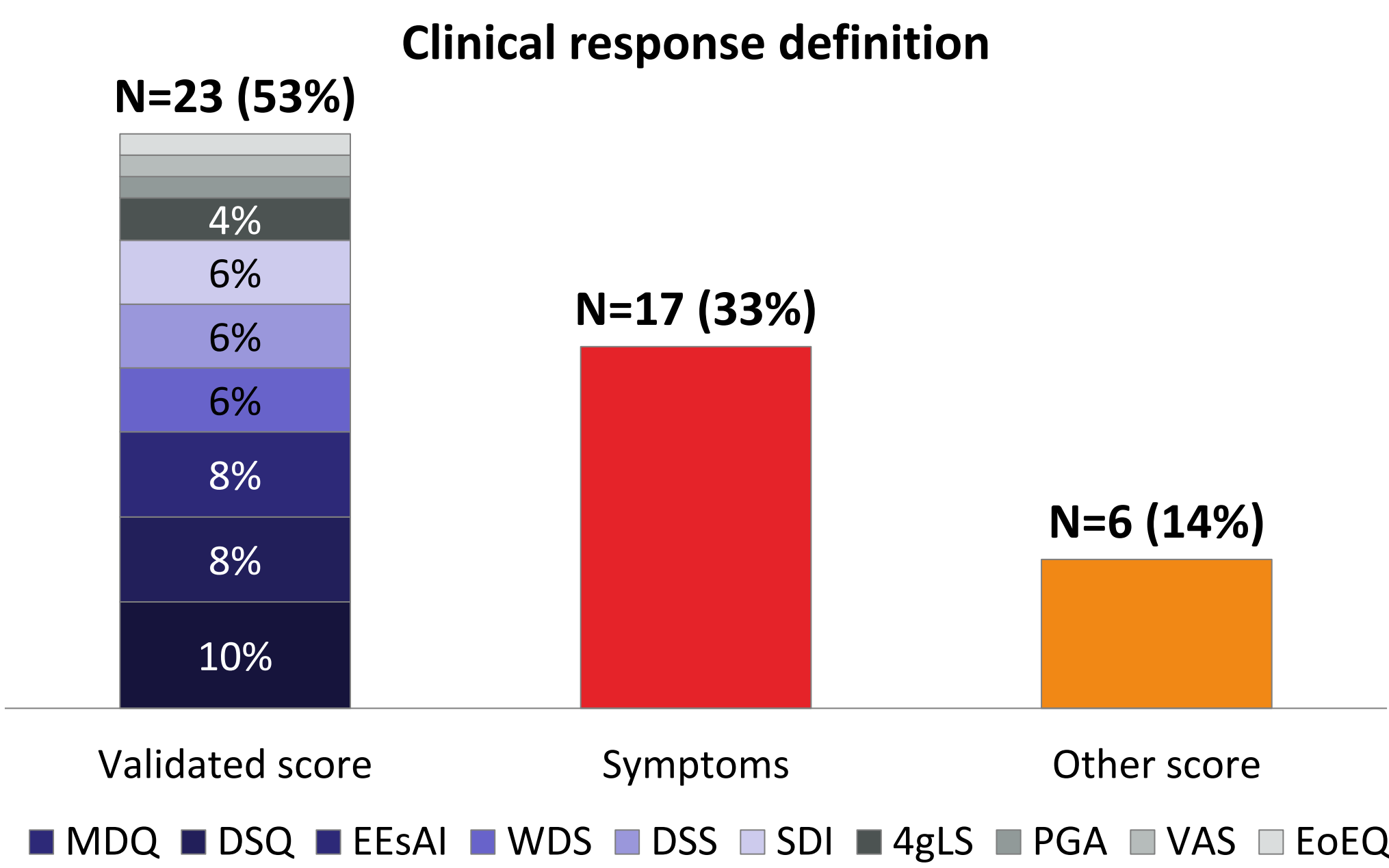


Figure 3. Description of the population enrolled in the included studies

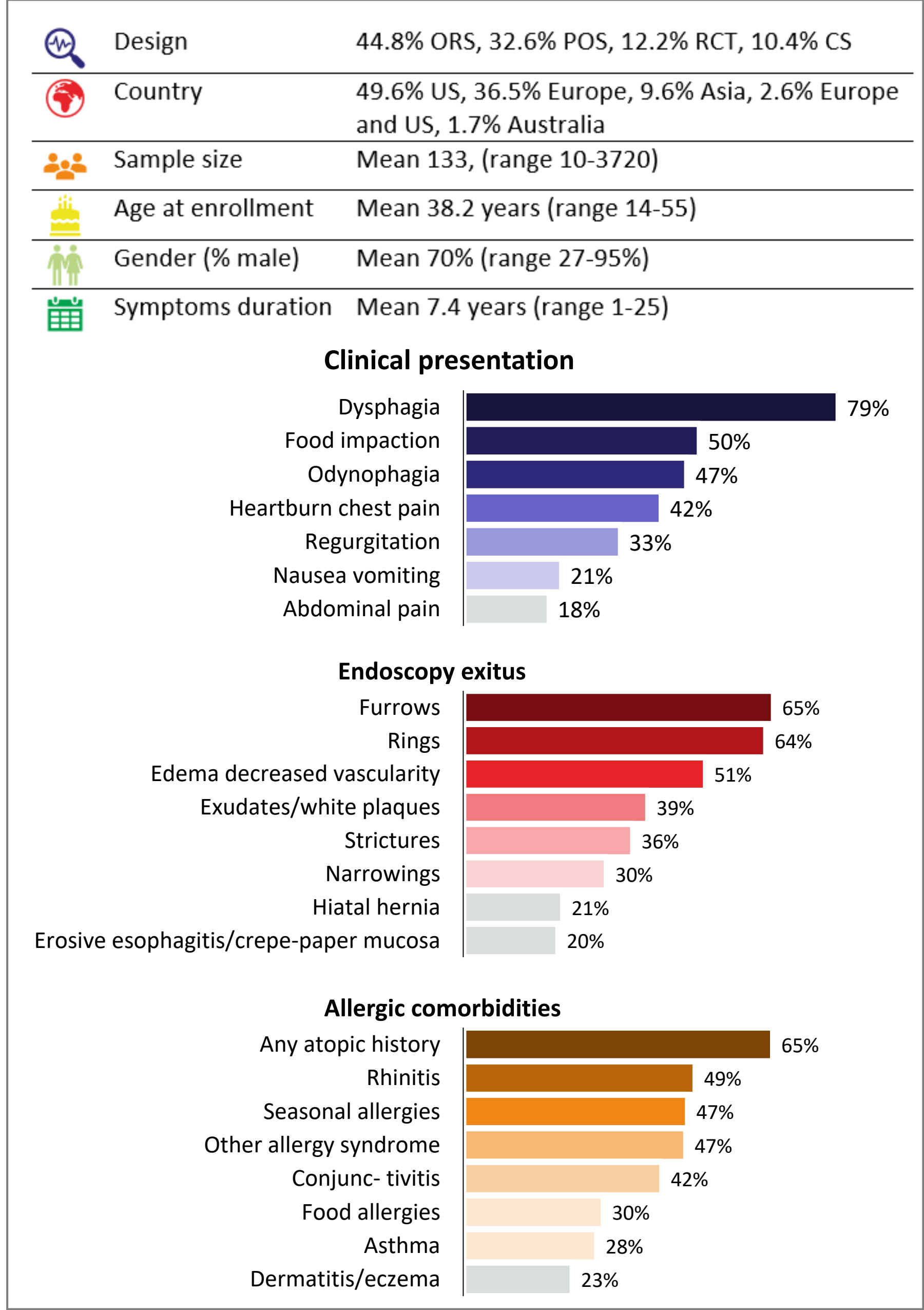
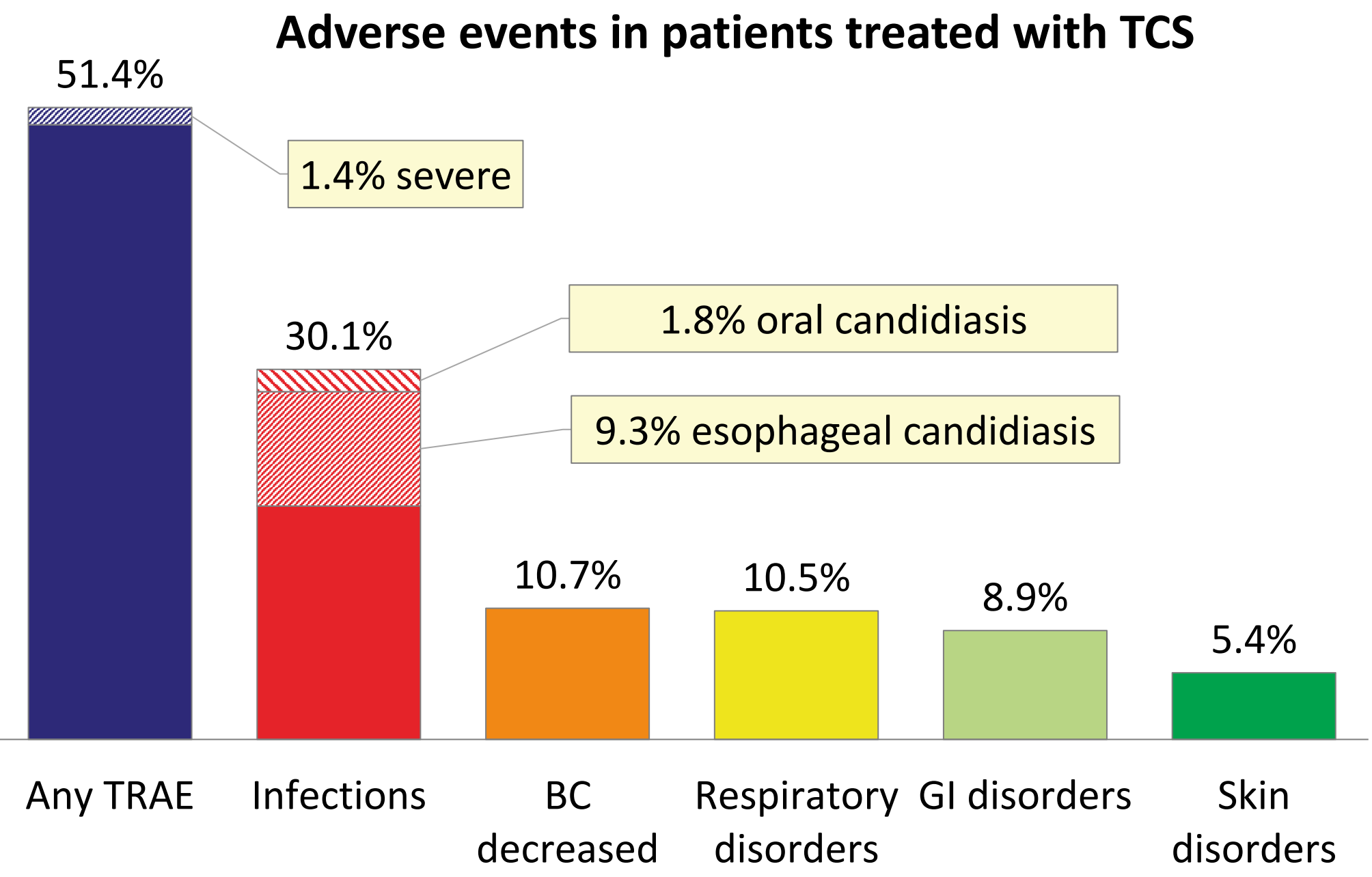


Table 1. Results of meta-analyses for the histologic, clinical and endoscopic outcomes

Efficacy outcome	PPI	TCS
Histologic response	Estimate (95% CI)	Estimate (95% CI)
% eos/hpf <15	45.0% (38.0 to 52.1)	64.0% (58.0 to 69.9)
% eos/hpf <5-7	32.7% (24.0 to 41.4)	55.7% (47.0 to 64.5)
% eos/hpf <1	25.1% (15.8 to 34.5)	45.0% (33.4 to 56.5)
Clinical response	Estimate (95% CI)	Estimate (95% CI)
% symptoms improvement	64.8% (51.9 to 77.7)	63.8% (55.3 to 72.4)
% symptoms resolution	54.4% (44.0 to 64.8)	46.2% (13.7 to 78.8)
SMD in symptoms' score	-1.98 (-3.12 to -0.84)	-1.09 (-1.40 to -0.82)
Endoscopic response	Estimate (95% CI)	Estimate (95% CI)
Baseline EREFS	3.03 (2.17 to 3.89)	4.27 (3.52 to 5.01)
Mean reduction	-1.72 (-2.09 to -1.34)	-1.76 (-2.40 to -1.11)

SMD: standardized mean difference

Figure 6. Adverse events in patients treated with TCS



BC: Blood cortisol; GI: gastrointestinal; TRAE: treatment related adverse events

Conclusions

- Efficacy of PPI and TCS in EoE patients ≥12 years has been deeply investigated in published literature while less information are available on adverse events associated to corticosteroids therapy. Quality of life associated to EoE drug-treatments should be further investigated.
- In summary, TCS are associated to better response than PPI but higher adverse events risk (generally not severe).
- In light of this literature review, who showed limited efficacy on disease control (clinical, histological and endoscopic) of EoE conventional therapies (PPI/TCS), there is still more than 35% of patients with a significant unmet medical need who can benefit from more effective and targeted treatments.

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Conflict of interest: PM and PL are employees of AdRes. FF, GR, BC and JPS are employees of Sanofi and may hold stock/stock options in Sanofi.