

In response to an enquiry from the West of Scotland Upper GI Surgery Unit, Department of Oesophagogastric Surgery, Glasgow Royal Infirmary.

Number 5 March 2012

**In patients with severe medically refractory gastroparesis (such as those requiring nutritional support), how effective and cost effective is gastric electrical stimulation (*Enterra*<sup>TM</sup> device) in reducing symptoms, reducing requirement for nutritional support or hospitalisation and improving quality of life, when compared with medical or alternative surgical management?**

## What is a scoping report?

Scoping reports ascertain the quantity and quality of the published clinical and cost effectiveness evidence on health technologies under consideration by decision makers within NHSScotland. They also serve to clarify definitions related to the research question(s) on that topic. They are intended to provide an overview of the evidence base, including gaps and uncertainties, and inform decisions on the feasibility of producing an evidence review product on the topic. Scoping reports are undertaken in an approximately 1 month period. They are based upon a high level literature search and selection of the best evidence that Healthcare Improvement Scotland could identify within the time available. The reports are subject to peer review but do not undergo external consultation. Scoping reports do not make recommendations for NHSScotland.

## Key definitions

**Gastroparesis:** a chronic disorder associated with delayed emptying of the stomach in the absence of mechanical obstruction.

**Gastric electrical stimulation (GES):** an option for the treatment of patients with chronic, intractable (drug-refractory) nausea and vomiting secondary to gastroparesis. Low energy electrical stimuli are delivered to the stomach via a surgically implanted system that consists of two intramuscular leads and a neurostimulator.

## Background

Gastroparesis is a frequent complication of diabetes, making it increasingly common, as the prevalence of diabetes rises<sup>1</sup>. It may also arise idiopathically or following gastric surgery<sup>2</sup>. The most common symptoms are severe nausea and vomiting, abdominal pain and bloating and oesophageal reflux which lead to reduced quality of life. Hospitalisation may be required due to dehydration, excessive weight loss and requirement for ongoing nutritional support. Diet and lifestyle changes and pharmacological treatments (prokinetic and antiemetic agents) are effective in most cases, but around 2% of patients with the condition have refractory gastroparesis.

Based on incidence data taken from an Ontarian Health Technology Assessment (2006) it is estimated that between 8–58 new patients with severe refractory gastroparesis could be identified in Scotland each year<sup>3</sup>. There is uncertainty around this estimate due to variation in the definition of the severity of the condition.

In 2010, based on communication with the device manufacturer, it was estimated that a total of 80–100 patients in the United Kingdom have received an *Enterra*<sup>TM</sup> implant for provision of GES<sup>4</sup>.

GES treatment is a non-standard treatment in Scotland and is presently considered on a case by case basis and carried out only in a small number of centres.

## The following question was scoped:

**In patients with severe gastroparesis refractory to pharmacological treatment, what is the evidence for clinical and cost effectiveness of GES (*Enterra*<sup>TM</sup> device) in reducing symptoms, reducing requirement for nutritional support or hospitalisation and improving quality of life, when compared with medical or alternative surgical treatments.**

## Literature search

A systematic search of the secondary and primary literature was carried out between the 1–6 June 2011. Key secondary resources were searched for policy documents, reviews, economic studies and ongoing trials. Terms used for these searches included: gastric electrical stimulation, gastric pacing, gastroparesis, gastric motility, gastric emptying.

As very little evidence was located in the secondary literature, the primary literature was searched using the following databases:

- Medline
- Medline in process
- Embase

All databases searched used the OVID SP platform. Results were limited to 2000–2011.

A full list of resources searched and primary literature search strategies are available on request.

## Evidence base

**Table 1 Included evidence sources**

Publications type	Number of publications	References
Health technology assessment	1	3,4
Meta-analysis	1	1
Randomised controlled trial (RCT)	2	5,6
Case series	1	2
Other cost studies	1	1*,2,4,7,8

\*Unpublished evidence appraisal report for the NHS North East Specialised Commissioning Team.

## Findings

### 1. Clinical effectiveness

A well conducted meta-analysis examined the evidence for efficacy of GES, primarily in patients with medically refractory gastroparesis of diabetic or idiopathic origin<sup>1</sup>. The paper identified articles up to August 2008 and included 13 studies. Only one of these was a randomised comparison (n=33)<sup>6</sup>. There were nine prospective case series and three retrospective case series.

Focusing, where possible, on 12 month outcomes, the meta-analysis reported that GES was associated with statistically significant and clinically important reductions from baseline in total symptom severity (n=77), nausea and vomiting severity (n=92), vomiting frequency (n=57) and the need for enteral or parenteral nutritional support (n=187). There were also statistically significant improvements in SF-36 physical composite and mental composite quality of life scores (n=110).

Device removal due to complications (predominantly associated with infection) was documented in 8.3% of the patients who received the implant.

A retrospective review of 188 cases with a mean follow up period of 56 months (range 12–131 months), found similar outcomes in terms of symptoms of nausea and vomiting<sup>2</sup>. The device was removed due to complications in 11% of the patients. The patients in this study overlapped with some of those assessed in the meta-analysis.

The RCT encompassed within the meta-analysis (Abell 2003) recruited only 33 patients and was sponsored by the device manufacturer. It had a 2 month double blind crossover study period immediately following device implantation. Although there was a greater reduction in the

number of vomiting episodes per week in those patients with the device switched on, this benefit was not apparent when the diabetic and idiopathic groups were analysed separately.

Since the publication of the meta-analysis, one RCT that attempted to control for the strong placebo effect of surgery, reporting since publication of the meta-analysis, was identified. In patients with intractable diabetic gastroparesis (n=55) it was found that 6 weeks of *Enterra*<sup>TM</sup> therapy was associated with significantly reduced gastroparesis symptoms. After the 6 week initiation and postoperative recovery period, a 3 month randomised and double blinded crossover trial was commenced comparing sham with active stimulation (n=36). There was no difference between the two modes in symptom frequency or severity scores. It was proposed by the authors that the initial 6 week stimulation period produced effects which were sustained into the sham therapy period. A placebo effect or regression to the mean were also postulated<sup>5</sup>.

### 2. Cost effectiveness and resource impact

One small prospective study (n=18), carried out in the United States (US) examined healthcare resource use and costs, comparing intensive medical therapy for patients with intractable gastroparesis with GES. Overall healthcare costs declined over a 3 year period for the GES group but not for the medical therapy group<sup>7</sup>. This cost-consequence analysis had a number of limitations (eg uncertainty over the relevance of the comparator to the Scottish setting, small sample size, lack of randomisation, no summary measure of cost-benefit and no separate reporting of resource use and costs) compounded by uncertainty regarding the generalisability of the cost estimates (based on one US provider hospital) to NHSScotland<sup>8</sup>.

Two cost analyses were identified. One retrospective review of 188 cases with mean follow up of 56 months reported a significant reduction in days of hospitalisation (in the most recent year of follow up) compared to baseline. Patients with diabetes mellitus had an 87% reduction in days of hospitalisation from 52 days to 7 days (p<0.001). The US healthcare setting limits the generalisability of this finding<sup>2</sup>.

The NHS North East England Treatment Advisory Group recently conducted an appraisal of GES for gastroparesis that included a high level cost analysis. They estimated per patient costs of between £16,000–18,000 including all pre-, peri- and postoperative care and hardware costs, although noting additional costs may arise where there are complications. They also highlighted, but did not quantify, potential offset costs that may arise through the reduction in proportion of patients requiring nutritional support, reduced hospital admissions and where the device is used as an

alternative to major gastrointestinal surgery. They noted, however, limited potential for cost offsetting due to reduced medication costs since the commonly used drugs for management of gastroparesis are of low cost<sup>4</sup>.

There is currently a dearth of evidence on the costs and cost effectiveness of GES technology. Primary research, enumerating the costs and relative effectiveness and efficiency of GES compared to existing alternatives, would be required to assess cost effectiveness of this technology in NHSScotland.

## Safety alerts

In August 2009 the device manufacturer reported 15 cases of bowel obstruction and/or perforation of the bowel associated with *Enterra*<sup>TM</sup> therapy system leads since November 2002. An urgent field safety notice was issued (<http://www.mhra.gov.uk/home/groups/dts-bi/documents/fieldsafetynotice/con057111.pdf>).

“The lead can become entangled with or erode into the bowel, which can result in bowel obstruction and/or perforation. Either may lead to life-threatening intra-abdominal infections and may require laparotomy, bowel resection, and system revision. Avoid excess lead slack in the abdominal cavity. Post implant; consider lead entanglement or erosion as a possible etiology in patients with bowel obstruction symptoms”.

In July 2007 the device manufacturer reported 27 cases related to a patient sensation of shocking associated with electrical stimulation from the *Enterra*<sup>TM</sup> therapy system. An educational brief on implant techniques and patient management steps that are important in mitigating the potential for patient shocking sensation was issued by the manufacturer.

## Summary

The evidence base for GES consists mainly of uncontrolled observational studies. GES is associated with statistically significant reductions in symptom frequency and severity, reduced need for hospital admissions and improved quality of life for patients with severe medically refractory gastroparesis.

Around 10% of patients require device removal.

While there is evidence of symptom reduction with gastric electrical stimulation, there is a lack of cost effectiveness evidence.

An ongoing double blind randomised controlled trial (Medico-economic Evaluation of *Enterra*<sup>TM</sup> therapy) aims to recruit 220 patients and examine both the clinical effectiveness and healthcare utilisation associated with GES in patients with severe refractory symptoms over a 28 month study period. The results which are due in 2013 are likely to be influential.

## Further work for Healthcare Improvement Scotland

Healthcare Improvement Scotland considers that this scoping report has provided coverage of the current published clinical and cost effectiveness evidence base. It is therefore proposed that this report is published and that SHTG does not undertake any further review of the evidence until requested by the clinical community, dependent on new published reports.

## Equality and diversity

Healthcare Improvement Scotland is committed to equality and diversity in respect of the nine equality groups defined by age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion, sex, and sexual orientation. As a scoping report summarises information and does not provide recommendations a full EQIA assessment is not deemed necessary.

The process for producing scoping reports will be assessed when available, however no adverse impacts across any of the groups is expected.

## Acknowledgements

Healthcare Improvement Scotland would like to acknowledge the helpful contribution of the following, who gave advice on the content of this scoping report:

Grant Fullarton  
Lead Surgeon  
West of Scotland Upper GI Surgery Unit  
NHS Greater Glasgow and Clyde

William Horsley  
Lead Pharmacist  
North East Treatment Advisory Group  
NHS North of Tyne

Lorna Thompson  
Author/Health Services Researcher

Carolyn Sleith  
Knowledge and Information Skills Specialist

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