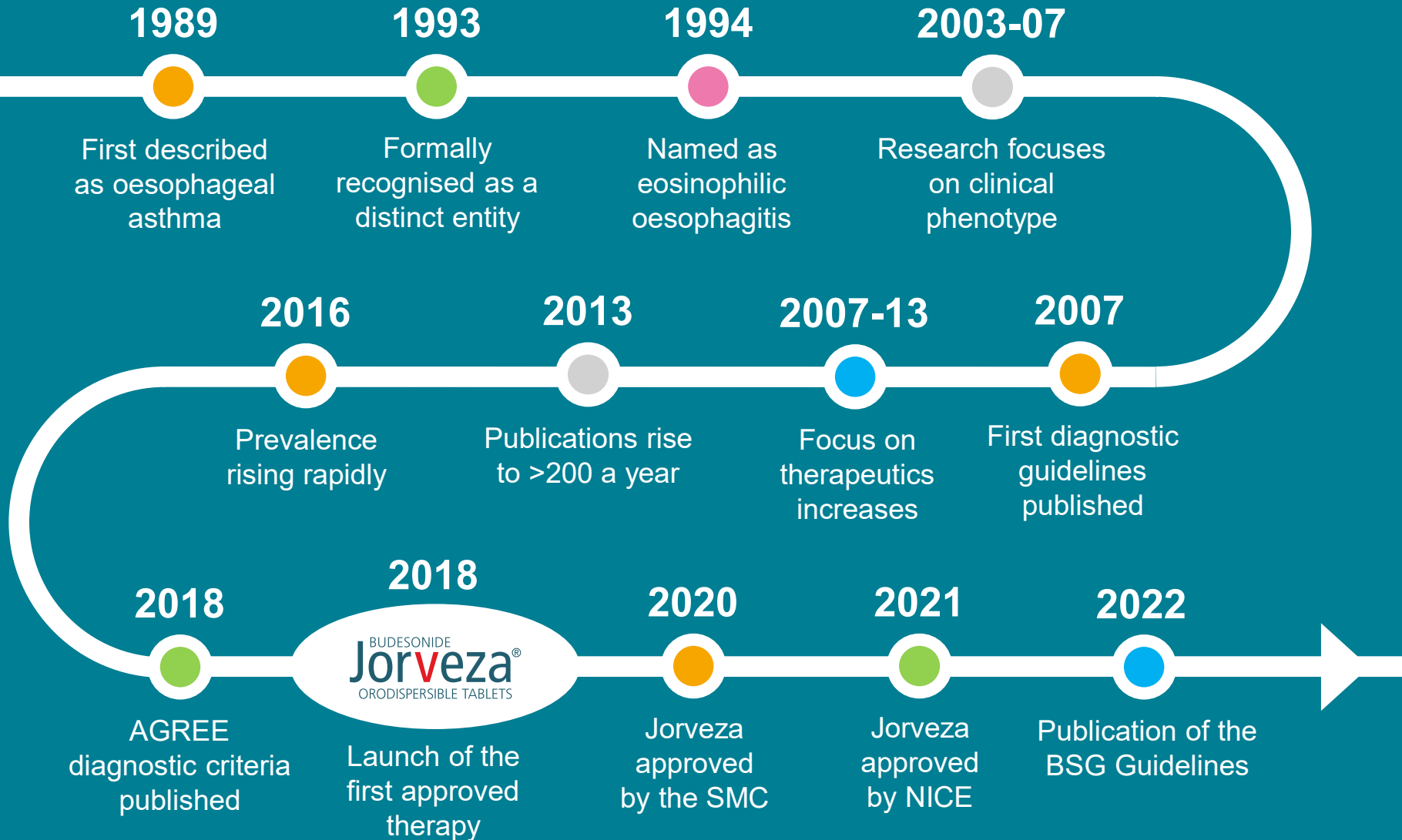


Eosinophilic oesophagitis background

Eosinophilic oesophagitis comes of age



AGREE: A working Group on ppi-REE
BSG: British Society of Gastroenterology
NICE: National Institute for Health and Care Excellence
SMC: Scottish Medicines Consortium

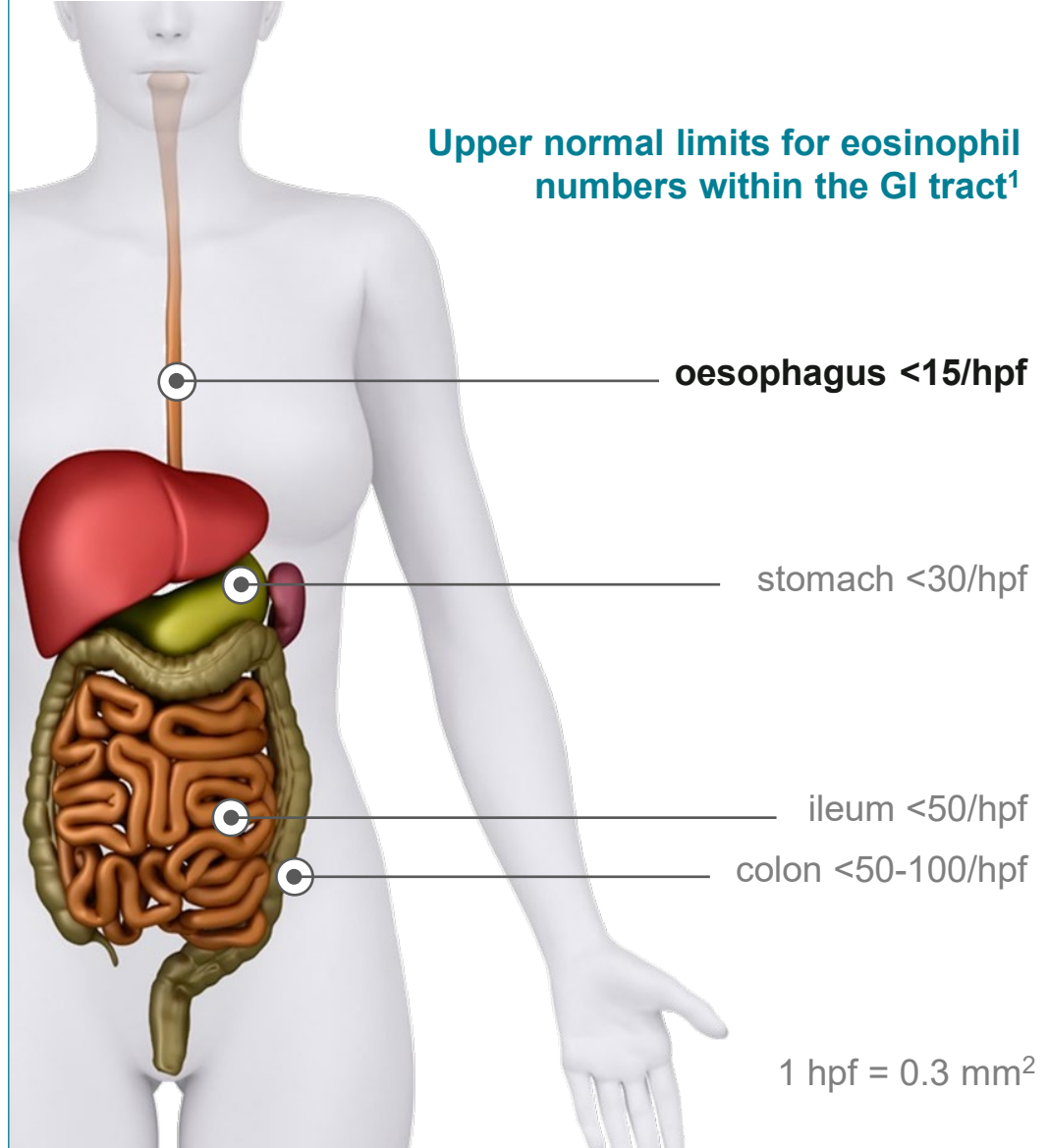
Eosinophil numbers typically increase as you go down the gut¹

1

Eosinophils are typically present throughout the GI tract since it is continuously exposed to foods, environmental allergens, toxins, and pathogens²

2

In healthy individuals, however, the oesophagus is unique in that eosinophils are generally absent²



1. Carr S, Watson W. Allergy Asth Immunol ma Clin 2011; 7(Suppl.1): S8.

2. Collins MH. Gastroenterol Clin North Am 2014; 43(2): 257-68.

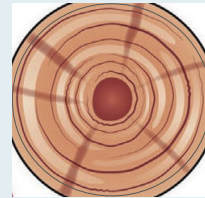
GI: gastrointestinal
hpf: high-power field

EoE is a chronic, progressive inflammatory disorder in which eosinophils infiltrate the oesophageal epithelium¹

Chronic eosinophilic inflammation leads to:^{2,3}

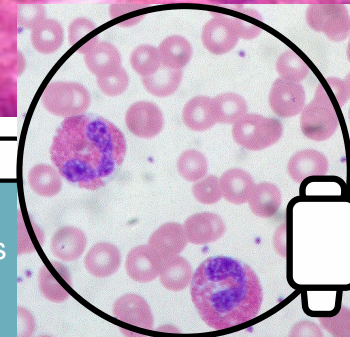
changes in oesophageal structure:

oesophageal rigidity, fibrostenotic features such as rings and ultimately strictures



changes in oesophageal function:

food feels like it is moving slowly/sticking in the chest after swallowing, food impaction



While symptoms such as swallowing difficulties point to EoE, it takes histology to confirm the diagnosis¹

EoE:

≥15 eos
per hpf
or
≥15 eos/
0.3 mm²

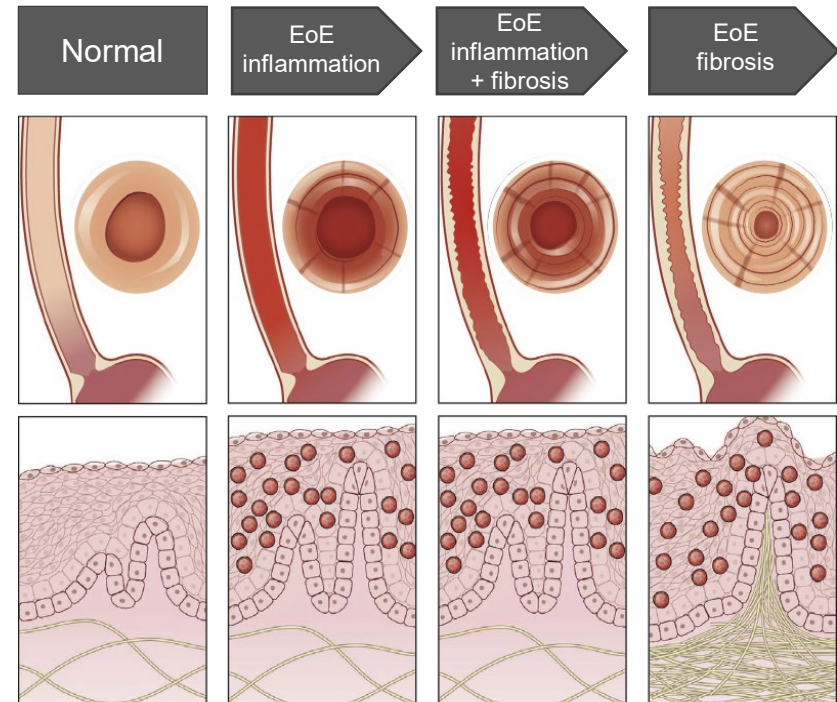
1. Oliva S, Dellon ES. Dig Liver Dis 2021; 53(11): 1476-8.
2. Attwood SE. Br J Hosp Med (Lond) 2019; 80(3): 132-8.
3. Dhar A *et al.* Gut 2022; 71(8): 1459-87.

EoE: eosinophilic oesophagitis
eos: eosinophils
hpf: high-power field

Natural history of EoE

- EoE is a relatively new disease, so uncertainties remain about its natural history and long-term consequences¹
- Untreated EoE is usually associated with persistent symptoms and inflammation, and it is thought that over time this leads to oesophageal remodelling resulting in stricture formation and functional abnormalities²
- There is some evidence that effective anti-inflammatory treatment may limit progression²
- There is no evidence that EoE is a pre-malignant condition²

Progression of EoE from inflammation to fibrosis*1



*Reprinted from *Gastroenterology*, vol. 154, Evan S, Dellon *et al.* Epidemiology and Natural History of Eosinophilic Esophagitis, 319-322. © 2018 with permission from Elsevier.

1. Dellon ES, Hirano I. *Gastroenterology* 2018; 154(2): 319-32.
2. Lucendo AJ *et al.* *United Eur Gastroenterol J* 2017; 5(3): 335-58.

Epidemiology of EoE

- A 2016 meta-analysis of 13 population-based studies from North America, Europe and Australia, examined the incidence and prevalence of EoE¹



EoE can now be classed as a **highly prevalent disorder**, with the incidence and prevalence rates rising further since this study was published²

1. Arias Á *et al.* *Aliment Pharmacol Ther* 2016; 43(1): 3-15.
2. Limketkai BN *et al.* *Gut* 2019; 68(12): 2152-60.

The progressive rise in the prevalence of EoE

Prevalence / 100,000 of the population¹⁻⁴



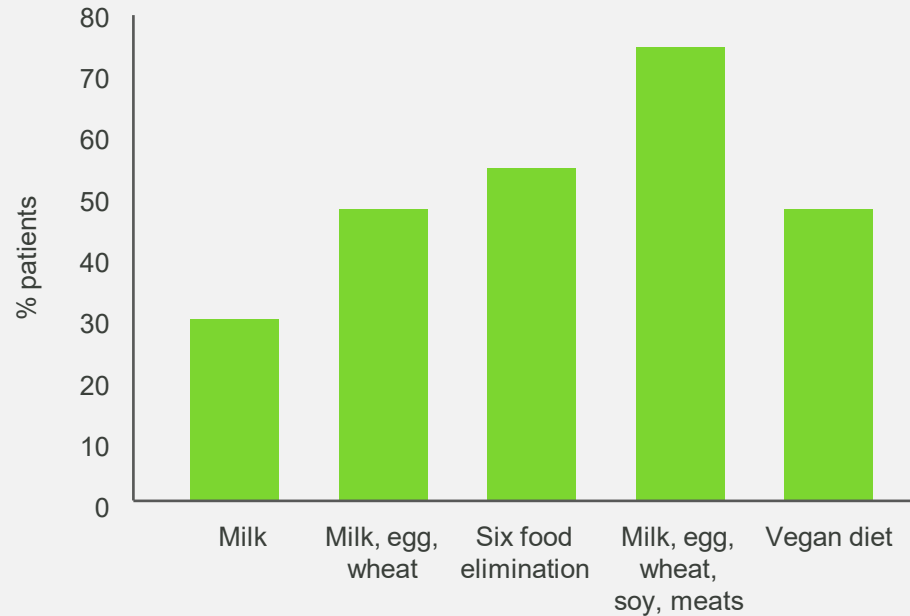
1. Navarro P *et al.* Aliment Pharmacol Ther 2019; 49(9): 1116-25.
2. Limketkai BN *et al.* Gut 2019; 68(12): 2152-60. (102,048 cases in population 133M)
3. Højgaard Allin K *et al.* United Eur Gastroenterol J 2022; 10(7): 640-50.
4. Plate J *et al.* United Eur Gastroenterol J 2022; 10(Suppl.8): 507.

EoE: eosinophilic oesophagitis

EoE is triggered by allergen exposure, typically food allergens

- Foods most commonly implicated in EoE are: milk, egg, wheat, soy, peanuts, beans, rye and beef¹
- The disease can be put into remission by removal of specific foods, either via elimination diets or hypoallergenic elemental formulas²

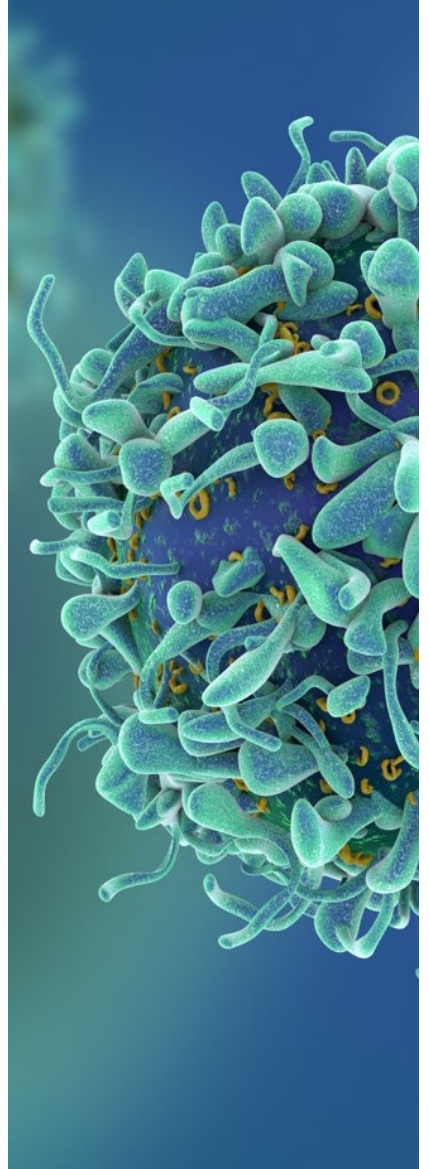
Success rate of various diet therapies in patients with EoE³



1. Ahmed M. World J Gastrointest Pharmacol Ther 2016; 7(2): 207-13.
2. Dellon ES, Hirano I. Gastroenterology 2018; 154(2): 319-32.
3. Spergel JM *et al.* J Allergy Clin Immunol 2012; 130(2): 461-7.

Immune system activation in EoE

- How the immune system is activated by food antigens in EoE isn't yet fully understood^{1,2}
 - food passage to the stomach is relatively rapid (within approximately 10 seconds)
 - the oesophageal mucosa is relatively impenetrable and lacking in antigen-presenting cells
 - ingested food is non-digested, with minimal exposure of antigen since it is enveloped in the complex food bolus
- In patients with active EoE, the oesophageal mucosal integrity is impaired³
 - it has been suggested that this could facilitate antigen penetration and subsequent activation of the immune system^{4,5}
 - complete avoidance of food allergens by an elemental diet restores the impaired oesophageal mucosal integrity³

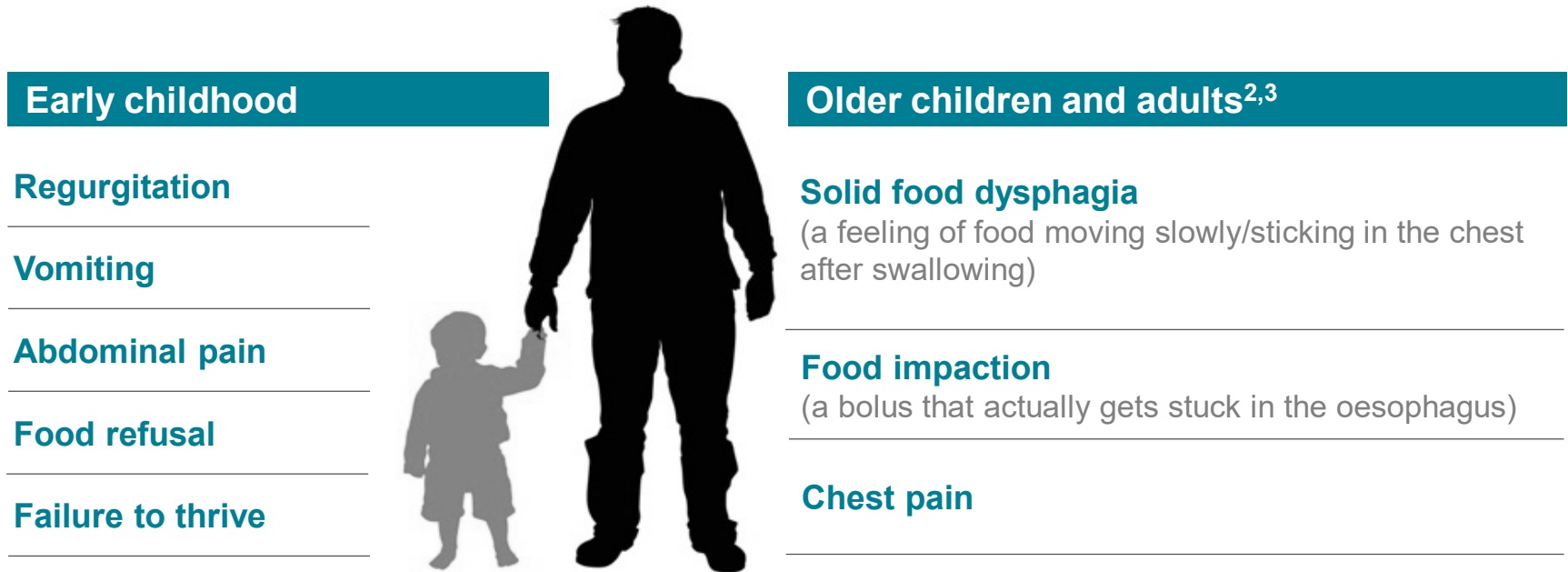


1. Katzka DA. Am J Gastroenterol 2017; 112(7): 1072-3.
2. Philpott H, Dellon ES. Gastroenterology 2017; 153(2): 605-6.
3. Warners MJ *et al.* Am J Gastroenterol 2017; 112(7): 1061-71.
4. Marietta EV *et al.* Aliment Pharmacol Ther 2017; 45(3): 427-33.
5. Kia L, Hirano I. Nat Rev Gastroenterol Hepatol 2015; 12(7): 379-86.

EoE: eosinophilic oesophagitis

The most common symptoms of EoE

- The clinical presentation of EoE tends to vary with patient age¹



While young children are more likely to present with non-specific symptoms, they may also present with dysphagia^{1,4}

1. Muir A, Falk GW. JAMA 2021; 326(13): 1310-18.
2. Biedermann L, Straumann A. Nat Rev Gastroenterol Hepatol 2023; 20(2): 101-19.
3. Attwood S, Epstein J. Frontline Gastroenterol 2020; 12(7): 644-9.
4. Fernandez-Becker NQ. Gastroenterol Clin North Am 2021; 50(4): 825-41.

What “dysphagia” means to those with EoE

- A patient with EoE typically has had the condition for many years¹
- As such, they can become used to the sensation of being aware of food travelling down the oesophagus^{1,2}
- They may adapt their eating in order to avoid these sensations, for example, drinking large amounts of water or only eating foods that are known to travel smoothly down the oesophagus¹
- They are prolonged chewers, slow to eat and the last to finish a meal²



1. Dellon ES. Available at: www.med.unc.edu/medicine/news/chairs-corner/podcast/eoe-dellon
Accessed on: 02/06/23.
2. Attwood S. Clin Med 2013; 13(6): s32-s35.

EoE-specific quality of life is correlated with symptoms and disease activity^{1,2}

- In a UK study, patients with EoE had reduced general energy/vitality levels – the condition also had a negative impact on their mental health¹
 - symptoms can be unpleasant, socially embarrassing and restricting^{1,3}
 - choking sensations can cause a sense of panic¹
 - ongoing or repeated courses of treatment may be required¹
 - serious complications requiring endoscopic dilatation may occur¹
 - dietary restrictions can lead to a significantly worse emotional impact³
- Reducing both symptoms and disease activity are important goals for improving QoL in adult patients²
 - having a diagnosis in itself can bring a sense of some relief¹



1. Hewett R *et al.* Dis Esophagus 2017; 30(1): 1-7.
2. Safroneeva E *et al.* Aliment Pharmacol Ther 2015; 42(8): 1000-10.
3. Lucendo AL *et al.* United European Gastroenterol J 2018; 6(1): 38-45.

EoE: eosinophilic oesophagitis
QoL: quality of life

Time to diagnosis of EoE is prolonged

- Despite increasing knowledge of the disease, the length of symptoms before a diagnosis of EoE is made is prolonged¹

Length of symptoms before diagnosis



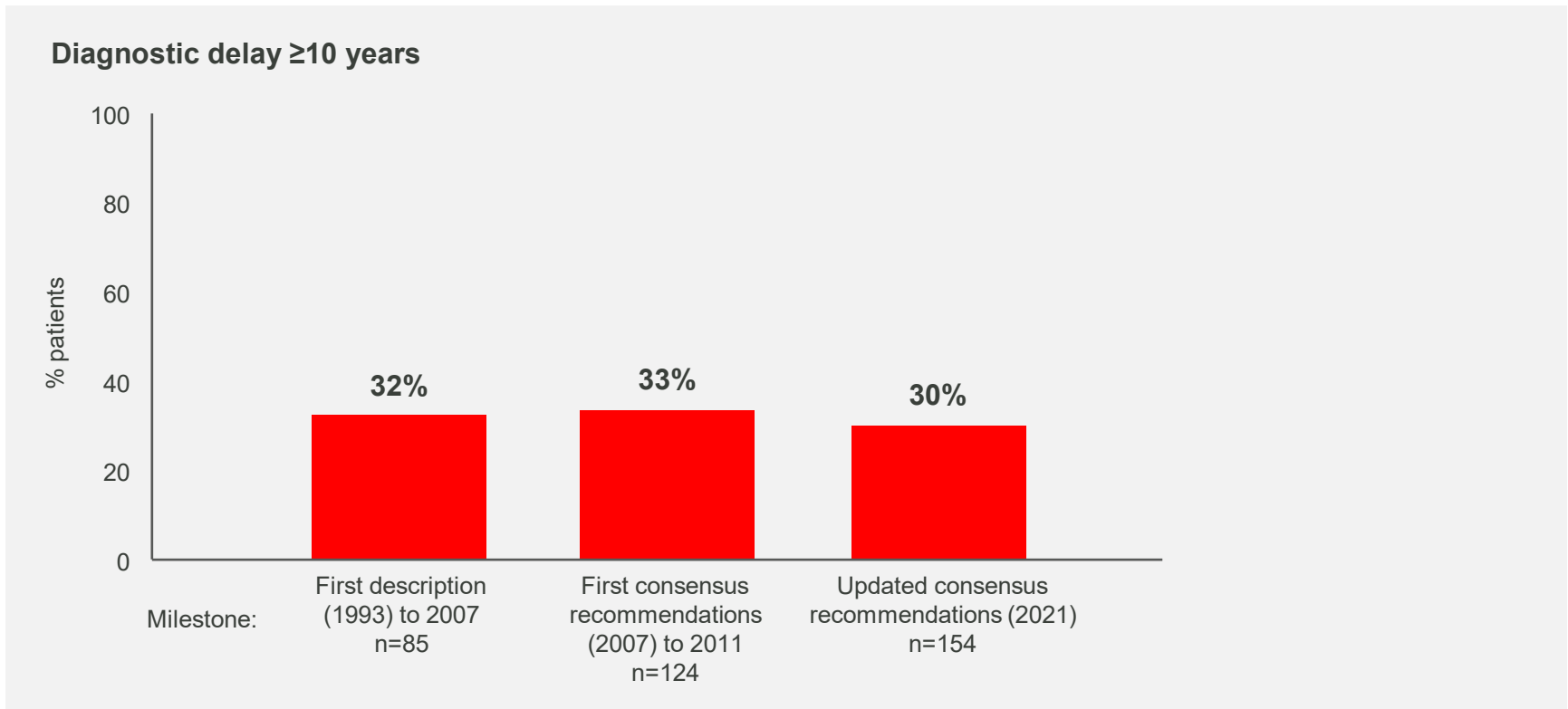
- With each additional year of undiagnosed EoE, the risk of stricture presence increases by 9%²

1. Reed CC *et al.* *Gastroenterology* 2017; 152(5, Suppl.1): S865.
2. Warners MJ *et al.* *Am J Gastroenterol* 2018; 113(6): 836-44.



Substantial efforts are warranted to increase awareness for EoE¹

- A persistently stable fraction of roughly one-third of all patients wait over 10 years for a diagnosis¹



Diagnosing EoE – a UK DGH experience¹

- Study investigating management of patients presenting with symptoms conducive with EoE to two district general hospitals over a year

Patients presenting with dysphagia/FBO undergoing gastroscopy (n=442)	
Female	58%
Average age	65
% of patients biopsied	50%
% of patients biopsied suspected of having EoE	40%
% of biopsies positive for EoE	8%

“EoE detection is likely to improve further if all patients with symptoms conducive with EoE (e.g. solid food dysphagia) routinely trigger an EoE biopsy protocol”

1. Osuha H *et al.* Gut 2015; 64(Suppl.1): A21.

DGH: district general hospital
EoE: eosinophilic oesophagitis
FBO: food bolus obstruction

Predicting EoE in dysphagic adults with a normal endoscopy¹

- Study investigating clinical risk factors predictive for EoE that could guide the endoscopist for when to take biopsies, thereby saving time and money

Patients presenting with dysphagia/FBO and a new diagnosis of EoE (eosinophils >15/hpf) (n=127)		Patients presenting with dysphagia/FBO but no evidence of EoE on biopsies (n=127)		“In patients presenting with dysphagia or FBO and a normal endoscopy, utilising a simple bedside tool comprising of age (<46 years) and male sex can reliably predict the presence of EoE”
Male	75%	Male	46%	
Average age	39	Average age	60	

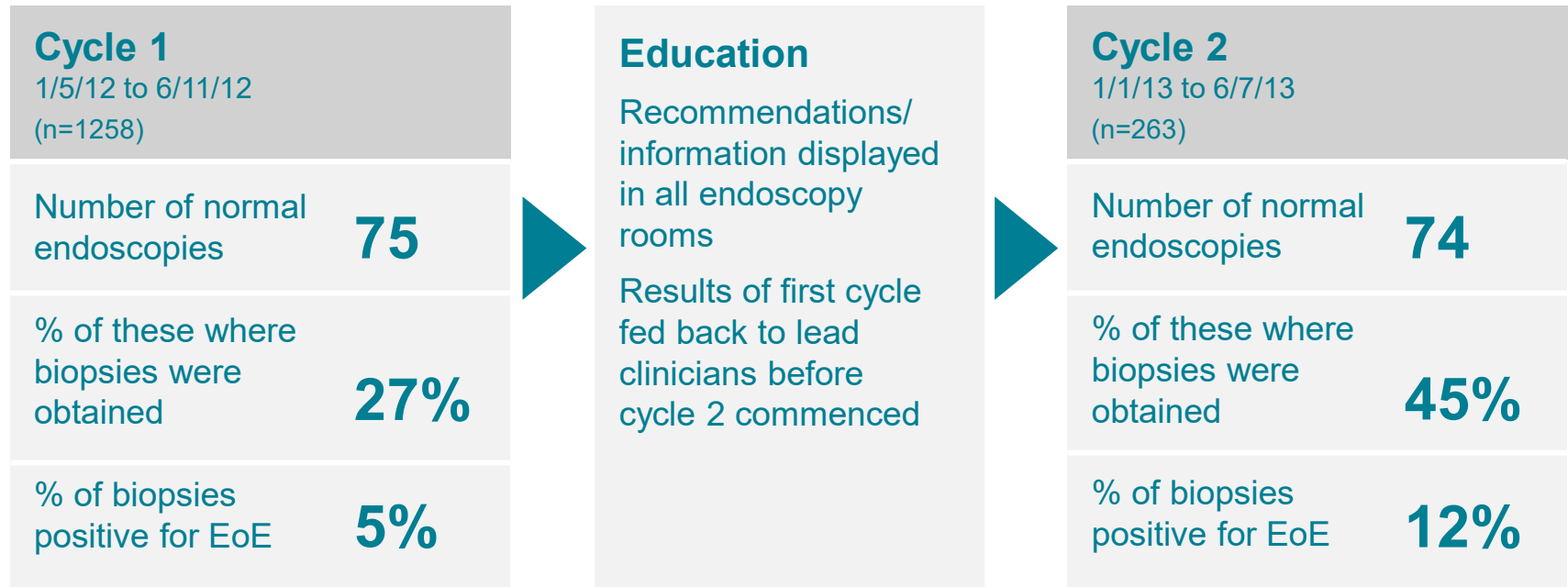
- A multivariate logistic regression analysis identified age ($p<0.001$) and sex ($p<0.001$) as the strongest predictors of EoE
 - the optimal cut-off for age was 46 years (sensitivity: 86%, specificity: 69%)

1. Ibraheim H *et al.* Gut 2017; 66(Suppl.2): A18-19.

EoE: eosinophilic oesophagitis
FBO: food bolus obstruction
hpf: high-power field

EoE diagnostic rates can be improved by education¹

- Study investigating the adherence to guidelines recommending obtaining biopsies in patients with dysphagia who have normal endoscopies



1. Davies A *et al.* Gut 2014; 63(Suppl.1): A46.

Differential diagnosis¹

Patient characteristics	Eosinophilic oesophagitis	Gastro-oesophageal reflux disease	Oesophageal cancer	Dysmotility
Dysphagia	Intermittent / continuous	Unusual	Progressive / continuous	Intermittent with long history
Heartburn	Less common	Characteristic	Previous history	Rare
Chest pain	Can be prominent feature	May occur	Rare	Common
Food impaction	Common	Rare	May occur rarely	Rare / occasional
Vomiting	More common in children	Rare	Rare	No
Regurgitation	Infrequent but secondary to food being stuck	Common but from stomach contents with foul taste	Infrequent but secondary to food being stuck	May occur
History of atopy	Common	No	No	No
Age	Uncommon >60	Any age	>50	Any age
Diagnostic tests				
Endoscopy	Oesophageal rings and vertical furrows may be seen	Distal oesophagitis / distal strictures may be seen	Diagnostic of a tumour	Frequently normal
Biopsy	>15 eos/hpf or >15 eos/0.3 mm ²	<5 eos/hpf or <5 eos/0.3 mm ²	Diagnostic	Normal
Barium swallow	May show strictures or narrow bore oesophagus	May show distal strictures	Can be diagnostic	May show dilation
24-hour pH studies	Normal	Abnormal	N/A	Usually normal
Manometry	Normal or distal obstruction	May be normal or hypomotility	Normal or obstruction	Diagnostic of dysmotility

1. Working Group. Data on file, Dr Falk.

eos: eosinophils
hpf: high-power field

Prescribing information

Please click on the following link for the prescribing information:

<https://www.dr Falk.co.uk/jorveza-1mg-oro-dipsersible-tablet/>

Jorveza® (budesonide) is indicated for the treatment of eosinophilic oesophagitis (EoE) in adults (older than 18 years of age)

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.mhra.gov.uk (UK residents) or www.hpra.ie (Irish residents). Adverse events should also be reported to Dr Falk Pharma UK Ltd at pv@drfalkpharma.co.uk.

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UK--2300098 Date of preparation: July 2023