



Topic Exploration Report ¹

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Report number	TER567
Topic	Gastroelectrical stimulation for the treatment of adults with severe, intractable gastroparesis
Summary of findings	<p>Gastroparesis is a chronic disorder characterised by delayed emptying of the stomach in the absence of mechanical obstruction. In severe cases, people may suffer dehydration, poor nutritional status and poor glycaemic control (in diabetics) which may require hospitalisation.</p> <p>A proportion of patients will be refractory to diet, medical and surgical interventions for gastroparesis. Gastroelectrical stimulation is an option for people with severe, intractable gastroparesis. The procedure involves a device, designed to stimulate the stomach, being placed under the skin of the abdomen. It sends electrical impulses to the stomach muscles to help them to work more normally.</p> <p>The National Institute for Health and Care Excellence (NICE) published Interventional Procedures Guidance Evidence in 2014, which supports the use of gastroelectrical stimulation gastroparesis. However, in 2016, the NHS Clinical Commissioning Policy did not recommend gastroelectrical stimulation for gastroparesis, even though it was largely based on the same evidence.</p> <p>NICE and NHS England guidance were mainly based on observational studies, but they also included two randomised controlled trials. Since this guidance, we identified an additional meta-analysis, randomised controlled trial and two economic evaluations.</p> <p>The evidence published since NICE and NHS England guidance appears to show benefits for reduction in vomiting, but does not show that gastroelectrical stimulation improves overall symptoms, quality of life, or accelerates gastric emptying for people with gastroparesis.</p> <p>Available economic evidence suggests that gastroelectrical stimulation may lead to improvements in quality of life and is cost-effective. It may also reduce costs associated with gastroparesis or vomiting. However, this evidence is based on uncontrolled studies and so must be interpreted with caution.</p>

¹ [Cyfieithu dogfennau HTW wedi'u cyhoeddi o'r Saesneg i'r Gymraeg](#)
[Translation of published technical HTW documents from English into Welsh](#)

Introduction and aims

Gastroparesis is a chronic disorder characterised by delayed emptying of the stomach in the absence of mechanical obstruction (NHS England 2016). Symptoms include nausea and vomiting. In severe cases, people may suffer dehydration, poor nutritional status and poor glycaemic control (in diabetics) which may require hospitalisation. A high prevalence of gastroparesis has been reported in people with diabetes (NHS England 2016). The prevalence of severe, symptomatic, and medically-refractory gastroparesis in the United States population was estimated at 17 per 100,000 people (Alberta Heritage Foundation for Medical Research, 2006).

Gastroparesis is usually managed by a change in diet, and/or anti-emetic medication (NHS England 2016). In cases of extremely severe gastroparesis that do not improve with changes to diet and/or medication, patients may benefit from more invasive surgical procedures. However, a proportion of patients will be refractory to these measures (NHS England 2016).

Gastroelectrical stimulation (GES) is an option for people with severe, intractable gastroparesis (NHS England 2016). The GES procedure involves a device, designed to stimulate the stomach, being placed into a small pocket made under the skin of the abdomen. The device sends electrical impulses to the stomach muscles to help them to work more normally. The amount of stimulation can be adjusted to suit the patient (NHS England 2016).

Gastroparesis can be debilitating and without alternative treatment options, such as GES, some patients may be nutritionally crippled by the disease and may progress through ever-more invasive and costly surgical treatments such as artificial feeding and gastrectomy (NHS England 2016).

The topic proposer reports that people in Wales with severe, intractable gastroparesis are referred to hospitals in England via the Individual Patient Funding Request (IPFR) process. They state that over the last four years, 13 patients in Wales were referred to hospitals in England via the IPFR process.

Health Technology Wales researchers searched for evidence on GES for gastroparesis. In 2014, the National Institute for Health and Care Excellence (NICE) published Interventional Procedures Guidance (IPG489) on GES for gastroparesis (NICE 2014). The literature search for IPG489 was to May 2013. Although a more recent NHS England Clinical Commissioning Policy exists for GES for the treatment of gastroparesis, they did not report the literature search date. As some of the evidence in NICE IPG489 and the NHS England Clinical Commissioning Policy came from RCTs, we only looked for RCT clinical evidence published after the date of the literature search for NICE IPG489. We did not include search limits or study design filters for cost-effectiveness evidence.

Evidence overview

NICE IPG489 and the NHS England Clinical Commissioning Policy both provide guidance on use of GES for severe, intractable gastroparesis. Since publication of these, a meta-analysis of crossover randomised controlled trials (RCT) was identified, as well as an additional RCT, and two cost-effectiveness studies.

The systematic review and meta-analysis, published since NICE IPG489 and the NHS England Policy, consisted of five RCTs of 185 participants treated with or without GES for gastroparesis. Of these participants, 50% had diabetic gastroparesis. Follow-up times ranged from eight days to six months (Levinthal & Bielefeldt, 2017).

Evidence overview

The crossover RCT on GES for refractory vomiting with or without gastroparesis, published since NICE and NHS England guidance, recruited 172 participants with idiopathic, diabetic, or postsurgical gastroparesis from a number of centres in France. Participants were randomised to a four-month period of activation or inactivation and then crossed over to the other group for a further four months (Ducrotte et al. 2020).

Two economic evaluations of GES were identified since NICE and NHS England guidance. Klinge et al. (2017) estimated the cost-effectiveness of GES from the perspective of the Danish healthcare system. Gourcerol et al. (2021) estimated the impact of GES from a French-societal perspective. The impact of GES was judged by comparing values before and after the intervention was used.

HTA Assessments and Guidance

NICE published IPG489 on GES for gastroparesis in 2014. This IPG reports that current evidence on the efficacy and safety of GES for gastroparesis is adequate to support the use of this procedure.

NICE IPG489 was based on 1,765 participants from two systematic reviews of mainly observational studies (O'Grady et al. 2009; Chu et al. 2012), two crossover RCTs (McCallum et al. 2010; McCallum et al. 2013), and six observational studies (McCallum et al. 2013; McCallum et al. 2011; Zehetner et al. 2013; Timratana et al. 2013; Keller et al. 2013; O'Loughlin et al. 2013).

In 2016, an NHS England Clinical Commissioning Policy stated that there was not enough evidence to routinely commission GES for gastroparesis. The NHS England Clinical Commissioning Policy was based on the same evidence as NICE IPG489, but also included a costing report on GES for gastroparesis for the Northeast Specialised Commissioning Team (Horsley et al. 2010).

Evidence

Total symptom-severity

NICE IPG489 and NHS England included a meta-analysis of 169 patients with diabetic gastroparesis, 58 patients with idiopathic gastroparesis, and 33 patients with post-surgical gastroparesis treated by GES. This meta-analysis reported a significant improvement in total symptom-severity score (mean difference: 8.96, 95% confidence interval [CI]: 6.1 to 11.8; mean difference: 7.5, 95% CI: 5.4 to 9.7; and mean difference: 8.3, 95% CI: 5.5 to 11.1, respectively) (Chu et al. 2012).

Five crossover RCTs in the meta-analysis by Levinthal and Bielefeldt (2017) found no difference between activation and inactivation periods on overall symptom severity (mean difference: 0.17, 95% CI: -0.06 to 0.4). Similarly, no differences were found on other measures, including subjective intensity of vomiting, nausea severity, satiety, or bloating.

Frequency of vomiting

An RCT of 32 patients with gastroparesis of idiopathic origin reported that there was a significant reduction in weekly vomiting frequency, from 61% with GES to 87% without GES (McCallum et al. 2013).

The crossover RCT by Ducrotte et al. (2020) found that GES reduced the frequency of refractory vomiting in patients with and without diabetes. The trial reports that vomiting frequency was significantly reduced during activation of the device (mean score: activation, 2.2 versus inactivation, 1.8) with around 30% of participants reporting an improvement of at least 1 point.

Gastric emptying

NICE IPG489 and NHS England included a meta-analysis of 378 patients treated by GES. The meta-analysis reported a significant improvement in gastric emptying at four hours (mean difference: 13.0, 95% CI: 7.4 to 18.6). Subgroup analysis showed that the improvement was statistically significant in patients with diabetic or idiopathic gastroparesis but not in patients with post-surgical gastroparesis (Chu et al. 2012).

The crossover RCT by Ducrotte et al. (2020) reported that GES did not accelerate gastric emptying, but only displayed this data in a graph and so it is not possible to accurately report the data in this TER.

Change in weight

NICE IPG489 and NHS England included a meta-analysis of 75 patients with gastroparesis treated by GES, which reported no statistically significant change in weight (mean difference: 3.7, 95% CI: -0.2 to 7.6) (O'Grady et al. 2009).

Need for nutritional support

A meta-analysis of 184 patients with gastroparesis treated by GES, included in NICE IPG489 and the NHS England Policy, reported a reduction in need for nutritional support from 44% of patients at baseline to 11% at follow-up (odds ratio: 5.5, 95% CI: 2.8 to 11.1) (O'Grady et al. 2009).

Hospital stay

In NICE IPG and NHS England guidance, a crossover RCT of 32 participants reported that there was a significant reduction in hospitalisation days at 12 months following GES treatment (0 days) compared to baseline levels (median 2 days, interquartile range: 0 to 9) (McCallum et al. 2013).

Death

A comparative, observational study in NICE IPG489 and the NHS England Policy reported that death within 30 days occurred in 3% (2/72) of patients treated by GES, due to small bowel infarction and heart failure, and 3% (1/31) of patients treated by gastrectomy, due to myocardial infarction (Zehetner et al. 2013).

Adverse events

Erosion through the skin (six patients), device migration (one patient) and pain at implantation site (four patients) resulting in device removal or replacement were reported in a systematic review of 364 patients, included in NICE IPG489 and NICE England guidance (O'Grady et al. 2009).

The crossover RCT by Ducrotte et al. (2020) reported a total of 101 adverse events, with 45 therapy or device-related events: abdominal wall pain at the implantation site (n = 28), infections at the abdominal pouch level (n = 16), hematoma (n = 1). In 3 cases, the device-related adverse events were serious enough to prompt device removal.

Gastric perforation related to an episode of vomiting (two months after the procedure) was reported in one patient in an observational study of 17 patients, included in NICE IPG489 (O'Loughlin et al. 2013).

Treatment failure

Treatment failure was reported in 26% (19 out of 72) of patients treated by GES in an

Evidence overview

observational study of 103 patients, included in NICE IPG489 and the NHS England Policy document. Reasons included 'failure to respond' (14 patients), device malfunction (1 patient) and damage to the device (1 patient) (McCallum et al. 2013).

Quality of life

A meta-analysis of 78 patients, in NICE IPG489 and the NHS England Policy, reported a significant improvement in Short Form-36 (SF-36) physical component score (mean difference: 8.1, 95% CI 5.0 to 11.1) and the mental component score (mean difference: 8.16, 95% CI: 4.9 to 11.5) (O'Grady et al. 2009).

An RCT of 55 patients reported a significant improvement in SF-36 physical component score from 29.5 (standard deviation [SD] 7.0) at baseline to 36.4 (SD 10.0) at 12-month follow-up (McCallum et al. 2010).

The crossover RCT by Ducrotte et al. (2020) found that GES did not significantly improve quality of life. The Hospital Anxiety and Depression Scale score was 15.9 ± 8.1 during the OFF period of GES and 16.1 ± 8.4 during the ON period of GES.

Cost effectiveness

NHS England (2016) included results from the Northeast Treatment Advisory Group, who produced a costing report of GES for gastroparesis in 2010. Their report estimated that the cost for implantation of an Enterra GES device is between £16,000 and £18,000 per patient, but noted that additional costs may arise where there are complications (Horsely, 2010).

Klinge et al. (2017) reported the total cost of implantation of the GES system as €19,500 (~£16,700) per patient. The incremental cost effectiveness ratio (ICER) was estimated to be €104 per quality adjusted life year (QALY) gained.

Gourcerol et al. (2021) followed the population from Ducrotte et al. (2020) for 21 months after the end of the crossover study, where all participants' GES devices were activated. They report that mean overall healthcare costs decreased from the pre- to post-implantation period (per-patient per-year costs, US\$8,873 vs. US\$5,525).

Patient and public involvement

NICE IPG489 received 27 questionnaires from patients who had undergone GES for gastroparesis, and summarised that *"Overall people were very positive about the procedure in improving the way their stomach empties. All patients stated they would have the procedure again and also would recommend the procedure to another patient with gastroparesis."*

Areas of uncertainty

GES for gastroparesis is supported by NICE. However, the length of follow-up was unclear in most of the analyses within the NICE IPG, and the IPG notes that there may be some overlap of patients in the studies included in the analyses. A more recent NHS England Clinical Commissioning Policy states that there is not enough evidence to make the treatment available. It is unclear why there is this discrepancy as both were largely based on the same evidence.

All RCTs identified in this TER compared outcomes with and without GES. It is unclear what the most appropriate comparator is in NHS Wales. It is also unclear whether any of the identified evidence was conducted in the UK.

Areas of uncertainty

Some of the evidence showed favourable outcomes in people with diabetic gastroparesis compared to non-diabetic gastroparesis. Additionally, some of the studies included patients without gastroparesis (e.g. intractable vomiting). Should this topic progress to full appraisal, the type of gastroparesis included within the scope would need to be considered.

Available economic evidence suggests that GES is cost-effective and may also reduce costs associated with gastroparesis or vomiting. However, this evidence is based on uncontrolled studies and so must be interpreted with caution.

Literature search results

Health technology assessments and guidance

[HTW](#)

No relevant evidence identified

[NHS England](#)

NHS England. Clinical Commissioning Policy: Gastroelectrical stimulation for gastroparesis (16025/P) (2016): <https://www.england.nhs.uk/wp-content/uploads/2018/07/Gastroelectrical-stimulation-for-gastroparesis.pdf>

[NICE](#)

NICE. Interventional Procedures Guidance (IPG489) (2014). Gastroelectrical stimulation for gastroparesis: <https://www.nice.org.uk/guidance/ipg489>

[Healthcare Improvement Scotland](#)

No relevant evidence identified

[Hand search published SIGN Guidelines](#)

No relevant evidence identified

[Health Information and Quality Authority](#)

No relevant evidence identified

[EUnetHTA](#)

No relevant evidence identified

[International HTA Database](#)

No relevant evidence identified

[International Guidelines Library](#)

No relevant evidence identified

Evidence reviews and economic evaluations

Alberta Heritage Foundation for Medical Research. Gastric Electrical Stimulation (Enterra™ Therapy system) for the Treatment of Gastroparesis. Edmonton (AL): Alberta Heritage Foundation for Medical Research, 2006. Available from: <http://www.health.alberta.ca/documents/ahtdp-ges-ahfmr-hta.pdf>

Chu H, Lin Z, Zhong L et al. (2012) Treatment of high-frequency gastric electrical stimulation for gastroparesis. *Journal of Gastroenterology and Hepatology*. 27 (6):1017-26: <https://doi.org/10.1111/j.1440-1746.2011.06999.x>

Gourcerol et al. (2021). Impact of Gastric Electrical Stimulation on Economic Burden of Refractory Vomiting: A French Nationwide Multicentre Study. *Clinical Gastroenterology and Hepatology*. Online. <https://doi.org/10.1016/j.cgh.2020.11.011>

Horsley W. Gastroelectrical stimulation for gastroparesis. Newcastle upon Tyne: NHS North East Treatment Advisory Group, 2010. Available from: <http://www.netag.nhs.uk/files/appraisal-reports/Gastroelectrical%20stimulation%20-%20NETAG%20appraisal%20report%20-Apr10.pdf>

Klinge et al. (2017). Early Assessment of Cost-effectiveness of Gastric Electrical Stimulation for Diabetic Nausea and Vomiting. *Journal of Neurogastroenterology and Motility*, 2017; 23(4): 541-549. <https://doi.org/10.5056/jnm16179>

Levinthal, D.J. and Bielefeldt, K., 2017. Systematic review and meta-analysis: Gastric electrical stimulation for gastroparesis. *Autonomic Neuroscience*, 202, pp.45-55: <https://doi.org/10.1016/j.autneu.2016.03.004>

O'Grady G, Egbuji JU, Du P et al. (2009) High-frequency gastric electrical stimulation for the treatment of gastroparesis: a meta-analysis. *World Journal of Surgery*. 33 (8):1693-1701: <https://link.springer.com/article/10.1007/s00268-009-0096-1>

Individual studies

Ducrotte et al. (2020). Gastric Electrical Stimulation Reduces Refractory Vomiting in a Randomized Crossover Trial. *Gastroenterology*, 158, 506-514. <https://doi.org/10.1053/j.gastro.2019.10.018>

Keller DS, Parkman HP, Boucek DO et al. (2013) Surgical outcomes after gastric electric stimulator placement for refractory gastroparesis. *Journal of Gastrointestinal Surgery* 17: 620-626: <https://link.springer.com/article/10.1007/s11605-013-2147-z>

McCallum RW, Snape W, Brody F et al. (2010) Gastric electrical stimulation with Enterra therapy improves symptoms from diabetic gastroparesis in a prospective study. *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association* 8: 947-54: <https://doi.org/10.1016/j.cgh.2010.05.020>

McCallum, R. W., Sarosiek, I., Parkman, H. P., Snape, W., Brody, F., Wo, J., and Nowak, T(2013). Gastric electrical stimulation with Enterra therapy improves symptoms of idiopathic gastroparesis. *Neurogastroenterology and Motility*.25 (10) 815-e636: <https://doi.org/10.1111/nmo.12185>

McCallum RW, Lin Z, Forster J et al. (2011) Gastric electrical stimulation improves outcomes of patients with gastroparesis for up to 10 Years. *Clinical Gastroenterology and Hepatology*. 9 (4):314-9: <https://doi.org/10.1016/j.cgh.2010.12.013>

O'Loughlin PM, Gilliam AD, Shaban F et al. (2013) Pre-operative gastric emptying time correlates with clinical response to gastric electrical stimulation in the treatment of gastroparesis. *Surgeon Journal of the Royal Colleges of Surgeons of Edinburgh & Ireland* 11: 134-40: <https://doi.org/10.1016/j.surge.2012.10.006>

Timratana P, El-Hayek K, Shimizu H et al. (2013) Laparoscopic gastric electrical stimulation for medically refractory diabetic and idiopathic gastroparesis. *Journal of Gastrointestinal Surgery* 17: 461-70: <https://doi.org/10.1007/s11605-012-2128-7> [Get rights and content](#)

Zehetner J, Ravari F, Ayazi S et al. (2013) Minimally invasive surgical approach for the treatment of gastroparesis. *Surgical Endoscopy* 27: 61-6: <https://link.springer.com/article/10.1007/s00464-012-2407-0>

Date of search	September 2024
Concepts used	Gastroparesis, Gastroelectrical stimulation, gastric emptying

Proposed research question and evidence selection criteria (if selected)

Proposed Research question	What is the clinical and cost effectiveness of gastroelectrical stimulation for adults with severe, intractable gastroparesis?
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	Inclusion criteria	Exclusion criteria
Population	Adults with severe, intractable gastroparesis	Children
Intervention	Gastroelectrical stimulation	
Comparison/ Comparators	Medical therapy Supplemental feeding Endoscopic injection of botulinum toxin Total gastrectomy No treatment	
Outcome measures	Severity of symptoms Frequency of vomiting Gastric emptying Need for nutritional support Hospital stay Adverse events Health related QoL Resource use Economic outcomes	

Proposed speciality	Digestive system
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