The Hidden Clinical and Economic Costs of PPI Treatment Failures in Severe Erosive Oesophagitis

EE710

P. Svangren [1], P. Miller [2]

[1] Svangren Life Science Consulting, Barsebäck, Sweden, per@svangrenconsulting.com [2] Miller Economics LTD, Alderley Edge, United Kingdom, paul@millereconomicsltd.com

Unhealed Severe Erosive Oesophagitis:
A clinical and economic tipping point - driving progression to serious complications, major surgery, and even cancer, while profoundly diminishing quality of life.

INTRODUCTION

Severe erosive oesophagitis (LA grades C/D) causes significant suffering through persistent heartburn, regurgitation, and sleep disturbance. While proton pump inhibitors (PPIs) remain the standard treatment, a substantial proportion of patients remain unhealed despite 8 weeks of therapy.

Key question: What happens to patients who don't heal?

Current guidelines[1, 2] recommend PPI optimization strategies - switching, dose escalation, or adding H2 antagonists - but the downstream clinical and economic impact of persistent non-healing remains poorly understood in the UK context.

OBJECTIVE

This research aims to understand the clinical and economic consequences of unhealed severe erosive oesophagitis and explore 3 key research questions:

- How many patients with severe erosive oesophagitis remain unhealed despite standard-of-care treatments?
- What are the clinical consequences of unhealed severe erosive oesophagitis?
- What are the economic consequences of unhealed severe erosive oesophagitis?

METHOD

We conducted a systematic literature review update building on NICE CG184 evidence (to September 2012), searching for RCT data on PPI efficacy in severe erosive oesophagitis from 2012 onwards.

Targeted literature reviews identified clinical complications and healthcare resource utilization associated with unhealed disease in the UK NHS setting.

Key focus: Healing rates at 8 weeks, relapse during maintenance, progression to complications, and associated costs.

RESULTS

Non-healing remains common

- Around **10-30%** of patients (Figure 1) with severe erosive oesophagitis remain unhealed after 8 weeks of standard-dose PPI therapy across multiple RCTs, regardless of which PPI is used.
- During maintenance treatment, **16-45%** (Figure 2) experience relapse depending on the regimen.

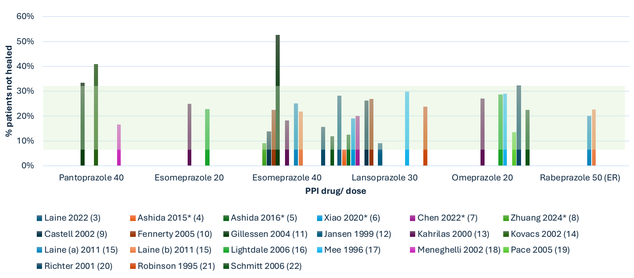

Figure 1: RCT evidence - % of erosive esophagitis patients (LA Grade C or D) not healed at 8 weeks

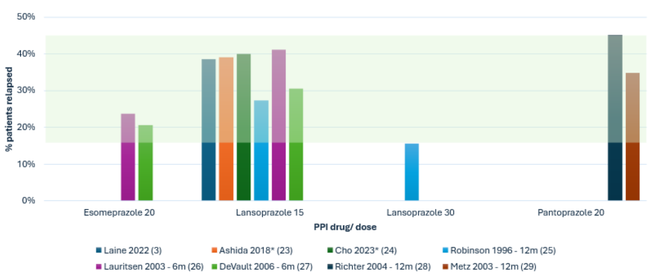

Figure 2: RCT evidence - % erosive esophagitis patients (LA Grade C or D) relapsed during maintenance treatment

Clinical cascade [2, 30-33]

Unhealed disease triggers a progression pathway:

- Around **11%** develop strictures requiring repeated dilation
- Circa **5-10%** progress to Barrett's oesophagus requiring ablation and lifelong surveillance
- An estimated **29%** per year with high-grade dysplasia develop oesophageal adenocarcinoma (OA)
- The 5-year (OA) cancer survival is **20%**

Quality of life [36]

Patients with unhealed disease experience utility as low as 0.56 (vs 0.86 in general population), with nocturnal symptoms severely impacting sleep and daily function.

Economic impact [1, 34, 35]

The journey from unhealed oesophagitis through complications generates substantial costs (Figure 3).

Most patients will have specialist referral and diagnostic endoscopy (up to £929). Many will be considered for Fundoplication surgery (£7,143 - £8,756).

Patients developing strictures will need dilation treatment (£1,120 day case - £2,261elective inpatient), which may be repeated. Those developing Barrett's oesophagus will need endoscopic radiofrequency ablation (£1,120 day case - £2,261elective inpatient) and regular endoscopic monitoring (£650 - £745).

Oesophageal adenocarcinoma is treated with chemoradiotherapy/ chemotherapy (£3,268 -£7,298) +/- Pembrolizumab (£35,000+) and/or surgical resection: oesophagectomy (£8,567 - £16,052).

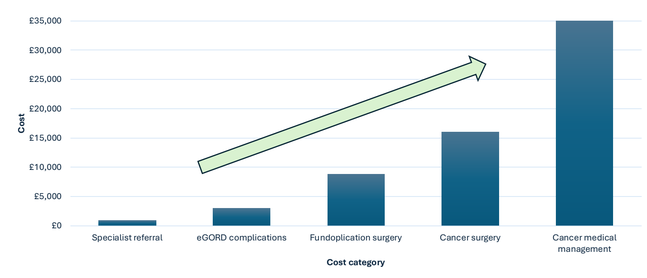

Figure 3: Economic consequences of unhealed oesophagitis (UK NHS costs 2023/24)

CONCLUSIONS

Severe erosive oesophagitis that remains unhealed represents a critical unmet clinical need with serious consequences. Current treatments, including double-dose proton pump inhibitor (PPI) therapy, often fail, leaving a substantial patient population refractory to care. Treatment failure leads to:

- Increased specialist referrals and surgical interventions
- Long-term complications
- Significant quality of life impairment

These issues contribute to a considerable clinical and economic burden.

There is an urgent need for therapeutic alternatives beyond conventional PPI approaches.

The economic rationale for investing in improved treatments is strong due to the high costs associated with treatment failure and complications.

REFERENCES

1. NICE (2019) Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. National Institute for Health and Care Excellence. https://www.nice.org.uk
2. Chait MM. Optimal Management of Erosive Esophagitis: An Evidence-based and Pragmatic Approach. J Transl Gastroenterol. 2025;3(1):39-46.
3. Laine L, DeVault K, Katz P, et al. Vonoprazan versus lansoprazole for healing and maintenance of healing of erosive esophagitis: a randomized trial. Gastroenterology. 2022;164:61–71
4. Ashida K, Sakurai Y, Nishimura A, et al. Randomised clinical trial: a dose-ranging study of vonoprazan, a novel potassium-competitive acid blocker, vs lansoprazole for the treatment of erosive oesophagitis. Aliment Pharmacol Ther 2015;42:685–695
5. Ashida K, Sakurai Y, Hori T, et al. Randomised clinical trial: vonoprazan, a novel potassium-competitive acid blocker, vs lansoprazole for the healing of erosive oesophagitis. Aliment Pharmacol Ther 2016;43:240–251
6. Xiao Y, Zhang S, Dai N, et al. Phase III, randomised, double-blind, multicentre study to evaluate the efficacy and safety of vonoprazan compared with lansoprazole in Asian patients with erosive oesophagitis. Gut 2020; 69:224–230
7. Chen S, Liu D, Chen H, et al. The efficacy and safety of keverprazan, a novel potassium-competitive acid blocker, in treating erosive oesophagitis: a phase III, randomised, double-blind multicentre study. Aliment Pharmacol Ther 2022;55:1524–1533
8. Zhuang Q, Liao A, He Q, et al. The efficacy and safety of fexuprazan in treating erosive esophagitis: a phase III, randomized, double-blind, multicenter study. J Gastroenterol Hepatol 2024;39:658–666
9. Castell DO, Kahrilas PJ, Richter JE, Vakil NB, Johnson DA, Zuckerman S et al. Esomeprazole (40 mg) compared with lansoprazole (30 mg) in the treatment of erosive esophagitis. Am J Gastroenterol 2002; 97(3):575-583
10. Fennerty MB, Johanson JF, Hwang C, Sostek M. Efficacy of esomeprazole 40 mg vs lansoprazole 30 mg for healing moderate to severe erosive oesophagitis. Aliment Pharmacol Ther 2005; 21(4):455-463
11. Gillessen A, Beil W, Modlin IM, Gatz G, Hole U. 40 mg pantoprazole and 40 mg esomeprazole are equivalent in the healing of esophageal lesions and relief from gastroesophageal reflux disease-related symptoms. J Clin Gastroenterol 2004; 38(4):332-340
12. Jansen JB, Van Oene JC. Standard-dose lansoprazole is more effective than high-dose ranitidine in achieving endoscopic healing and symptom relief in patients with moderately severe reflux oesophagitis. The Dutch Lansoprazole Study Group. Aliment Pharmacol Ther 1999; 13(12):1611-1620
13. Kahrilas PJ, Falk GW, Johnson DA, Schmitt C, Collins DW, Whipple J et al. Esomeprazole improves healing and symptom resolution as compared with omeprazole in reflux oesophagitis patients: a randomized controlled trial. The Esomeprazole Study Investigators. Aliment Pharmacol Ther 2000; 14(10):1249-1258.
14. Kovacs TO, Wilcox CM, DeVault K, Miska D, Bochenek W. Comparison of the efficacy of pantoprazole vs nizatidine in the treatment of erosive oesophagitis: a randomized, active-controlled, double-blind study. Aliment Pharmacol Ther 2002; 16(12):2043-2052
15. Laine L, Katz PO, Johnson DA, Ibegbu I, Goldstein MJ, Chou C et al. Randomised clinical trial: a novel rabeprazole extended release 50 mg formulation vs esomeprazole 40 mg in healing of moderate-to-severe erosive oesophagitis - the results of two double-blind studies. Aliment Pharmacol Ther 2011; 33(2):203-212
16. Lightdale CJ, Schmitt C, Hwang C, Hamelin B. A multicenter, randomized, double-blind, 8-week comparative trial of low-dose esomeprazole (20 mg) and standard-dose omeprazole (20 mg) in patients with erosive esophagitis. Dig Dis Sci 2006; 51(5):852-857
17. Mee AS, Rowley JL. Rapid symptom relief in reflux oesophagitis: a comparison of lansoprazole and omeprazole. Aliment Pharmacol Ther 1996; 10(5):757-763
18. Meneghelli UG et al. Efficacy and tolerability of pantoprazole versus ranitidine in the treatment of reflux esophagitis and the influence of Helicobacter pylori infection on healing rate. Dis Esophagus 2002; 15(1):50-56
19. Pace F, Annese V, Prada A, Zambelli A, Casalini S, Nardini P et al. Rabeprazole is equivalent to omeprazole in the treatment of erosive gastro-oesophageal reflux disease. A randomised, double-blind, comparative study of rabeprazole and omeprazole 20 mg in acute treatment of reflux oesophagitis, followed by a maintenance open-label, low-dose therapy with rabeprazole. Dig Liver Dis 2005; 37(10):741-750
20. Richter JE, Kahrilas PJ, Johanson J, Maton P, Breiter JR, Hwang C et al. Efficacy and safety of esomeprazole compared with omeprazole in GERD patients with erosive esophagitis: a randomized controlled trial. Am J Gastroenterol 2001; 96(3):656-665
21. Robinson M, Sahba B, Avner D, Jhala N, Greski-Rose PA, Jennings DE. A comparison of lansoprazole and ranitidine in the treatment of erosive oesophagitis. Multicentre Investigational Group. Aliment Pharmacol Ther 1995; 9(1):25-31
22. Schmitt C, Lightdale CJ, Hwang C, Hamelin B. A multicenter, randomized, double-blind, 8-week comparative trial of standard doses of esomeprazole (40 mg) and omeprazole (20 mg) for the treatment of erosive esophagitis. Dig Dis Sci 2006; 51(5):844-850
23. Ashida K, Iwakiri K, Hiramatsu N, et al. Maintenance for healed erosive esophagitis: phase III comparison of vonoprazan with lansoprazole. World J Gastroenterol 2018;24:1550–1561
24. Cho YK, Kim JH, Kim HS, et al. Randomised clinical trial: comparison of tegoprazan and lansoprazole as maintenance therapy for healed mild erosive oesophagitis. Aliment Pharmacol Ther 2023;57:72–80
25. Robinson M, Lanza F, Avner D, Haber M. Effective maintenance treatment of reflux esophagitis with low-dose lansoprazole. A randomized, double-blind, placebo-controlled trial. Ann Intern Med 1996; 124(10):859–867
26. Lauritsen K, Deviere J, Bigard MA, Bayerdorffer E, Mozsik G, Murray F et al. Esomeprazole 20 mg and lansoprazole 15 mg in maintaining healed reflux oesophagitis: Metropole study results. Aliment Pharmacol Ther 2003; 17 Suppl 1:24–27.
27. DeVault KR, Johanson JF, Johnson DA, Liu S, Sostek MB. Maintenance of healed erosive esophagitis: a randomized six-month comparison of esomeprazole twenty milligrams with lansoprazole fifteen milligrams. Clin Gastroenterol Hepatol 2006; 4(7):852–859.
28. Richter JE, Fraga P, Mack M, Sabesin SM, Bochenek W. Prevention of erosive oesophagitis relapse with pantoprazole. Aliment Pharmacol Ther 2004; 20(5):567–575.
29. Metz DC, Bochenek WJ. Pantoprazole maintenance therapy prevents relapse of erosive oesophagitis. Aliment Pharmacol Ther 2003; 17(1):155–164.
30. Yadlapati R, Hubscher E, Pelletier C, Jacob R, Brackley A, Shah S. Induction and maintenance of healing in erosive esophagitis in the United States. Expert Rev Gastroenterol Hepatol. 2022 Oct;16(10):967-980
31. Shaheen NJ, Patel DA, Abeynayake I, Bui B, Gopal M, Jacob R, Chastek B, Steiger C, Shah ED. Economic and treatment burden among newly diagnosed patients with erosive esophagitis in the US: a national retrospective cohort study. Diseases of the Esophagus (2025), 38,1–10
32. Katz PO, Gerson LB, Vela MF. Guidelines for the Diagnosis and Management of Gastroesophageal Reflux Disease. American Journal of Gastroenterology 108(3):p 308-328, March 2013
33. Mei-Juan L, Qing L, Min S, Li-Qin L. Comparative effectiveness and acceptability of the FDA-licensed proton pump inhibitors for erosive esophagitis. A PRISMA-compliant network meta-analysis. Medicine 96(39):p e8120, September 2017
34. UK NHS costs (NHS England: National Schedule of costs 2023/24; last updated 29/7/25) https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/
35. https://www.nice.org.uk/guidance/ta737
36. Grant et al (2008). The effectiveness and cost-effectiveness of minimal access surgery amongst people with gastro-oesophageal reflux disease – a UK collaborative study. The REFLUX trial. Health Technology Assessment 2008; Vol. 12: No. 31.

* Asian patients only study

FINANCIAL DISCLOSURE: This research was funded by Cinclus Pharma Holding AB, Sweden