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Stent placement versus surgical palliation for malignant gastric outlet obstruction (Protocol)

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[Intervention Protocol]

Stent placement versus surgical palliation for malignant gastric outlet obstruction

Emma Upchurch[1], Roberto Cirocchi[2], Mark Ragusa[3]

[1]Department of Colorectal and Upper Gastrointestinal Surgery, Gloucestershire Hospitals NHS Foundation Trust, Cheltenham, UK. [2]Department of General Surgery, University of Perugia, Terni, Italy. [3]Perugia University Medical School, Terni, Italy

Contact address: Emma Upchurch, Department of Colorectal and Upper Gastrointestinal Surgery, Gloucestershire Hospitals NHS Foundation Trust, Sandford Road, Cheltenham, Gloucestershire, GL53 7AN, UK. em_upchurch@hotmail.com, emma.upchurch@glos.nhs.uk.

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the benefits and harms of endoscopic stent placement versus surgical palliation for patients with malignant gastric outlet obstruction.

BACKGROUND

Description of the condition

Gastric outlet obstruction (GOO) is the clinical and pathological consequence of a disease process, which results in a mechanical obstruction to gastric emptying at the distal (bottom) end of the stomach. It is the end result of a variety of pathological processes that culminates in compression and subsequent blockage of the gastric outlet (the area of the stomach by which food exits, and enters the small bowel). The causes are typically divided into those resulting from benign (i.e. non-cancerous) disease and those resulting from malignant (i.e. cancerous) disease. The incidence of GOO from benign disease, predominantly peptic ulcer disease, has declined substantially since the identification of *Helicobacter pylori* and the use of proton pump inhibitors, as this has diminished the incidence of peptic ulcers, and consequently, their complications (Shone 1995).

Malignant disease now accounts for 50% to 80% of cases of GOO, although the exact incidence is unclear (Chowdhury 1996; Johnson 1990; Johnson 1995; Shone 1995). This is likely due to the wide range of cancers that can result in GOO, which leads to difficulties in recording incidence. In addition, the development of this condition is often a near-terminal or terminal event and therefore, this complication may not be documented, leading to difficulties in accurately predicting the number affected.

The most common malignancy that results in GOO is pancreatic malignancy, with 15% to 20% of patients presenting with GOO (Tendler 2002). In 2013, there were 9408 new cases of pancreatic cancer and thus, approximately 1400 to 1900 cases of GOO present in this cohort each year. The obstruction is typically the result of disease extension to the duodenum or stomach, or external compression at the level of the gastric outlet, reflecting the anatomical position of the pancreas in relation to the stomach. A

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significant proportion of these patients also have biliary obstruction.

Distal gastric, and more rarely, duodenal cancers, result in intraluminal obstruction; although this is typically a late complication, it may be the presenting symptom in these patients. Rarer malignancies, including ampullary carcinoma and cholangiocarcinomas, can result in this condition, due to their anatomical position. Lymphoma and metastatic disease, if affecting the lymph nodes and structures surrounding the gastric outlet, can also be the cause.

Gastric outlet obstruction typically presents with progressive symptoms. Vomiting is the predominant feature; this may initially follow solid food intake before ultimately progressing to vomiting following liquid intake. Overtime, significant weight loss occurs as a result of both reduced calorie intake and the disease process itself, and thus, the majority of patients presenting with GOO are frail, with poor physiological reserve. In addition, continual vomiting can be extremely distressing for the patient.

The median survival in this patient cohort may be as short as three to four months, although this depends on the exact tissue type of cancer, volume of metastatic disease, and patient co-morbidities (Jeurnick 2007; Lopera 2004). Without intervention, the absence of nutritional intake, alongside the electrolyte imbalance that occurs as a result of continual vomiting, would be a terminal event for the patient. In view of the short timeframe, the ideal procedure that would alleviate these symptoms would restore oral intake swiftly, with minimal complications.

See Appendix 1 for a glossary of terms.

Description of the intervention

Traditionally, the treatment approach for patients with gastric outlet obstruction was surgical bypass, consisting of an open gastrojejunostomy. This was first performed in 1881 by Rydygier, for a patient with a duodenal ulcer (Pach 2008). Later that same year, a similar operation was performed by Wolfer, for a patient with pyloric carcinoma that had extended into the pancreas (Robinson 1960).

The operation involves an upper midline incision to gain access to the abdomen. The obstruction is bypassed by forming an anastomosis between the stomach above the level of the obstruction to the small bowel below the level of the obstruction, typically the jejunum. The anastomosis usually takes the form of a roux-en-y loop, which is an end to side anastomosis, and can be positioned behind or in front of the transverse colon. The anastomosis can either be hand sewn or stapled, and to date, there is no evidence favouring either technique.

Developments in minimal access surgery have resulted in the ability, in suitable patients, to perform this procedure laparoscopically. In laparoscopic gastrojejunostomy, the surgical access to the abdominal cavity is via a central port, typically placed just below the umbilicus. The abdominal cavity is distended using carbon dioxide pneumoperitoneum, and further ports, typically three 5 mm to 10 mm incisions, are placed for additional instruments. The surgery can be performed entirely laparoscopically, with either laparoscopic stitches, or more commonly, laparoscopic staples, used for the anastomosis.

Palliative stent placement for gastric outlet obstruction was first reported in the 1990s (Kozarek 1992). Conscious sedation is used, and with the patient in the left lateral position, the area of obstruction is reached with an endoscope. A guidewire is passed through the obstruction, and with fluoroscopic guidance, a stent is deployed through the working channel of the endoscope, to cover the obstruction. A variety of stents are available. They are self-expanding metal stents (SEMS), and can be covered or uncovered, depending on whether they are coated. The advantage of covered stents is that they can prevent tumour ingrowth, however, they have a higher rate of stent migration. There is no evidence indicating that either is preferred.

How the intervention might work

Patients who develop gastric outlet obstruction as a result of their malignancy are usually in the terminal stages of their disease, and thus, an intervention that alleviates their symptoms and improves their quality of life with minimal recovery time is required.

Surgical palliation is associated with a not insignificant risk of complications. Complication rates of 25% to 35% are reported, with a perioperative mortality rate of 2% (Isla 2000; Johnsson 2004; Lillemoe 1999; Maetani 2005; Mittal 2004). Complications include chest infections, wound infections, and anastomotic leak at the site of the bypass. An anastomotic leak can be a devastating complication, resulting in abdominal sepsis, and in some cases, the need for a second operation.

Laparoscopic surgery may reduce the surgical insult, and lead to reduced complications and a shorter hospital stay. This has been shown to be the case in other surgical procedures when comparing an open to a laparoscopic approach (Bijen 2009; Keus 2006; Reza 2006; Talseth 2014; Walsh 2009).

In addition to the early complications seen in patients who have undergone gastrojejunostomy, delayed gastric emptying has been reported to be around 20% (Watanapa 1992), and as high as 57% in some studies (Doberneck 1987). For an intervention where restoration of oral intake, and hence, quality of life is paramount, this is unquestionably high.

Endoscopic stent placement would reduce the surgical burden placed on the patient and reduce the incidence of complications and length of hospital stay, while producing similar, if not better, improvements in quality of life. However, endoscopic stent replacement is not without its own complications. These include occlusion of the stent, either from food bolus or tumour ingrowth, resulting in a return of symptoms and the need for a further endoscopic procedure. Stent migration can lead to the return of symptoms, necessitating a further endoscopy to correct the position. In

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rare instances, stent migration can lead to perforation of the stomach or small bowel, as the stent erodes through the bowel wall.

Why it is important to do this review

With the avoidance of general anaesthetic and surgical burden of gastrojejunostomy, the potential advantages of endoscopic stent placement for malignant gastric outlet obstruction are desirable. The improvement in symptoms as well as the longevity of any improvement has to be ensured before this method can be widely recommended as the technique of choice. There are current concerns regarding a high rate of late complications caused by stent migration and occlusion, which would preclude its preferential use (Espinel 2001; Lopera 2004). This review aims to address these concerns, and determine if either method produces better results in a cohort of patients where timely improvement in symptoms is paramount.

OBJECTIVES

To assess the benefits and harms of endoscopic stent placement versus surgical palliation for patients with malignant gastric outlet obstruction.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs). We will include studies reported as full text, those published as abstract only, and unpublished data.

Types of participants

We will include adults undergoing intervention for gastric outlet obstruction which is secondary to a malignant process. We will exclude participants if the underlying cause of their gastric outlet obstruction is benign disease, or if the cause is unknown.

Types of interventions

We will include trials that compare endoscopic stent placement (including metal stent and self-expanding metal stent (SEMS)) with surgical palliation (including open, laparoscopic-assisted and laparoscopic gastrojejunostomy).

We will exclude trials that compare either method to conservative management (i.e. symptom control with medication or a nasogastric tube).

Types of outcome measures

Primary outcomes

1. Measures of resolution of symptoms
   i) Time-to-reestablishment of oral intake
2. All cause mortality
   i) Short-term mortality (in-hospital mortality, or mortality within three months)

Secondary outcomes

1. Time-to-recurrence of obstructive symptoms (inability to swallow solids, liquids, or both, epigastric pain on swallowing, post-prandial vomiting, or both)
2. Serious adverse events (within three months, including the time point closest to three months). We will accept the following definitions of serious adverse events:
   i) Clavien-Dindo classification: Grade III or more (Clavien 2009; Dindo 2004);
   ii) International conference on harmonisation: good clinical practise guideline: serious adverse events are defined as any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or any combination (ICH-GCP 2015).
3. Length of hospital stay
4. Health-related quality of life (using any validated scale)
   i) Short term (measured between four weeks and three months);
   ii) Long term (measured beyond three months).

We based the choice of the above clinical outcomes on the necessity to assess whether stenting or surgical bypass resulted in the quickest resolution of symptoms with the shortest hospital stay. The goal for patients with malignant outlet obstruction is quality of life, thus, it is important to understand which method may be more likely to achieve this.

Reporting of the outcomes listed here will not be an inclusion criteria for the review.

Search methods for identification of studies

Electronic searches

We will conduct a literature search to identify all published and unpublished randomised controlled trials in all languages. We will

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translate non-English language papers and fully assess them for potential inclusion in the review as necessary.
We will search the following electronic databases:

- Cochrane Central Register of Controlled Trials (CENTRAL; Appendix 2);
- MEDLINE (1966 to present; Appendix 3);
- EMBASE (1988 to present; Appendix 4); and
- CINAHL (1982 to present).

Searching other resources

We will check reference lists of all primary studies and review articles for additional references. We will contact authors of identified trials and ask them to identify other published and unpublished studies.
We will search for errata or retractions from eligible trials on PubMed (www.ncbi.nlm.nih.gov/pubmed) and report the date this was done in the review.

Grey literature databases

- Health Management Information Consortium (HMIC) database www.ovid.com/site/catalog/DataBase/99.jsp
- National Technical Information Service (NTIS) database www.ntis.gov/products/ntisdb.aspx
- OpenGrey www.opengrey.eu
- PsycEXTRA www.apa.org/pubs/databases/psycextra/index.aspx

Clinical trials registers and trial result registers

We will also conduct a search of clinical trial registers/trial result registers:

- AstraZeneca Clnical Trials
- Bristol-Myers Squibb Clinical Trial Registry
- Clinical Trials.gov
- Current Controlled Trials metaRegister of Controlled Trials (mRCT)
    - active registers www.controlled-trials.com/mRCT
    - archived registers www.controlled-trials.com/mrct/archived
- Eli Lilly and Company Clinical Trial Registry
    - www.lillytrials.com
    - www.lillytrials.com/initiated/initiated.html
- EU Clinical Trials Register
- GlaxoSmithKline Clinical Study Register
- International Clinical Trials Registry Platform Search Portal
- International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Clinical Trials Portal
- Roche Clinical Trials Results Database

Data collection and analysis

Selection of studies

Two review authors (EU, RC) will independently screen titles and abstracts of all the potential studies we identify as a result of the search, and code them as 'retrieve' (eligible, potentially eligible, or unclear) or 'do not retrieve'. We will retrieve the full text of study reports or publications, and two review authors (EU, RC) will independently screen the full text, identify studies for inclusion, and identify and record reasons for exclusion of the ineligible studies. We will resolve any disagreement through discussion; if required, we will consult a third person [MR].
We will identify and exclude duplicates, and collate multiple reports of the same study, so that each study, rather than each report, is the unit of interest in the review. We will record the selection process in sufficient detail to complete a PRISMA flow diagram and 'Characteristics of excluded studies' table.

Data extraction and management

We will use a standard data collection form for study characteristics and outcome data, which has been piloted on at least one study in the review. Two review authors (EU, RC) will independently extract study characteristics from included studies. We will extract the following study characteristics:

1. Methods: study design, total duration of study and run in, number of study centres and location, study setting, withdrawals, date of study.
2. Participants: number, mean age, age range, gender, primary tumour, tumour stage, histological subtype, performance status, ASA status (ASA 2014), inclusion criteria, exclusion criteria.
3. Interventions: intervention, comparison, concomitant interventions.
4. Outcomes: primary and secondary outcomes specified and collected, time points reported.
5. Notes: funding for trial, notable conflicts of interest of trial authors.

Two review authors (EU, RC) will independently extract outcome data from the included studies. If outcomes were reported multiple times for the same timeframe (for example, short-term health-related quality of life reported at six weeks and three months), we will extract the data for the latter time point (i.e. three months). We will note in the 'Characteristics of included studies' table if outcome data were not reported in a usable format. We will resolve disagreements by consensus, or by involving a third person (MR). One review author (EU) will copy the data from the data collection form into the Review Manager (RevMan) file. A second review author will double check that the data are entered correctly by comparing the study reports with the data in RevMan.

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Assessment of risk of bias in included studies

Two review authors will independently assess the risk of bias for each study, using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Any disagreement will be resolved by discussion, or by involving a third assessor. We will assess the risk of bias according to the following domains:

1. Random sequence generation;
2. Allocation concealment;
3. Blinding of participants and personnel;
4. Blinding of outcome assessment;
5. Incomplete outcome data;
6. Selective outcome reporting;
7. Other bias.

We will grade each potential source of bias as high, low, or unclear, and provide a quote from the study report and justification for our judgement in the 'Risk of bias' table. We will summarise the risk of bias judgements across studies for each of the domains listed. We acknowledge that blinding of participants and personnel will be impossible, but blinding of outcome assessors is possible. We will consider blinding separately for different key outcomes where necessary, e.g. for unblinded outcome assessment, risk of bias for all cause mortality may be different than for a patient-reported quality of life scale, since lack of blinding is unlikely to bias all cause mortality, while lack of blinding is likely to introduce a significant bias in quality of life). Where information on risk of bias relates to unpublished data or correspondence with a trialist, we will note this in the 'Risk of bias' table.

When considering treatment effects, we will take into account the risk of bias for the studies that contribute to that outcome, as part of the GRADE methodology.

Assesment of bias in conducting the systematic review

We will conduct the review according to this published protocol and report any deviations form it in the 'Differences between protocol and review' section of the systematic review.

Measures of treatment effect

We will analyse dichotomous data (short-term mortality, proportion of people with serious adverse events) as risk ratios. We will analyse continuous data as hazards ratios where the trials have been analysed with survival techniques (e.g. time-to-reestablishment of oral intake, time-to-recurrence of symptoms), as mean differences when the outcome is reported or converted to the same unit in all the trials (e.g. hospital stay, number of days before returning to work), or as standardised mean differences when different scales are used for measuring the same outcome (e.g. quality of life). We will ensure that higher scores for continuous outcomes have the same meaning for the particular outcome, explain the direction to the reader, and report where the directions were reversed if this was necessary.

We will calculate the rate ratio for outcomes such as serious adverse events, where it is possible for the same person to develop more than one serious adverse event. If the authors have calculated the rate ratio of serious adverse events in the intervention versus control based on Poisson regression, we will obtain the rate ratio by the Poisson regression method in preference to ratio:ratio calculated based on the number of serious adverse events during a certain period (Poisson).

We will undertake random effects meta-analyses only where this is meaningful i.e. if the treatments, participants, and the underlying clinical question are similar enough for pooling to make sense.

A common way that trialists indicate they have skewed data, is by reporting medians and interquartile ranges. When we encounter this, we will note that the data are skewed and consider the implication of this. If the data are skewed, we will not perform a meta-analysis, but will provide a narrative summary instead.

Where multiple trial arms are reported in a single trial, we will include only the relevant arms. If two comparisons (e.g. stent placement versus no intervention and surgical palliation versus no intervention) must be entered into the same meta-analysis, we will halve the control group to avoid double counting.

Unit of analysis issues

The unit of analysis will be individual patients undergoing treatment for gastric outlet obstruction. We do not anticipate any cluster-randomised trials, but if any are identified, we will obtain the effect estimate adjusted for the clustering effect. If this is not available, we will perform a sensitivity analysis excluding the trial from the meta-analysis, as the variance of the effect estimate unadjusted for cluster effect is less than the actual variance that is adjusted for cluster effect, giving inappropriately more weight to the cluster RCT in the meta-analysis.

Dealing with missing data

We will contact investigators or study sponsors in order to verify key study characteristics and obtain missing numerical outcome data as indicated (e.g. when a study is identified as abstract only). If we are unable to obtain the information from the investigators or study sponsors, we will impute the mean from the median (i.e. consider median as the mean) and the standard deviation from the standard error, interquartile range, or P values, according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will assess the impact of including such studies in a sensitivity analysis. If we are unable to calculate the standard deviation from standard error, interquartile range, or P values, we will impute standard deviation as the highest standard deviation in the remaining trials included in the outcome, fully aware that this method of imputation will decrease the weight of the studies in

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the meta-analysis of mean difference, and shift the effect towards no effect for standardised mean difference.

Assessment of heterogeneity

We will use the I^2 statistic to measure heterogeneity among the trials in each analysis (Higgins 2003). If we identify substantial heterogeneity as per the *Cochrane Handbook for Systematic Reviews of Interventions* (greater than 50% to 60%), we will explore it by pre-specified subgroup analysis (Higgins 2011). We will also assess heterogeneity by evaluating whether there is good overlap of confidence intervals.

Assessment of reporting biases

If we are able to pool more than 10 trials, we will create and examine a funnel plot to explore possible publication biases. We will use Egger's test to determine the statistical significance of the reporting bias (Egger 1997). We will consider $P < 0.05$ to be a statistically significant reporting bias.

Data synthesis

'Summary of findings' table

We will create a 'Summary of findings' table with the following outcomes: time-to-reestablishment of liquid diet, time-to-reestablishment of solid diet, all cause mortality, recurrence of obstructive symptoms, serious adverse events, length of hospital stay, and health-related quality of life. We will use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of the body of evidence based on the studies that contributed data to the meta-analyses for each outcome, classifying it as high, moderate, low or very low. We will use the methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook* for *Systematic Reviews of Interventions* (Higgins 2011), and GRADEpro GDT software (GRADEpro GDT). We will justify all decisions to downgrade or upgrade the quality of the evidence in the footnotes, and where necessary, provide comments to aid the reader's understanding of the review. We will consider whether there is additional outcome information that was not incorporated into the meta-analyses, note this in the comments, and state if it supports or contradicts the information from the meta-analyses.

Subgroup analysis and investigation of heterogeneity

We plan to carry out the following subgroup analyses:

1. Analysis based on primary malignancy
2. Open versus laparoscopic gastrojejunostomy
3. Different anaesthetic risk patients (ASA I or II (a healthy patient or mild systemic disease) versus ASA III or more (a patient with severe systemic disease of worse).

All of the primary outcomes will be used in the subgroup analysis. We will use the formal Chi^2 test for subgroup differences to test for subgroup interactions.

Sensitivity analysis

We will perform sensitivity analysis to assess the robustness of our conclusions. This will involve:

1. Excluding trials at unclear or high risk of bias (one or more of the risk of bias domains (other than blinding of surgeon) classified as unclear or high);
2. Excluding trials in which either the mean or standard deviation, or both were imputed;
3. Excluding cluster RCT in which the adjusted effect estimates were not reported;
4. Different methods of dealing with multi-arm trials (please see 'Measures of treatment effect').

Reaching conclusions

We will only base our conclusions on findings from the quantitative or narrative synthesis of studies included in this review. We will avoid making recommendations for practice; our implications for research will give the reader a clear sense of the needed focus of future research and remaining uncertainties in the field.

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We thank Karin Dearness, Managing Editor, Cochrane Upper Gastrointestinal and Pancreatic Diseases Group (UGPD) for providing administrative and logistical support for the conduct of this current review; and Racquel Simpson, former Trials Search Co-ordinator, UGPD for developing the search strategies.

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. Glossary of terms

Ampullary Carcinoma: A cancerous growth that occurs at the Ampulla of Vater. This is the area in the small bowel where the biliary system drains into the GI tract.

Anastomosis: An anastomosis is a surgical connection (join) between two tubular structures. In a gastrojejunostomy, the anastomosis is between the stomach (gastric) and jejunum (small bowel).

Anastomotic Leak: The breakdown in the join between two structures. This results in leakage of the contents of the structures into the abdominal cavity resulting in significant problems.

Benign: This refers to conditions that are not cancerous.

Bile duct: The tubular structures which drain bile (greenish liquid which is necessary for the digestion and absorption of fat) from the liver and gallbladder to the small bowel.

Biliary Obstruction: Blockage of the bile ducts due to any cause, which includes cancers. This typically results in jaundice (yellowing of the skin).

Cholangiocarcinoma: A cancer (malignant growth) of the bile ducts.

Distal: The area that is at the bottom end. For example: the distal end of the stomach is the bottom end of the stomach.

Duodenum: The first part of the small bowel which begins after the stomach.

Electrolyte Imbalance: A change in the concentration of salts in the blood (e.g.: potassium, sodium) which are essential for normal cellular function. This can occur, for example, after vomiting.

Epigastrium: This describes the area of the body that sits below the chest in the centre. Epigastric pain refers to pain that is felt in this area.

Endoscope: The instrument used to look inside the stomach and small bowel during an endoscopy. It consists of a hollow tube, about the size of your 5^{th} finger, with a light and camera. Instruments can be passed down the tube to take tissue samples from the stomach and small bowel.

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Endoscopy: Endoscopy is the process of looking inside the body with a camera attached to a scope. In gastroscopy, the camera is inserted via the mouth to the stomach and small bowel.
Fluoroscopic: This relates to the radiological technique which uses specialised dye and x-ray. It is typically used to monitor the placement of devices, including stents, in the body as it allows exact placement to be monitored.
Gastric: Refers to the stomach.
Gastric Outlet: The area of the stomach through which food passes on its route to the small bowel. The gastric outlet is in the part of the stomach that is known as the pylorus.
Gastric Outlet Obstruction (GOO): This describes the obstruction to the passage of food and liquid at the distal end of the stomach, also known as the gastric outlet.
Gastrojejunostomy: This describes a connection between the stomach (gastric) and small bowel (jejunum).
Helicobacter pylori: This is the name given to the bacteria that has been shown to be associated with peptic ulcer disease.
Intra-luminal: This refers to the inside of a hollow structure.
Jaundice: The yellow discoloration of the skin which can occur as a result of reduced drainage of bile (or biliary obstruction).
Jejunum: The middle part of the small bowel which is distal to the duodenum.
Laparoscopic: This is also referred to as minimal access surgery. This is surgery via small incisions on the abdomen through which specialised instruments are passed. This alleviates the need for large incisions on the abdomen.
Lateral: This term is used to describe the position of a structure or object. Lateral describes objects or structures to the side, whereas, medial describes objects or structure lying along the middle or centre.
Lymphoma: This is a cancer that affects the lymph nodes of the body.
Malignant: This refers to a cancerous process.
Metastatic Disease: This is disease that has spread from the organ that it originates from to lymph nodes or other organs around the body. Metastatic disease typically refers to an advanced stage of cancer.
Migration: the movement from the original position to another position. In stent migration, this refers to movement of the stent from the position it was placed to a different, and typically worse, position.
Morbidity: Complications or events that impact on the patients' ability to function and return to their normal level of functioning. For example; a chest infection that prevents walking is said to have caused morbidity.
Mortality: Death rate
Occlusion: Blockage. This can be partial or complete.
Palliation: The control of symptoms without the treatment of, or attempt to treat, the underlying cause of the symptoms.
Pathological: The result of the underlying disease process.
Peptic Ulcer: A break or erosion in the lining of the stomach or small bowel.
Perforation: A small hole that appears in part of the GI tract as a cause of disease or an intervention. For example; a gastric perforation is a hole in the stomach from which stomach contents can escape into the rest of the abdominal cavity.
Peri-operative: At the time of operation. For example; a peri-operative complication would be something at occurs during the operation.
Physiological Reserve: This refers to the capacity, predominantly in terms of heart and lung function, that a person has to withstand various insults to the body.
Pneumoperitoneum: In laparoscopic surgery, carbon dioxide is placed inside the abdomen to create space. This is known as a pneumoperitoneum.
Port: A port is a specialised device used in laparoscopic surgery through which the specialised instruments are passed. A port is either 5mm or 12mm in size and, thus, the incisions are approximately this size.
Post-prandial: Occurs following eating.
Proton-pump Inhibitor (PPI): A medicine that reduces the production of acid in the stomach. This helps to treat ulcerations in the stomach.
Pylorus: The name given to the distal end of the stomach where the gastric outlet sits. A pyloric carcinoma is a cancer that grows at the pylorus.
Roux-en-y anastomosis: This describes a surgically created end-to-side anastomosis, usually between the stomach and small bowel.
Self Expanding Metal Stent (SEMS): A stent which is able to expand and fit the patient depending on the space and external forces encountered.
Stent: A hollow tube, wither plastic or metal, or self-expanding, which is used to keep a passageway within the body open.
Terminal: This refers to conditions for which there is no cure and for which this will be the cause of death. This does not mean that the symptoms cannot be treated or improved.
Umbilicus: The area at the belly-button or navel.

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Appendix 2. CENTRAL search strategy

1. exp Gastric Outlet Obstruction/
2. (gastric adj2 outlet adj2 obstruction$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
3. GOO.mp.
4. or/1-3
5. Stents/
6. stent$.mp.
7. (endoscop$ adj2 clip$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
8. Equipment Design/
9. Prosthesis Design/
10. endoscopy, gastrointestinal/ or duodenoscopy/ or gastroscopy/
11. or/5-10
12. (surgical adj2 palliation).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
13. Palliative Care/mt [Methods]
14. Surgical Instruments/
15. or/12-14
16. 4 and (11 or 15)

Appendix 3. MEDLINE search strategy

(We had drafted a MEDLINE search strategy for a previous version of this protocol, which has been included below, for future revision)
1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. drug therapy.fs.
6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. or/1-8
10. exp animals/ not humans.sh.
11. 9 not 10
12. exp Gastric Outlet Obstruction/
13. (gastric adj2 outlet adj2 obstruction$).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
14. GOO.mp.
15. or/12-14
16. Stents/
17. stent$.mp.
18. (endoscop$ adj2 clip$).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
19. Equipment Design/
20. Prosthesis Design/
21. endoscopy, gastrointestinal/ or duodenoscopy/ or gastroscopy/
22. or/16-21
23. (surgical adj2 palliation).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
24. Palliative Care/mt [Methods]
25. Surgical Instruments/
26. or/23-25
27. 15 and (22 or 26)

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28. 11 and 27

Appendix 4. EMBASE search strategy

1. Clinical trial/
2. Randomized controlled trial/
3. Randomization/
4. Single-Blind Method/
5. Double-Blind Method/
6. Cross-Over Studies/
7. Random Allocation/
8. Placebo/
9. Randomi?ed controlled trial$.tw.
10. Rct.tw.
11. Random allocation.tw.
12. Randomly allocated.tw.
13. Allocated randomly.tw.
14. (allocated adj2 random).tw.
15. Single blind$.tw.
16. Double blind$.tw.
17. ((treble or triple) adj blind$).tw.
18. Placebo$.tw.
19. Prospective study/
20. or/1-19
21. Case study/
22. Case report.tw.
23. Abstract report/ or letter/
24. or/21-23
25. 20 not 24
26. stomach obstruction/
27. (gastric adj2 outlet adj2 obstruction$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
28. GOO.mp.
29. or/26-28
30. stent$.mp.
31. (endoscop$ adj2 clip$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
32. Equipment Design/
33. prosthesis/
34. gastrointestinal endoscopy/ or duodenoscopy/ or gastroscopy/
35. or/30-34
36. (surgical adj2 palliation).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
37. palliative therapy/ or cancer palliative therapy/
38. surgical instrument/
39. metal implantation/
40. or/36-39
41. 29 and (35 or 40)
42. 25 and 41

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CONTRIBUTIONS OF AUTHORS

Conceiving the protocol: EU

Designing the protocol: EU

Coordinating the protocol: EU

Designing search strategies: RC

Writing the protocol: EU

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