NIHR | National Institute for Health and Care Research

Journals Library

Check for updates

Health Technology Assessment

Volume 29 • Issue 68 • December 2025

ISSN 2046-4924

Cost-effectiveness of endoscopic treatments for obesity: a clinical evidence map and systematic review to inform a model-based cost-effectiveness analysis

Esther Albon, Nafsika Afentou, Janine Dretzke, James Hall, Chidubem Okeke Ogwulu, Malcolm J Price, Ken Clare, Rishi Singhal, Abd Tahrani, Emma Frew and David J Moore

DOI 10.3310/PWKQ2310

Health Technology Assessment

Extended Research Article

Cost-effectiveness of endoscopic treatments for obesity: a clinical evidence map and systematic review to inform a model-based cost-effectiveness analysis

Esther Albon,[1] Nafsika Afentou,[1] Janine Dretzke,[1*] James Hall,[1] Chidubem Okeke Ogwulu,[1] Malcolm J Price,[1] Ken Clare,[2] Rishi Singhal,[3] Abd Tahrani,[4†] Emma Frew[1†] and David J Moore[1*†]

[1]Department of Applied Health Sciences, University of Birmingham, Birmingham, UK
[2]Obesity UK, Halifax, UK
[3]University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
[4]Department of Metabolism and Systems Science, University of Birmingham, Birmingham, UK

[*]**Corresponding authors** d.j.moore@bham.ac.uk, j.dretzke@bham.ac.uk
[†]Guarantors

Published December 2025
DOI: 10.3310/PWKQ2310

This report should be referenced as follows:

Albon E, Afentou N, Dretzke J, Hall J, Ogwulu CO, Price MJ, *et al*. Cost-effectiveness of endoscopic treatments for obesity: a clinical evidence map and systematic review to inform a model-based cost-effectiveness analysis. *Health Technol Assess* 2025;**29**(68). https://doi.org/10.3310/PWKQ2310

৳# Health Technology Assessment

ISSN 2046-4924 (Online)

Impact factor: 4

A list of Journals Library editors can be found on the NIHR Journals Library website

Launched in 1997, *Health Technology Assessment* (HTA) has an impact factor of 4 and is ranked 30th (out of 174 titles) in the 'Health Care Sciences & Services' category of the Clarivate 2022 Journal Citation Reports (Science Edition). It is also indexed by MEDLINE, CINAHL (EBSCO Information Services, Ipswich, MA, USA), EMBASE (Elsevier, Amsterdam, the Netherlands), NCBI Bookshelf, DOAJ, Europe PMC, the Cochrane Library (John Wiley & Sons, Inc., Hoboken, NJ, USA), INAHTA, the British Nursing Index (ProQuest LLC, Ann Arbor, MI, USA), Ulrichsweb™ (ProQuest LLC, Ann Arbor, MI, USA) and the Science Citation Index Expanded™ (Clarivate™, Philadelphia, PA, USA).

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta.

Criteria for inclusion in the *Health Technology Assessment* journal
Manuscripts are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

This article

The research reported in this issue of the journal was commissioned and funded by the HTA programme as award number NIHR133099. The protocol was agreed in October 2021. The draft manuscript began editorial review in April 2024 and was accepted for publication in March 2025. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' manuscript and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this article.

This article presents independent research funded by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care.

This article was published based on current knowledge at the time and date of publication. NIHR is committed to being inclusive and will continually monitor best practice and guidance in relation to terminology and language to ensure that we remain relevant to our stakeholders.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Newgen Digitalworks Pvt Ltd, Chennai, India (www.newgen.co).

Abstract

Background: Bariatric surgery is the most effective treatment for obesity, but access is limited. Endoscopic obesity treatments are potentially cheaper and less invasive options, which may be similarly effective. There is currently a lack of evidence to inform decisions on whether such treatments should be considered for people living with obesity.

Objective(s): What is the current evidence for the clinical and cost-effectiveness of endoscopic treatments compared to alternative weight management interventions for obesity?

Methods: Comprehensive searches were undertaken to January 2023 and a searchable evidence map of all quantitative studies (n > 2) on endoscopic treatments was constructed. The map was used where possible to inform the economic models. Indirect comparisons were undertaken where relevant direct evidence for the model was not available. A systematic review of cost-effectiveness studies was undertaken. Targeted searches were undertaken to identify additional evidence to inform model parameters. Three economic (Markov) models were designed to estimate the cost-effectiveness of endoscopic therapies compared to alternative weight management interventions from a United Kingdom National Health Service and Personal Social Services perspective.

Results: The evidence map included over 1500 records of studies of endoscopic therapies, most of which related to intragastric balloons and endoscopic sleeve gastrectomy. Three cost–utility analyses were identified, one of which was set in the United Kingdom and was used to inform the models.

Laparoscopic sleeve gastrectomy is likely cost-effective compared with endoscopic sleeve gastroplasty for patients' obesity class II and III (£10,593 per quality-adjusted life-year-gained). Endoscopic sleeve gastroplasty is likely cost-effective compared with semaglutide for patients' obesity class I and II (£7267 per quality-adjusted life-year-gained). Semaglutide is dominant (cheaper and more effective) than intragastric balloon in patients' obesity class I and II. Probabilistic sensitivity analysis found a degree of confidence in the estimates. The 5-year time horizon may not capture longer-term benefits from endoscopic sleeve gastroplasty or laparoscopic sleeve gastrectomy.

Limitations and conclusions: The effectiveness evidence base was greater and more wide-ranging than anticipated. However, for the interventions compared within the economic models, there were no randomised controlled trials and either limited, or an absence of, direct comparative evidence. There was also limited long-term data on interventions. These limitations necessitated the use of assumptions in modelling.

Future work: Future research should focus on longer-term effectiveness of endoscopic treatments, studies directly comparing endoscopic therapies against semaglutide or other emerging weight loss drugs and studies which better reflect the complex treatment pathways of obesity and different obesity classes. Such studies could provide more robust evidence for informing future cost-effectiveness models beyond a 5-year time horizon.

Study registration: This study is registered as PROSPERO CRD42022302942.

Funding: This award was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme (NIHR award ref: NIHR133099) and is published in full in *Health Technology Assessment*; Vol. 29, No. 68. See the NIHR Funding and Awards website for further award information.

Contents

List of tables

List of figures

List of supplementary material

Report Supplementary Material 1 Supplementary material

Supplementary material can be found on the NIHR Journals Library report page (https://doi.org/10.3310/PWKQ2310).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

The supplementary materials (which include but are not limited to related publications, patient information leaflets and questionnaires) are provided to support and contextualise the publication. Every effort has been made to obtain the necessary permissions for reproduction, to credit original sources appropriately, and to respect copyright requirements. However, despite our diligence, we acknowledge the possibility of unintentional omissions or errors and we welcome notifications of any concerns regarding copyright or permissions.

Glossary

Cost-effectiveness acceptability curves The cost-effectiveness acceptability curve presents the uncertainty surrounding the incremental cost-effectiveness ratio across various cost-effectiveness thresholds. It portrays a spectrum of cost-effectiveness thresholds on the horizontal axis against the probability of the intervention being cost-effective at each threshold on the vertical axis.

Cost-effectiveness planes The cost-effectiveness plane is a scatterplot illustrating the incremental health outcomes between two treatments on the horizontal axis and incremental costs on the vertical axis. Usual care typically serves as the origin, with horizontal and vertical values indicating incremental effects and costs compared to usual care. The plane consists of four quadrants:

- The northeast quadrant depicts new treatments offering greater health gains at higher costs.
- The northwest quadrant represents a new intervention yielding fewer health gains at a higher cost.
- Both southern quadrants reflect lower intervention costs, with lower intervention health outcomes in the southwest quadrant and higher health gains in the southeast quadrant.
- Cost-effectiveness planes usually display numerous points forming a 'cloud', each point corresponding to a different iteration of the model generated during probabilistic sensitivity analysis, visually representing uncertainty around the cost-effectiveness result.

Cost–utility analysis Cost–utility analysis evaluates health economic outcomes in terms of quality-adjusted life-years compared with their cost.

Incremental cost-effectiveness ratio The incremental cost-effectiveness ratio is a key measure in cost-effectiveness analysis, indicating the economic value of a healthcare intervention. It calculates the cost per unit of health outcome by dividing the difference in cost between two interventions by the difference in health outcome measures.

Markov model In health economic analyses, a Markov model employs health states to predict the likely consequences of an intervention. These states are mutually exclusive and exhaustive, ensuring each individual within the model occupies only one state at any given time. Patients move states over time reflective of their prognosis.

National Institute for Health and Care Excellence cost-effectiveness threshold The National Institute for Health and Care Excellence employs a threshold of £20,000–30,000 per quality-adjusted life-year gained to assess various medical treatments and technologies. Generally speaking, treatments exceeding this threshold are considered not cost-effective and are not typically recommended for National Health Service adoption.

Probabilistic sensitivity analysis Probabilistic sensitivity analysis enables economic modellers to gauge the confidence level in their model results by reflecting uncertainty associated with all model input parameters. These parameters are often sourced from clinical trials, observational studies, or expert opinion and are represented as distributions around point estimates. A simulation package then randomly samples each parameter from these distributions to create thousands of model iterations.

Quality-adjusted life-year Quality-adjusted life-year serves as a generic measure of disease burden, incorporating both the quality and quantity of life lived. It is widely utilised in economic analyses to evaluate the value of medical interventions as the generic measure can be used across disease areas.

Sham procedure An inactive procedure that is designed to mimic as closely as possible the active procedure being studied in a clinical trial.

Transition probability The transition probability represents the proportion of patients within a health state in a Markov model who transition to a particular health state within one model cycle.

Utility value A utility value, ranging from 0 to 1, represents the quality of life of a particular patient or patient group. Utility values are used within the quality-adjusted life-year framework to assess the quality of life, where 1 signifies full health and 0 represents death.

List of abbreviations

AE	adverse event
AOM	anti-obesity medication
APC	argon plasma coagulation
AWL	absolute weight loss
BMI	body mass index
Botox	botulinum toxin
BPD	biliopancreatic diversion
CBA	cost–benefit analysis
CBT	cognitive–behavioural therapy
CDSR	Cochrane Database of Systematic Reviews
CEA	cost-effectiveness analysis
CEAC	cost-effectiveness acceptability curve
CENTRAL	Cochrane Central Register of Controlled Trials
CHD	coronary heart disease
CPRD	Clinical Practice Research Datalink
CUA	cost–utility analysis
CVD	cardiovascular disease
DALY	disability-adjusted life-year
DJBL/DJBS	duodenal–jejunal bypass liner/sleeve
DMR	duodenal mucosal resurfacing
DSA	deterministic sensitivity analyses
EGCP	endoluminal greater curvature plication
EQ-5D	EuroQol-5 Dimensions
ESD	endoscopic submucosal dissection
ESG	endoscopic sleeve gastroplasty
EVG	endoluminal vertical gastroplasty
EWL	excess weight loss
GERD	gastro-oesophageal reflux disease
GJA	gastro jejunal anastomosis
GLP-1	glucagon-like peptide-1
ICER	incremental cost-effectiveness ratio
IGB	intragastric balloon
IOP	Incisionless Operating Platform
ITT	intention to treat
LAGB	laparoscopic adjustable gastric band
LGB	laparoscopic gastric bypass
LGCP	laparoscopic greater curvature plication
LGP	laparoscopic gastric plication
LMGB	laparoscopic mini gastric bypass
LOCF	last observation carried forward
LSG	laparoscopic sleeve gastrectomy
LSI	lifestyle intervention
LYG	life-year gain/gained
MA	meta-analysis
MBSAQIP	Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program
NAFLD	non-alcoholic fatty liver disease
NASH	non-alcoholic steatohepatitis
NICE	National Institute for Health and Care Excellence
NR	not reported
ONS	Office of National Statistics
ORC	obesity-related complications
POSE	Primary Obesity Surgery Endoluminal
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
PSA	probabilistic sensitivity analysis
PSS	Personal Social Services
QALY	quality-adjusted life-year
QoL	quality of life
RCT	randomised controlled trial
ROSE	restorative obesity surgery endoluminal
RYGB	Roux-en-Y gastric bypass
SAEs	serious adverse events
SG	semaglutide

SF-36	36-Item Short Form Survey
SR	systematic review
T2D	type 2 diabetes
TBWL	total body weight loss
TERIS	transoral endoscopic restrictive implant system
TOGA	transoral gastroplasty
TORe	transoral outlet reduction by endoscopy
TPS	TransPyloric Shuttle™
WET	Weight-Loss Endoscopy Trial
WHO	World Health Organization
WL	weight loss
WTP	willingness to pay

Plain language summary

Treating obesity can improve the health and quality of life of people living with obesity and reduce the burden of obesity-associated medical problems. It also has wide-ranging economic benefits. Bariatric (weight loss) surgery remains the most effective long-term treatment and is good value for money for the United Kingdom healthcare system. However, there are barriers to accessing this surgery including a lack of resources and variability in service availability. Endoscopy is a non-surgical procedure that uses a flexible tube (an endoscope) passed through the mouth to look at the digestive tract. Small tools located at the end of the endoscope can be used to help weight loss by changing the size or shape of the stomach or by inserting a liner or balloon. Endoscopic weight loss therapies may be cheaper, more acceptable alternatives as they are less invasive and need a shorter hospital stay.

We undertook a wide-ranging systematic search of the published literature and identified a large number of articles (1574) looking at endoscopic therapies. We also identified many different types of endoscopic therapies. We have produced an extensive list of these studies to aid future understanding of the effects of these therapies. There were limited studies on the value for money of endoscopic therapies.

Therefore, we built three models to compare the cost-effectiveness between treatments over 5 years. These models found that laparoscopic sleeve gastrectomy (a bariatric surgery procedure) is likely to be better value for money than endoscopic sleeve gastroplasty (an endoscopic approach to reducing stomach size). Endoscopic sleeve gastroplasty is likely to be better value for money than semaglutide (a weight loss drug). Semaglutide is likely to be better value for money than a gastric balloon placed via endoscopy. This suggests that both endoscopic sleeve gastroplasty and semaglutide are feasible options for weight loss. The choice may depend on the stage a patient is at in their weight loss journey and their preference. Despite the findings of the models, it is important to realise that the data did not originate from high-quality studies directly comparing these therapies and some assumptions on how effective the therapies would be over long periods of time had to be used. Future studies should directly compare the therapies, follow patients for longer and consider that some patients receive multiple treatments for obesity over time.

Scientific summary

Background

Obesity is a common disease associated with poorer quality of life (QoL), increased risk of multiple metabolic, vascular, physical and mental health complications and mortality, and significant economic impact. Bariatric surgery is currently the most effective obesity treatment for sustained long-term weight loss and improvements in obesity complications. Despite its effectiveness, access to bariatric surgery is limited due to multiple factors including lack of resources among others. Lifestyle behavioural interventions (LSIs) are known to have modest effectiveness that is difficult to sustain long term. Endoscopic obesity treatments are becoming increasingly available globally and in the UK. Compared to bariatric surgery, they are less invasive, require a shorter hospital stay and are potentially cheaper, while replicating some of the anatomical and physiological changes that occur after bariatric surgery. This makes them a potential alternative, or bridge to, bariatric surgery. It is important to determine whether endoscopic treatments are both clinically effective and cost-effective to inform decision-making from the UK NHS/Personal Social Services (PSS) perspective on their potential for treating people living with obesity.

Aims and objectives

What is the current evidence for the clinical and cost-effectiveness of endoscopic treatments compared to alternative weight management interventions for obesity?

The specific objectives were:

- To produce a map of the evidence on the effectiveness of endoscopic therapies for obesity based on randomised, non-randomised controlled and uncontrolled studies.
- To undertake one or more systematic reviews of the clinical effectiveness of different endoscopic treatments, with the potential for undertaking meta-analyses, subgroup analyses and a network meta-analysis to determine the relative effectiveness of different treatments. As this was not feasible due to the vast numbers of studies, interventions and comparators, greater emphasis was placed on the evidence map with more detailed analysis limited to evidence that could be used to inform the economic model.
- To undertake a systematic review of available economic evidence on the use of endoscopic treatments for obesity.
- To undertake a model-based cost-effectiveness analysis comparing endoscopic treatments with other alternative treatments from the UK NHS/PSS perspective; in consultation with the steering group, three separate economic models were developed to enable key endoscopic therapies to be compared to laparoscopic bariatric surgery or pharmacotherapy.

Methods

The review was registered on PROSPERO (CRD42022302942) and reporting followed the general principles of the Preferred Reporting Items for Systematic Reviews and Meta Analyses.

Evidence map

Searches and study selection

Databases [Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE] were searched from inception to January 2023. There were no restrictions by study design, language, date of publication or publication type. Two reviewers independently undertook title and abstract screening and full-text selection. Disagreements were resolved by a third reviewer or by consensus and reasons for exclusion were recorded.

Eligibility criteria

Studies of patients of any age with obesity (as defined by the study authors) who received any endoscopic treatment were eligible. Any randomised, non-randomised controlled or single-arm study design was eligible (with $n \geq 2$). Any, or no, comparators were eligible (e.g. bariatric surgery, LSI, pharmacotherapy, a different endoscopic treatment) and any obesity-related outcome was eligible (e.g. weight loss, change in diabetes status, adverse events, QoL).

Construction and reporting of evidence map

A searchable database map of all available evidence for endoscopic treatments for obesity was constructed in Microsoft Excel® (Microsoft Corporation, Redmond, WA, USA). Details on the population, intervention(s), comparator(s) where relevant, study design, sample size and length of follow-up were extracted by a single reviewer based on the abstract. Information on randomised controlled trials (RCTs) was checked by a second reviewer. Key descriptors were added to the evidence map via drop-down menus to enable filtering. Summary tables were used to collate the evidence from the map into four overarching categories: (1) restrictive procedures, (2) space-occupying devices, (3) malabsorption devices and procedures and (4) other endoscopic procedures. For all RCTs and non-randomised controlled studies, a brief narrative description was also provided.

Use of the evidence map to inform the economic evaluation

A full systematic review of effectiveness of all endoscopic treatments was not possible, given the vast volume of evidence and the numerous interventions and comparators. The map was therefore used to identify relevant evidence to inform the economic models.

Indirect comparisons

Where direct evidence on relevant interventions being compared was not available from the evidence map, indirect comparisons were undertaken. This is where treatments are compared indirectly across different studies based on the fact that they have the same comparator in common and are also similar in other aspects. RCTs were sought from existing systematic reviews and targeted searches of Cochrane CENTRAL. Stata® (version 17) (StataCorp LP, College Station, TX, USA) was used to undertake random effects meta-analyses, and results from pair-wise meta-analyses were used to perform indirect comparisons.

Systematic review of cost effectiveness

The broad searches used to identify effectiveness studies for the evidence map were also used to identify any model-based economic evaluations for this review. Trial-based or model-based economic evaluations comparing the costs and outcomes from two or more obesity treatments where at least one was an endoscopic therapy were eligible for inclusion. Appropriate risk of bias tools were applied and a narrative synthesis was undertaken.

Economic evaluation

Model development was informed by evidence from the evidence map, the indirect comparisons, evidence found through purposive literature searches beyond endoscopic procedures and clinical assumptions. Three state transition cohort Markov models were designed in Microsoft Excel 2018 to estimate the cost-effectiveness of endoscopic therapies compared to alternative weight management interventions for adult patients with obesity (body mass index of > 30 kg/m^2). A cost–utility analysis was conducted based on the outcome of cost per quality-adjusted life-year (QALY). The base-case analysis was from the perspective of the NHS and PSS over a 5-year time horizon. Costs and benefits were subjected to an annual discount rate of 3.5%, following the recommendation of National Institute for Health and Care Excellence. The comparison of the following treatments was conducted within three separate economic models for a 5-year time horizon: model 1: endoscopic sleeve gastroplasty (ESG) versus laparoscopic sleeve gastrectomy (LSG); model 2: ESG versus semaglutide; model 3: intragastric balloon (IGB) versus semaglutide. Patients could transition between four obesity health states and cycle length was 6 months for the first cycle and 12 months thereafter. Uncertainty was explored via both deterministic and probabilistic sensitivity analyses.

Results

Evidence map

There were 1574 records of relevant studies included in the evidence map, with 90% of these published after 2009. Most of these records were related to single-arm studies (73%), 18% related to non-randomised controlled studies, and 9% related to RCTs. The most common endoscopic interventions were space-occupying devices (mainly IGB), restrictive procedures (mainly variations of ESG) and to a lesser extent malabsorption devices (such as duodenal–jejunal bypass liner). The most common comparators were a different endoscopic treatment (or variation of the same treatment), bariatric surgery (often LSG) and LSI, with sham procedures and pharmacotherapy less well represented. Most studies reported weight loss and/or safety outcomes but could also include changes in body composition, satiety and gastric emptying, and biomarkers of metabolic and glycaemic control. Duration of follow-up varied from 1 week to 5 years but was most frequently between 6 and 12 months. The vast majority of studies were in adults, with very few records relating to studies undertaken in children or adolescents. Patients were enrolled for weight loss prior to surgery ('bridge to surgery') or following weight regain after previous obesity treatment in a small proportion of studies. A limitation of the map is the reliance on abstracts only for data extraction.

In terms of informing the economic models, non-randomised studies comparing ESG with LSG as well as studies reporting weight loss in the longer-term were identified from the evidence map.

Indirect comparisons

Seven RCTs were included in the indirect comparison, two RCTs comparing ESG with LSI, three RCTs comparing IGB with LSI and two RCTS comparing semaglutide with LSI. The analysis found little evidence of a difference in mean per cent of total body weight loss (95% confidence interval) between ESG and semaglutide at 6 months [2.15 (−29.47 to 33.76)] and 12 months [0.54 (−2.05 to 3.14)]. There was also little evidence of a difference between IGB and semaglutide at 6 months [0.37 (−6.25 to 6.98)] but good statistical evidence of a difference in favour of greater weight loss with semaglutide at 12 months [−7.91 (−11.14 to −4.67)]. Limitations of the analysis include some uncertainty around the transitivity assumptions made such as similarity of comparators and populations.

Systematic review of cost-effectiveness

Three cost–utility analyses were identified, conducted within a UK, USA, or Canadian setting. The studies explored three endoscopic therapies, ESG, swallowable IGB and aspiration therapy, compared against LSI or bariatric surgery. A lifetime horizon was used in models and primary outcomes were reported in terms of cost per QALY. Study findings could not be directly compared, given the differences in treatments compared and methods used, but overall findings suggested that endoscopic therapies were cost-effective when compared to LSI or no treatment but were dominated when compared to bariatric surgery. A common and significant limitation across all the studies was the scarcity of long-term data on the effectiveness of endoscopic therapies, and the lack of data on direct comparisons of different treatments. The UK cost–utility analysis was considered the most useful to inform the development of the new economic models because of the relevance of the setting (UK) and patient population.

Economic evaluation

Model 1 found that LSG is likely to be cost-effective compared with ESG, for the treatment of patients with obesity class II and III (£10,593 per additional QALY with LSG when compared with ESG in base case). This finding was robust to deterministic and probabilistic sensitivity analyses. Only the most pessimistic scenario regarding long-term efficacy with LSG led to an incremental cost-effectiveness ratio (ICER) approaching an upper threshold limit of £30,000/QALY.

Model 2 found that ESG is likely to be cost-effective compared with semaglutide for the treatment of patients with obesity class I and II (£7267 per additional QALY with ESG when compared with semaglutide in base case). This finding was more sensitive to deterministic sensitivity analyses, particularly cost, with a reduction in ESG costs by 10–20% resulting in ESG becoming dominant. The results were also sensitive to a reduction in assumed weight regain with semaglutide, resulting in an increased ICER for ESG.

Model 3 found that semaglutide is the dominant (cheaper and more effective) treatment option in the base case compared with IGB in patients with obesity class I and II, but the effect differences are very small. Semaglutide loses its dominance with a decrease of IGB costs by around 20%.

While the probabilistic sensitivity analysis (PSA) found a degree of confidence in the base-case estimates, there remains some uncertainty relating to the comparability of the included studies evaluating the different therapies. There were no RCTs directly comparing the interventions and it is possible the PSA could have overestimated certainty in the results. Other limitations include basing utility values and comorbidity costs on obesity health states rather than being directly associated with history of weight loss. Also, the 5-year time horizon may not capture longer-term benefits from ESG or LSG but was felt to be appropriate due to the lack of evidence on long-term weight trajectory following treatment. Weight loss beyond 12 months is based solely on clinical assumption for semaglutide and, as such, base-case estimates for models 2 and 3 should only be considered in the context of the sensitivity analyses.

Conclusions

A vast amount of research has been undertaken on a range of endoscopic therapies for obesity. The searchable evidence map provides a useful repository of evidence which can be used for planning and informing future research, including economic models. There were few economic evaluations of endoscopic therapies, and the models developed for this report will therefore add early evidence to the cost-effectiveness of endoscopic therapies. The three Markov models respectively found that over a 5-year time horizon, LSG was likely to be cost-effective compared with ESG (for obesity class II and III), and for obesity class I and II, ESG was likely to be cost-effective compared with semaglutide, and IGB was dominated by semaglutide. The model comparing ESG and LSG was robust to sensitivity analyses, while the other models were somewhat sensitive to intervention costs. There was substantial uncertainty around long-term weight loss for both semaglutide and IGB.

Future research

Future research should focus on longer-term studies evaluating effectiveness of endoscopic treatments, studies directly comparing endoscopic therapies against semaglutide and other emerging weight loss drugs, and studies which better reflect the complex treatment pathways of obesity. It could also explore the effectiveness of endoscopic therapies for patients in different obesity classes. Such studies could provide more robust evidence for informing future cost-effectiveness models beyond a 5-year time horizon.

Study registration

This study is registered as PROSPERO CRD42022302942.

Funding

This award was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme (NIHR award ref: NIHR133099) and is published in full in *Health Technology Assessment*; Vol. 29, No. 68. See the NIHR Funding and Awards website for further award information.

Chapter 1 Background

Introduction

Obesity is a common disease that has increased in prevalence globally over the last four decades and is associated with a poorer quality of life (QoL), increased risk of multiple metabolic, vascular, physical and mental health complications and mortality, and significant economic impact on the NHS and wider economy.[1] Weight loss (WL) is proven to reduce the health and economic burden of obesity and improve QoL.[1] Bariatric surgery is currently the most effective obesity treatment resulting in sustained long-term WL and improvements in obesity complications and QoL.[2] Endoscopic obesity treatments are increasingly performed globally[3] and are increasingly available in the UK. These treatments are less invasive than laparoscopic bariatric surgery, require shorter hospital stay, and are aimed at replicating some of the physiological changes that occur after surgery, which makes them a bridge, or a potential alternative, to bariatric surgery.[4] This chapter describes the classification and epidemiology of obesity and gives an overview of management approaches.

Classification of obesity

The World Health Organization (WHO) defines obesity as abnormal or excessive fat accumulation that presents a risk to health and defines a body mass index (BMI) over 25 and 30 to be consistent with overweight and obesity, respectively.[5] Different classes of weight are further defined by National Institute for Health and Care Excellence (NICE) as 'healthy weight' (BMI 18.5–24.9 kg/m^2), 'overweight' (BMI 25–29.9 kg/m^2), 'obesity class 1' (BMI 30–34.9 kg/m^2), 'obesity class 2' (BMI 35–39.9 kg/m^2) and 'obesity class 3' (BMI 40 kg/m^2 or above).[6] Due to differences in body composition and higher health risks, BMI cut-offs to define obesity vary by ethnicity with lower cut-offs for overweight and obesity defined for South and East Asian populations.[7] More recently, studies have found that other measurements such as fat mass index, waist-to-hip ratio, and waist-to-height ratio may have more consistent associations with inflammatory markers and mortality and thus may be more suitable for targeting healthcare interventions.[8–10]

Epidemiology of obesity

Obesity prevalence continues to increase globally with 2.6 billion (38% of the world population) with obesity and overweight in 2020 that is expected to rise to over 4 billion (over 50% of the world population) by 2035.[11] The prevalence of obesity (BMI ≥ 30 kg/m^2) is also expected to rise from 14% to 24% over the same period, with nearly 2 billion adults, children and adolescents affected by 2035.[11] In England, obesity affects 26% of men and 29% of women.[12] This is a steep increase from 1993 and was accompanied by an increase in the prevalence of severe obesity (BMI ≥ 40 kg/m^2) from 1% in 1993 to 3% in 2018.[12] The high prevalence of obesity affects all ethnicities and age groups, with a peak in men and women aged 45–64 years.[12,13] Obesity is associated with poorer QoL and an increased risk of type 2 diabetes (T2D), cancers, and cardiovascular disease (CVD).[14–17] In England, obese adults are five times more likely to be diagnosed with T2D than healthy weight adults.[18] There is also a greater risk of asthma, depression, metabolic syndrome, gastro-oesophageal reflux disease (GERD) and obstructive sleep apnoea among others.[6] In addition, obesity is associated with increased mortality and reduced survival of between 3 and 14 years. Obesity and being overweight contribute to at least 1 in every 13 deaths in Europe.[15–17,19] More recently, obesity was associated with an increased risk of severe COVID-19.[20]

Cost of obesity

The World Obesity Federation has estimated that the economic impact of overweight and obesity will reach almost 3% of global gross domestic product (around $4.32tn) annually by 2035.[21] The NHS spent £6.1B on overweight or obesity-related ill-health in 2014–5 with an estimated cost to wider society of £27B.[22] These annual costs are projected to reach £9.7B for the NHS, and £49.9B for society by 2050.[22] Besides excess healthcare expenditure, costs from obesity also stem from lost productivity as a result of lost work days, lower productivity at work, mortality and permanent disability.[23]

Management of obesity

Overall obesity management options can be classified into three categories including lifestyle behavioural interventions, pharmacotherapy and laparoscopic bariatric surgery.[24] In the UK, obesity care is delivered via clinical pathways for obesity, which has four tiers. Tier 1 represents public health interventions, tier 2 represents lifestyle interventions (LSIs) that can be delivered widely (e.g. through apps), tier 3 is medical weight management and tier 4 is bariatric surgery.[25] Tier 3 is commonly delivered over a 2-year period and usually precedes moving to tier 4. Tier 4 usually includes a 2-year follow-up after bariatric surgery.

National Institute for Health and Care Excellence recommends adjusting the level of interventions for people with overweight and obesity based on the presence of obesity complications and the severity of the disease as well as patients' wishes and considerations.[8] NICE recommends referral to tier 3 in the following if:

- the underlying causes of overweight or obesity need to be assessed
- the person has complex disease that cannot be managed adequately in tier 2
- conventional treatment has been unsuccessful
- drug treatment is being considered for a person with a BMI of more than 50 kg/m^2
- specialist interventions (such as a very-low-calorie diet) may be needed
- surgery is being considered.

In addition, NICE recommends referral for bariatric surgery if the patient:

- has a BMI of 40 kg/m^2 or more, or between 35 and 39.9 kg/m^2 with a significant health condition that could be improved if they lost weight *and* agrees to the necessary long-term follow-up after surgery (e.g. lifelong annual reviews).

Lower cut-offs are recommended for non-White European ethnicities. NICE also recommends that expedited assessment for bariatric surgery can be offered for patients with T2D duration < 10 years with a BMI above 30 kg/m^2.

Due to the high prevalence of obesity and the complex biological and environmental drivers, it is likely that a combination of policy addressing the obesogenic environment with improved access to obesity treatments are needed to reduce the burden of the current obesity pandemic.

Lifestyle behavioural interventions

Lifestyle interventions include a variety of treatment strategies that usually combine dietary interventions with exercise and address the behavioural drivers for obesity and increased energy intake. Their efficacy is largely modest, but the impact of even modest adiposity loss has important favourable effects on obesity-related complications.[26] However, a major challenge for WL via LSIs is the difficulty in maintaining the WL in the majority of patients; even 5% WL is regained within 2 and 5 years in 50% and 80% of patients, respectively.[27–33] This weight regain is driven by complex neurohormonal metabolic adaptations.[28–30,33] Hence, there is a need for treatment strategies that can maximise WL and WL maintenance. Some of the above-mentioned metabolic adaptations such as changes in satiety hormone levels are addressed by pharmacotherapy or bariatric surgery which result in more sustained long-term WL.[34,35]

Pharmacotherapy

Pharmacotherapy may be included as a WL intervention where LSIs alone have failed. There are a range of WL drugs available with different mechanisms of action. NICE currently recommends orlistat for a BMI ≥ 30 kg/m^2 (or ≥ 28 kg/m^2 with associated risk factors) and liraglutide or semaglutide for a BMI ≥ 35 kg/m^2 (with lower thresholds depending on ethnicity and other risk factors).[8]

Both liraglutide 3.0 mg daily (Saxenda) and semaglutide 2.4 mg weekly (Wegovy®, Bagsvaerd, Denmark) are glucagon-like peptide-1 (GLP-1) receptor agonists, which mimic the GLP-1 hormone that is released in response to eating and result in reduced blood glucose and reduced appetite.[36,37] Semaglutide is more effective than liraglutide for lowering body weight, glycated haemoglobin and waist circumference.[36] The most common adverse events (AEs) for semaglutide are gastrointestinal disorders, which are generally mild and transient.[36] Rare serious side effects can include gall bladder disorders and pancreatitis.[36] NICE currently recommend the use of semaglutide and liraglutide for weight management in specific populations for a maximum of 2 years alongside LSIs.[37,38]

Laparoscopic bariatric surgery

The most common bariatric procedures in the UK are the Roux-en-Y gastric bypass (RYGB), laparoscopic sleeve gastrectomy (LSG), laparoscopic adjustable gastric banding (LAGB)[39] and, more recently, single anastomosis gastric bypass. Currently RYGB is the most commonly performed procedure in the UK, but LSG is increasing rapidly while LAGB is diminishing. The mechanisms of action of bariatric surgery are complex and multifactorial ranging from vagal stimulation to complex neurohormonal interactions caused by the anatomical changes from the surgery, a summary of these mechanisms can be found here.[2] Length of hospital stay is around 2–3 days for gastric bypass, 1–2 days for sleeve gastrectomy and 0–1 day for gastric banding.[40] Originally, bariatric surgery was performed through the open method, but these days procedures are primarily performed laparoscopically as this method is associated with fewer complications and shorter hospital stay.[41]

All bariatric surgery comes with the risk of complications. For gastric bypass, complications include leaks, anastomotic stenosis, staple line bleeding, internal hernia, acute gastric dilation and intestinal obstruction.[40] For sleeve gastrectomy, it includes wound disruptions, postoperative anastomosis leak or bowel obstruction.[42] Gastric band complications can include acute band slippage or migration, splenic or oesophageal injury, band erosion and reservoir deflation/leak.[40]

Bariatric surgery, especially gastric bypass, has been shown to be the most cost-effective procedure compared with weight management programmes and very-low-calorie diets in the Health Technology Assessment-funded REBALANCE mixed-methods systematic review and economic evaluation.[43] The WL after LAGB is around 15% on average with LSG and RYGB achieving 25–30% WL that is sustained for more than 10 years.[2,44]

However, despite the above-mentioned NICE guidelines, access to bariatric surgery is limited in the UK with around 4000–5000 primary bariatric surgery per year.[45] This is one of the lowest number of bariatric surgeries in Europe, which is surprising considering that the UK obesity prevalence is one of the highest in Europe.[46] The limited access to bariatric surgery is driven by lack of financial resources and variation in the provision and commissioning of weight management services across the country and worsened by obesity stigma.[47,48] Privately funded bariatric surgery saw an increase of 79% in the UK between 2014 and 2018, rising from 1153 cases to 2065 cases.[39] However, due to the difficulty in access and the challenges of scaling up bariatric surgery to treat the large number of people living with obesity, there is a need for other interventions that are clinically and cost effective.

Endoscopic obesity treatments

Endoscopic procedures have emerged as a possible alternative to laparoscopic bariatric surgery.[49,50] These endoscopic treatments are expected to be more affordable than bariatric surgery and are less invasive requiring less time in hospital.[51] Hence, endoscopic treatments might address some of the barriers of access to bariatric surgery and

TABLE 1 Overview of endoscopic procedures for obesity[52–56]

Type of device or procedure	Examples of commercial devices	Brief description	Length of placement, reversibility of procedure
(a) Restrictive procedures			
Variations on endoscopic sleeve gastrectomy/gastroplasty (ESG) using different approaches to suturing or stapling. All result in reduction of gastric volume	OverStitch™ suturing device (Apollo Endosurgery, Austin, TX, USA)	Endoscope equipped with a mounted suturing platform. A tissue grasper device is used to capture the desired location of the suture at the gastric wall. The tissue is then retracted into the suturing arm of the device. A small sleeve is created along the greater curvature of the stomach using full-thickness running sutures	Permanent but potentially reversible
	Endomina™ suturing device [Endo Tools SA (STT), Gosselies, Belgium]	Creation of an endoscopic gastroplasty alongside the greater curvature of the stomach. Over-the-scope triangulation platform attached to an endoscope, which allows application of anterior-to-posterior greater curvature plications	Permanent but potentially reversible
	EndoCinch suturing system (C.R. Bard Inc., Murray Hill, NJ, USA)	Stomach tissue is suctioned into capsule attached to endoscope and sutures are deployed in a continuous and cross-linked fashion from the proximal fundus to the distal body of the stomach to create a narrow tube-like passage	Permanent but potentially reversible
	Restore Suturing System (Bard Davol, Warwick, RI, USA)	Modified version of EndoCinch; allows multistitch suturing and suture fastening during single intubation	Permanent but potentially reversible
	Primary Obesity Surgery Endoluminal (POSE) Incisionless Operating Platform (USGI Medical San Clemente, CA, USA)	Endoscopic plication of the stomach in the region of the fundus and distal body to reduce gastric volume. Transmural plications are placed at eight to nine locations in the gastric fundus with an additional three plications in the distal part of the stomach	Permanent but potentially reversible
	Transoral gastroplasty (TOGA) system (Satiety Inc., Palo Alto, CA, USA)	Endoscopically guided flexible staplers (introduced over a guide wire) that enable the creation of a restrictive pouch along the lesser curvature of the stomach	Permanent but potentially reversible
Restrictive implant	Trans-Oral Endoscopic Restrictive Implant System (TERIS, Barosense, Inc., Menlo Park, CA, USA)	Placement of a restrictor with a 10 mm central channel for food passage at the gastric cardia, thereby creating a restrictive pouch. Involves plication formation and placement of five anchors around the cardia	Permanent, but removal or modification is possible

Type of device or procedure	Examples of commercial devices	Brief description	Length of placement, reversibility of procedure
Transoral outlet reduction	TORe	Endoscopic revision procedure for post-RYGB patients with weight regain. Endoscopic suturing at the gastro-jejunal anastomosis site to reduce the size of the stomal opening	Permanent but potentially reversible
(b) Gastric-occupying devices			
Endoscopically placed fluid filled intragastric balloon (IGB)	BioEnterics (Orbera) Intragastric Balloon System and Orbera 365 (OIBS; Apollo Endosurgery, Inc., Austin, TX, USA); ReShape and ReShape Integrated Dual Balloon System (ReShape Medical, Inc., San Clemente, CA, USA), Spatz3, (Spatz Medical, Fort Lauderdale, FL, USA), Silimed (Silimed, Rio de Janeiro, Brazil), MedSil (Medsil, Moscow, Russia)	Space-occupying silicone balloon filled with saline	Up to 6 months, except for the Spatz and Orbera365 (12 months). Removal by endoscopy
Endoscopically placed air-/gas-filled IGB	Heliosphere (Helioscopie Medical Implants, Vienne, France), Ballobes (Ballobe, DOT ApS, Rödovre, Denmark), Garren-Edwards gastric bubble (American Edwards Laboratories, Santa Ana, CA, USA)	Double-bag polymer balloon covered with a silicone envelope	Up to 6 months. Removal by endoscopy
Swallowable fluid-filled IGB	Allurion (formerly Elipse, Allurion, Natick, MA, USA)	Swallowable capsule containing deflated balloon and attached to tube. Capsule is filled with saline once in stomach	Up to 4 months. Sutures closing balloon valve degrade over time and balloon deflates and is passed naturally
Swallowable air-/gas-filled IGB	Obalon (Obalon Therapeutics Inc., Carlsbad, CA, USA)	Swallowable capsule containing deflated balloon. Capsule is inflated via microcatheter inflated once in stomach	Up to 4 months. Removal by endoscopy
	Ullorex (Phagia Technologies, Inc., Fort Lauderdale, FL, USA)	Swallowable capsule that is injected with citric acid. After 4 minutes, the injected acid reacts with sodium-bicarbonate and the gas product of this reaction (carbon dioxide) inflates the balloon	Balloon has a plug that is degraded by gastric acid over 25–30 days, thereby allowing the balloon to deflate and to be passed naturally
Other endoscopically placed space-occupying devices	Transpyloric shuttle (BAROnova Inc., Goleta, CA, USA)	Silicone device consisting of a large spherical bulb connected to a smaller cylindrical bulb by a flexible catheter	Up to 12 months. Endoscopic removal
	SatiSphere (EndoSphere, Inc., Columbus, OH, USA)	Nitinol guidewire with mounted polyethylene terephthalate oval balloons implanted into pylorus and duodenum	Up to 3 months. Endoscopic removal

continued

TABLE 1 Overview of endoscopic procedures for obesity[52–56] (*continued*)

Type of device or procedure	Examples of commercial devices	Brief description	Length of placement, reversibility of procedure
Orally administered capsules ingested before a meal	Gelesis100 (Gelesis, Boston, MA, USA)	Modified cellulose cross-linked with citric acid; creates three-dimensional matrix. When hydrated in stomach it occupies about one-fourth of stomach volume	Broken down by enzymes
(c) Malabsorptive/metabolic therapies			
Duodenal–jejunal bypass liner (also termed duodenal–jejunal bypass sleeve or endoluminal bypass liner)	EndoBarrier Gastrointestinal Liner (GI Dynamics Inc., Lexington, MN, USA)	Flexible, endoscopically implanted, and removable 60-cm long sleeve that is impermeable to nutrients; open at both ends, anchored in the duodenal bulb and extended into the proximal jejunum. Provides a physical barrier to the duodenal mucosa	3–12 months, endoscopic removal
Duodenal mucosal resurfacing (DMR)	Revita DMR system (Fractyl Laboratories, Inc., Lexington, KY, USA)	Up to 10 cm of the duodenal mucosa is lifted and then hydrothermally ablated, with subsequent regeneration of the mucosa. Endocrine cells renew their function and incretin secretion. Primarily developed to restore insulin sensitivity in T2D patients	Effect in T2D patients may last up to 1–2 years
Endoscopic anastomosis devices	Incisionless Magnetic Anastomosis System [IMAS, GI Windows (Boston, MA, USA)]	Self-assembling magnets placed in proximal jejunum and ileum by simultaneous upper and lower endoscopy. This causes necrosis in the tissue between them, leading to the formation of a jejunal–ileal anastomosis	After the anastomosis has been established, the coupled magnets will be passed naturally
(d) Gastric aspiration			
Aspiration devices	AspireAssist (Aspire Bariatrics, King of Prussia, PA, USA)	Endoscopic placement of a gastrostomy tube and the AspireAssist siphon assembly. Gastric contents aspirated about 20 minutes after a meal to remove about 30% of ingested food	Up to 4 years
(e) Gastric botulinum toxin A injection			
Gastric botulinum toxin A injection	N/A	Between 5 and 20 injections of botulinum toxin A into the area of the gastric antrum and/or fundus. This delays gastric emptying and induces early satiety	Effect of treatment limited to 3–6 months

N/A, not applicable; TORe, transoral outlet reduction by endoscopy.

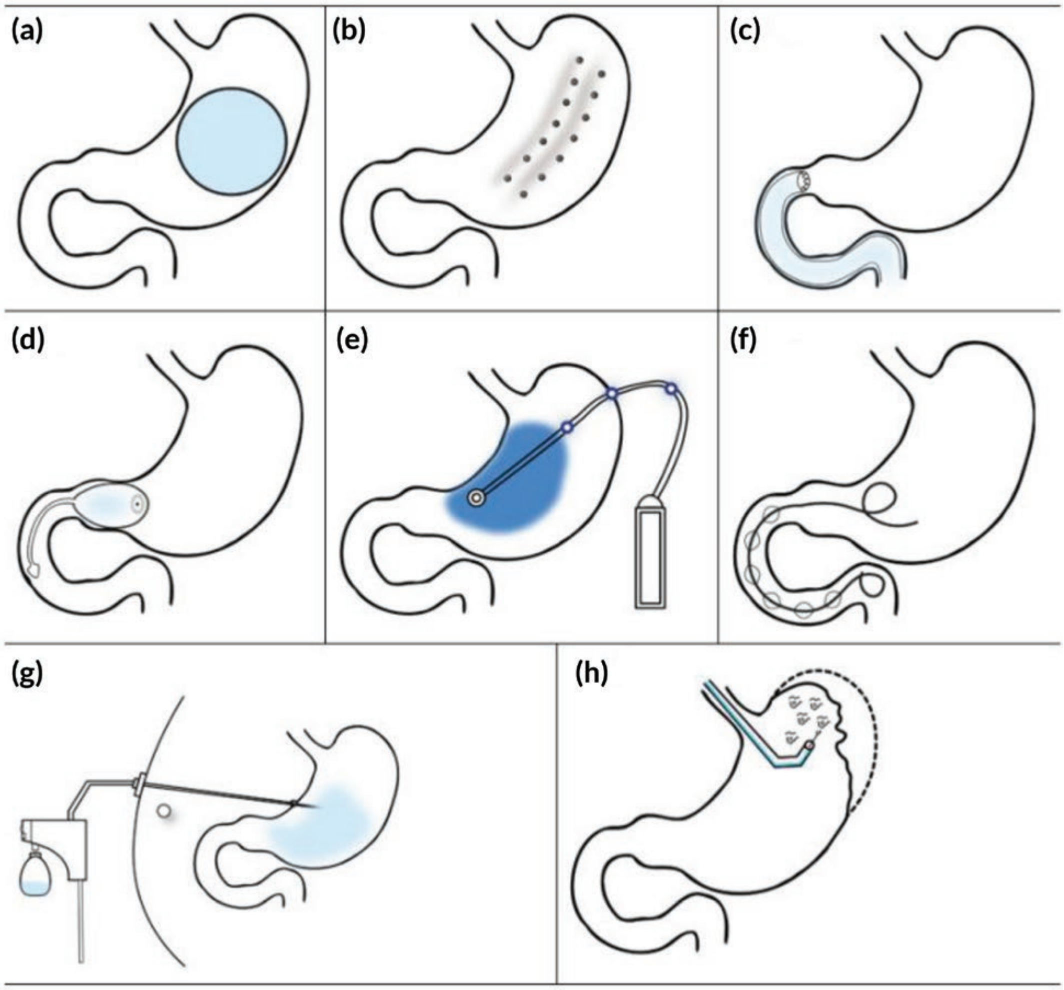

FIGURE 1 Overview of endoscopic bariatric procedures. (a) Intragastric balloon placement; (b) endoscopic sleeve gastroplasty; (c) duodenojejunal bypass; (d) TransPyloric Shuttle; (e) electrical stimulation; (f) SatiSphere; (g) aspiration therapy; (h) Primary Obesity Surgery Endoluminal (POSE). Reproduced with permission from Král *et al*.[53] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The figure includes minor additions and formatting changes to the original text.

could be a treatment option in patients with contraindications to bariatric surgery. The number of endoscopic obesity treatments performed is still low in the NHS, but most bariatric surgeons anticipate these procedures will become a bridge, or a possible alternative, to traditional bariatric surgery.

Endoscopic procedures can be broadly grouped into gastric-occupying devices, restrictive procedures, malabsorptive/metabolic therapies, gastric aspiration and other approaches. *Table 1* gives an overview of different endoscopic procedures.[52–56]

A brief description of the more commonly used devices and procedures is provided in the following and shown in *Figure 1*.

Restrictive procedures

Endoscopic sleeve gastrectomy

Endoscopic sleeve gastroplasty (ESG) is a similar, but less invasive, procedure to LSG. It aims to reduce gastric volume, which leads to early satiety, delay in gastric emptying and potential changes in gut and metabolic hormones.[55,57]

ESG is performed under general anaesthesia using a video-endoscope and a device that places sutures or staples through the stomach.[53] A commonly used device is the OverStitch suturing system (Apollo Endosurgery, Austin, TX, USA), which is comprised of a double-channel endoscope with a mounted suturing platform.[54] A sleeve is created through a series of uninterrupted full-thickness sutures along the lesser curvature of the stomach.[52] The procedure is designed to be permanent, and, as such, is likely to lead to more sustained WL compared with temporary procedures.[58] While potentially less effective than LSG for WL, it may have fewer AEs associated with it and may be suitable for patients who are not eligible candidates for LSG.[59] There are also studies investigating whether combining ESG with pharmacotherapy may improve WL.[55] Repeating ESG (redo ESG) may also be an option in patients with WL failure.[60] A more recent device is the Endomina suturing system, which uses a triangulation platform attached to an endoscope and creates plications alongside the greater curvature of the stomach resulting in a gastroplasty.[54] There is limited evidence on the comparative effectiveness of the OverStitch and Endomina systems, with one study finding similar amounts of WL.[61] ESG complications can include nausea, vomiting and abdominal pain (common), symptomatic GERD, intra- or post-procedural bleeding, subcutaneous emphysema, and rarely, pneumoperitoneum, pulmonary embolism or pneumothorax.[55,56]

Primary Obesity Surgery Endoluminal

Primary Obesity Surgery Endoluminal (POSE) is an endoscopic plication technique which uses the Incisionless Operating Platform (IOP, USGI Medical San Clemente, CA, USA) to perform tissue apposition with full-thickness plication in the gastric fundus.[55] Using specialised suture anchors, stomach tissue is plicated in eight or nine locations in the fundus and in three or four locations in the distal body.[52] After an initial trial found limited WL,[62] POSE has undergone technique adjustments, with POSE 2.0 making the gastric reservoir for food smaller leading to potentially greater WL.[60] Complications may include bleeding, hepatic abscess, abdominal pain, nausea and vomiting.[59]

Transoral gastroplasty system

The transoral gastroplasty (TOGA) system (Satiety Inc., Palo Alto, CA, USA) uses a set of flexible, endoscopically guided staplers that enable the creation of a restrictive pouch along the lesser curvature of the stomach.[56] Studies have shown that the technique is feasible in terms of WL: however, the evidence is limited, and future application of this technique is uncertain.[54] Common AEs include vomiting, pain, nausea, and transient dysphagia.[53] Rare, serious AEs of respiratory insufficiency and pneumoperitoneum have also been reported.[56]

Space-occupying devices

Intragastric balloons

Intragastric balloons (IGB) are space-occupying devices placed within the stomach. They are thought to work by taking up space in the stomach leading to a reduction in food intake, an early sense of satiety and a delay in gastric motility and emptying.[59] They also affect complex hormone signalling processes potentially involving ghrelin, a hormone involved in weight regulation.[63]

A common balloon is the Orbera (Apollo Endosurgery, Inc., Austin, TX, USA), which is a silicone balloon inserted endoscopically into the stomach under light sedation and then filled via a catheter with around 400–800 ml of saline stained with methylene blue.[56] It is designed to remain in place for 6 months before endoscopic removal, but a 12-month version is now also available (Orbera356).[58] The Spatz balloon (Spatz Medical, Fort Lauderdale, FL, USA) is similar to the Orbera, but the amount of saline is adjustable; starting with a lower volume of saline may increase tolerability, while a greater volume may increase efficacy.[53] Some balloons [e.g. Heliosphere (Helioscopie Medical Implants, Vienne, France)] are filled with air rather than saline which may improve tolerance but result in less WL.[56] Swallowable versions of IGB are also emerging which avoids the need for endoscopic placement, and in some cases removal where balloons are naturally passed through the gastrointestinal tract.[58] Such balloons are inflated with air or saline once they are in the stomach [e.g. Obalon (Obalon Therapeutics Inc., Carlsbad, CA, USA)], or in the case of the Ullorex balloon (Phagia Technologies, Inc., Fort Lauderdale, FL, USA) are self-inflating.[56]

While balloons can be used as a stand-alone procedure, patients must adhere to LSIs in conjunction with the balloon in order to achieve significant WL, and weight regain after balloon removal is expected.[63] Additional treatments may be needed, for example pharmacotherapy, additional bariatric surgery or placement of repeat balloons (with a wash-out period).[63] Balloons can also be used as a 'bridge' to surgery where the initial WL achieved with the balloon decreases the risk and complexity of subsequent surgery. The most common AEs after IGB placement are nausea, vomiting and abdominal pain, rarer side effects include intestinal bacterial overgrowth, pancreatitis, gastric erosion, ulceration and, very rarely, death, while balloon-related complications may involve early balloon deflation and migration.[55,56]

Malabsorptive procedures

Duodenal–jejunal bypass liner (EndoBarrier)

The EndoBarrier (GI Dynamics Inc., Lexington, MN, USA) is a flexible Teflon sleeve which is open at both ends and is implanted endoscopically for up to 12 months. It is anchored in the duodenal bulb and extended into the jejunum[56] and allows food to pass undigested to the distal jejunum while preventing contact with the duodenal mucosa.[53] As such, it aims to imitate a gastric bypass without changing gastrointestinal anatomy. In addition to facilitating WL, the EndoBarrier also improves glycaemic control in patients with T2D.[54] Common side effects include abdominal pain and nausea, while rarer, more serious complications include gastrointestinal bleeding, device migration and the formation of hepatic abscesses.[54] As with other temporary procedures, weight regain is common after removal.

Endoscopic anastomosis devices

The Incisionless Magnetic Anastomosis System [IMAS, GI Windows (Boston, MA, USA)] uses self-assembling magnets which are positioned via simultaneous colonoscopy and endoscopy in adjacent bowel loops and compress the intestinal wall to create a non-surgical jejuno-jejunal anastomosis.[55] This results in a formation of a partial jejunal diversion, which diverts bile acids and nutrients into the ileum resulting in decreased absorption.[59] There is limited study data on this device in humans, with a pilot study showing progressive WL up to 12 months.[64]

Aspiration therapy

The AspireAssist device (Aspire Bariatrics, King of Prussia, PA, USA) involves placement of a gastrostomy tube and the AspireAssist siphon assembly. This enables patients to directly aspirate about 30% of the gastric content after a meal through an external skin port before calories are absorbed into the body.[56] The AspireAssist is placed for 1 year unless patients want to continue with longer treatment.[65] Studies have shown WL of up to 4 years.[55] AEs result mainly from placement of the tube and include peristomal irritation, granulation tissue, infection, nausea, vomiting, abdominal pain and dyspepsia. Rare AEs of peritonitis and prepyloric ulceration or tube removal have been reported.[55]

Guidance on use of endoscopic obesity treatments in the United Kingdom

Endoscopic treatments for obesity are currently not part of routine care in the NHS and their place in the treatment pathway is not well defined. The decision to use such treatments may depend on the number and type of previous failed treatments (including LSI, pharmacotherapy, previous bariatric surgery), patient BMI, patient fitness for a higher or lower risk procedure, patient preference, potential reversibility of the procedure and target WL.[3] Local availability and accessibility in either the public or private sector will also play a role.

Endoscopic bariatric procedures may be performed as (1) a single stand-alone procedure, (2) a repeat of the same endoscopic procedure, (3) as a bridge to further bariatric surgery, as lowering the BMI pre-surgery may reduce the risk of surgery, or (4) as a revision to previous bariatric surgery, for example if weight regain has occurred. They all require concomitant LSIs and can also potentially be combined with pharmacotherapy.

National Institute for Health and Care Excellence guidance published in February 2024 recommends the use of ESG as a treatment option for obesity, with eligibility criteria as for other bariatric surgery (described above).[66] The NICE Committee noted that the procedure may particularly benefit people with class 3 obesity for whom laparoscopic bariatric surgery is not suitable due to associated risks.[66] Further NICE guidance is limited to the duodenal–jejunal bypass liner (DJBL) for T2D (not obesity) published in 2015 and swallowable balloons (for WL) published in 2020. The efficacy and safety of the liner were deemed to be limited, and the use of the procedure for managing T2D was recommended only in the context of research.[67] The swallowable gastric balloon capsule was recommended for people who need to lose weight in the short term for medical reasons providing '*special arrangements are in place for clinical governance, consent and audit*'.[68] For long-term WL, the device is only recommended in the context of research. No guidance was identified for any other endoscopic devices or procedures.

In summary

Obesity is associated with high costs to patients, the NHS and wider society. LSIs have limited effectiveness for long-term WL. Laparoscopic bariatric surgery is known to be effective, but access to this is limited in the UK due to high upfront costs among other reasons. There are also risks to the patient and not all patients are suitable. Endoscopic obesity treatments may provide an alternative to bariatric surgery as they are less invasive, less costly and may be more acceptable to patients as well as potentially being more cost-effective. However, their role within the treatment pathway is uncertain.

Chapter 2 Aims

In order to make an informed decision on the use of endoscopic therapies for people of varying levels of obesity, evidence on the clinical and cost-effectiveness is required.

The aim of the research documented in this report was to address the question:

What is the current evidence for the clinical and cost-effectiveness of endoscopic treatments for obesity?

The specific objectives to address this aim were:

- To produce a map of the evidence on the effectiveness of endoscopic therapies for obesity based on randomised, non-randomised controlled and uncontrolled studies (see *Chapter 3*).
- If feasible, to undertake systematic reviews, meta-analyses and subgroup analyses, and if these are possible to assess the feasibility and undertake if appropriate, a network meta-analysis to determine relative effects of endoscopic therapies.
- To undertake a systematic review of available economic evidence on the use of endoscopy therapies for obesity (see *Chapter 4*).
- To undertake a model-based cost-effectiveness analysis (CEA) comparing endoscopic treatments with other alternative treatments from the UK NHS/Personal Social Services (PSS) perspective informed by the evidence map and the systematic review of cost-effectiveness of endoscopic therapies, wider evidence on model-based economic evaluations used in obesity, and patient, public and clinical input – employing deterministic and probabilistic sensitivity analysis (PSA) to explore the robustness of the results (see *Chapter 5*).

When this research was commissioned, the expectation was that the evidence base on effectiveness was much smaller than it actually is, and that the range of endoscopic therapies (and associated variants) was less extensive and diverse. Furthermore, both aspects also give rise to a wider range of comparators and populations studied.

Since this research was commissioned, there has been a sea change in the range of therapies available or used more commonly for obesity with the rise in prominence and use of pharmacotherapy – predominantly semaglutide [marketing approval 2021 (USA), 2022 (EU)].[69]

To accommodate both facets and in agreement with the steering group, we:

- Placed more emphasis on the evidence map of effectiveness studies, given how extensive and detailed it needed to be, and less emphasis on reviewing all the effectiveness evidence due to the infeasibility of this. Targeted evidence identification to inform economic modelling and model parameters were undertaken instead (see *Appendix 2*).
- Developed three rather than a single economic model to enable key endoscopic therapies to be compared to laparoscopic bariatric surgery and pharmacotherapy (as appropriate).

Chapter 3 Map of evidence for endoscopic treatments for obesity

Introduction

Endoscopic treatments for obesity have been available for some time but are not commonly performed in the UK. The aim of this chapter is to (1) describe the development of an evidence map of all currently available evidence on endoscopic obesity treatments and (2) present an overview of the volume and nature of the available evidence based on the findings of the evidence map. The evidence was also used, where possible, to inform a model-based CEA comparing endoscopic treatments with alternative treatments (see *Chapter 5*).

Methods

The review is registered on PROSPERO (CRD42022302942).[70]

Searches

Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, MEDLINE In Process and EMBASE via Ovid were searched from inception up to 25 January 2022 and updated to 25 January 2023. Appropriate index terms and free-text terms related to the population and interventions were combined to create a sensitive search strategy designed to be comprehensive. Searches were not restricted by study design, date, language or publication type. The full search strategy adapted for each bibliographic database can be found in *Appendix 1*. Reference lists of relevant systematic reviews were checked for additional primary studies. Searches included checking for ongoing studies in trial registries.

Study selection

Records retrieved by running the searches were exported into EndNote 20 Clarivate Analytics [Clarivate Analytics (formerly Thomson Reuters), Philadelphia, PA, USA]. Duplicate records were systematically removed. The resulting reference library was transferred to Rayyan[71] for screening and selection.

The eligibility criteria were applied to the title and abstract of each record and a decision was made by at least two reviewers independently to include, exclude, or to obtain and review the full text. A conservative approach was taken to excluding articles based on abstracts found to have limited information or no associated full text (e.g. conference abstracts). Details of the full inclusion and exclusion criteria are below and shown in *Appendix 1*, *Table 20*. Disagreements were resolved by consensus and involved a third reviewer if required. The selection process was documented using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart.[72]

The search strategies were designed to capture studies relevant to the systematic review of cost-effectiveness evidence (see *Chapter 4*). Screening and selection of existing studies of cost-effectiveness were carried out concurrently by labelling relevant records as having economic or cost content.

Eligibility criteria

Population

People of any age with obesity (as defined by study authors) with or without obesity-related comorbidities regardless of prior interventions for obesity and regardless of whether intervention was planned as a stand-alone treatment or as a bridge to bariatric surgery.

Intervention(s)

Any treatment for obesity carried out using endoscopy without planned additional laparoscopic intervention. Swallowable IGBs for obesity were also included as an important emerging technology. All endoscopic interventions were included regardless of current availability or licensing status, either in the UK or in other countries.

Comparator(s)

Any comparator or control including open or laparoscopic bariatric surgery, sham procedure, lifestyle and behavioural interventions, alternative endoscopic treatments, pharmacotherapy or no treatment. Studies without a comparator were also eligible for inclusion.

Outcomes

One or more outcomes from all weight-related outcomes [including BMI, total body weight loss (TBWL), excess weight loss (EWL)], changes in diabetes status or treatment and/or CVD risk, AEs, reintervention or revisional surgery for weight regain, obesity-related morbidity, mortality (all cause, CVD related, cancer related), QoL assessed by any tool, or micronutrient status.

Type of study

Any clinical study of any design (randomised or non-randomised controlled studies, uncontrolled studies) as well as observational studies including cohort and case-control studies and case series. Studies were eligible if they included two or more participants. All single case reports, letters, comments, narrative reviews, editorials and animal studies were excluded.

Systematic reviews were labelled and checked to identify additional potentially relevant primary studies.

Evidence map design and construction

A searchable database map of all available evidence for endoscopic treatments for obesity was constructed in Microsoft Excel® (Microsoft Corporation, Redmond, WA, USA). Author(s), date of publication, title, abstract and citation details were imported. A single reviewer used the title and abstract to extract details on the population, intervention(s), comparator(s) where relevant, study design, sample size (with breakdown for each study arm), maximum length of follow-up and whether the study was ongoing. Where applicable, the commercial brand of intervention was recorded. Any additional records found to be duplicates or not relevant were removed and logged as excluded with the reason (see *Appendix 1*, *Table 21*). Full texts were not routinely used for map data extraction except when an abstract was missing, or additional information was sought to enable extraction of the specified data item. An attempt was made to identify single studies from multiple published articles.

Mapped information was checked by a second reviewer for all studies recorded as randomised controlled trials (RCTs). Articles not recorded as RCTs were mapped by a single reviewer except when mapping information was not clear which resulted in the article being reviewed and discussed with a second reviewer.

To enhance the usability, consistency and searchability of the map, categorisation of terms for population, intervention, comparator and study design was required. To achieve this, each record was assigned key descriptors for each of these features from a defined but limited list. The range of key descriptors for each feature were drawn up, added to the database as drop-down menus, piloted and refined with input from clinical and methodological experts. The key descriptors for each feature are outlined below.

Population

The population was recorded as requiring 'weight loss pre-bariatric surgery' or 'weight loss pre- surgery', requiring further obesity intervention due to 'weight regain or plateau' or simply as 'obese' where no other information was available. Children or adolescent populations were recorded. Specific comorbidities were recorded when it could be ascertained that this applied to the whole study cohort.

Intervention

The endoscopic interventions were recorded using descriptors that included 'endoscopic sleeve gastroplasty', 'primary obesity surgery endoluminal', 'transoral outlet reduction by endoscopy', 'endoscopic intragastric balloon', 'swallowable intragastric balloon', 'duodenal–jejunal bypass liner', 'aspiration', and 'botox'. When it was not possible to determine the specific procedure or device used, the intervention was recorded in the first instance using a simplified descriptor, for example 'endoscopic suturing' or, if necessary, as described by the author. A combination of interventions used in a single study arm was recorded using 'with', for example DJBL with LSI. If further details were given, this was included in brackets, for example '(diet and exercise)'.

Comparator

Comparators were recorded using 'bariatric surgery', 'lifestyle intervention', 'other endoscopic intervention', 'pharmacotherapy', 'no intervention', or 'no comparator'. Brackets were used following this descriptor to record specific details, for example 'bariatric surgery (laparoscopic sleeve gastrectomy)'.

The description of interventions and comparators was not always clear, and terminology has changed or evolved over time, particularly for endoscopic restrictive procedures. Attempts were made to ascertain the procedure using title and abstract. Full text was checked where there was ambiguity.

Study design

The study design for each article was recorded as 'randomised controlled trial', 'non-randomised controlled study' or 'uncontrolled study'. These descriptions included interventional, observational, prospective and retrospective study designs. Studies having a comparative arm expressed either as a clear intervention and control or as results presented separately for intervention and control groups were classed as non-randomised controlled studies.

Reporting the evidence map

Due to the volume of evidence, careful consideration was given to the synthesis. Summary tables were used to collate the evidence from the map into categories. Four overarching categories were used: (1) restrictive procedures, (2) space-occupying devices, (3) malabsorption devices and procedures and (4) other endoscopic procedures. Within each category, subgroups were formed based on the intervention and then the comparator. Further subdivision was made based on the study design using the hierarchy of evidence. RCTs were grouped together, and non-randomised controlled studies were grouped separately for each section. Studies which did not clearly compare one therapy to another such as those that compared endoscopic intervention with pharmacotherapy to endoscopic intervention alone, or studies involving a comparison of case series in a different population (non-obese), are included in the map and are briefly mentioned at the end of each category. Studies with multiple intervention and comparator arms are described in all relevant sections.

For comparative studies, a narrative description is given containing details of intervention, comparator, follow-up and sample size. Population details are given if there was a specific age range, class of obesity (e.g. morbidly obese) or a specific comorbidity. For uncontrolled studies, the number included for each section are noted only, due to their number and limitations on space. All are however represented in the map.

Use of the evidence map to inform the economic evaluation

A full systematic review of all the evidence, even at the RCT level only, was beyond the capacity of this project due to the sheer volume of evidence and the numerous interventions this covered.

To inform the economic evaluation (see *Chapter 5*), the map was used to identify relevant studies containing evidence of effectiveness, effect and or AEs on the interventions to be modelled. Data on relevant characteristics and findings (including WL and AEs data) were extracted from such studies to inform the model parameters. Details on these studies and the data relevant to the modelling can be found in *Appendix 2*.

Results

Overview of evidence

The searches identified 12,793 records. Following the removal of duplicates, 9047 records were taken forward for screening using the title and abstract. The map of evidence (see Report Supplementary Material 1) includes 1574 articles after exclusion of those not representing a study meeting the inclusion criteria. A summary of the selection process is shown in *Figure 2*.

The evidence map shows all included articles. The following section highlights some general observations found in the evidence map before continuing into sections detailing the evidence available for each type of endoscopic therapy against comparator therapies.

Of the 1574 mapped articles of endoscopic treatments for obesity, 68 related to ongoing studies. Of these, 38 articles were reporting RCTs, 8 reported non-randomised controlled studies and 22 articles were for uncontrolled studies. These articles are not discussed further.

A breakdown by study design and category of intervention is shown in *Table 2*. The majority of articles were publications involving an uncontrolled study (73%), with non-randomised controlled studies accounting for 18%. Nine per cent of records were mapped as RCTs. Ninety per cent of all articles identified were published since 2009.

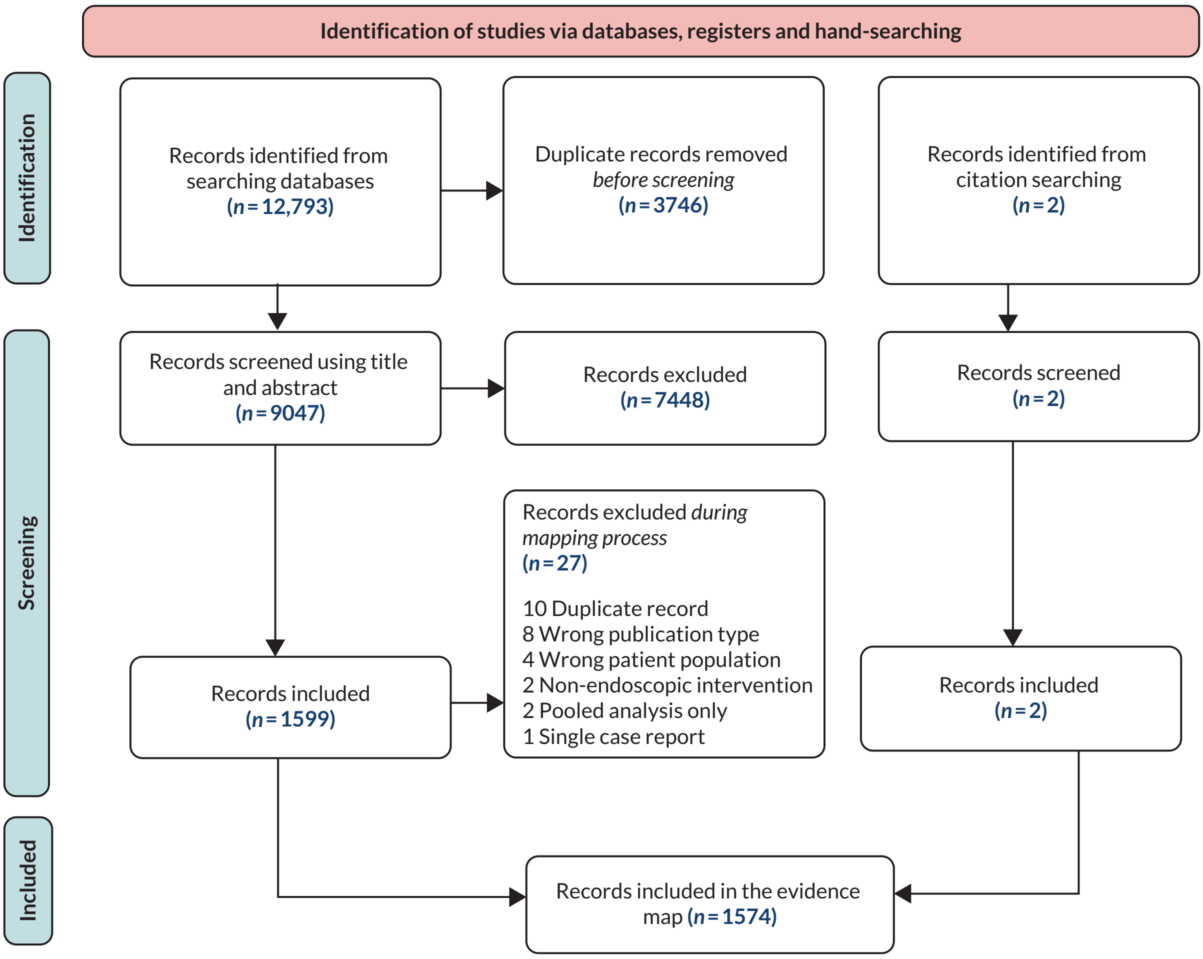

FIGURE 2 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for map of evidence.

TABLE 2 Number of articles by study design and intervention category

		Intervention category			
	Number of articles	Restrictive procedures[a]	Space-occupying devices	Malabsorption devices and procedures	Other endoscopic treatments
Published	1506	449	770	266	59
RCT	140 (9.3)[b]	41 (9.1)	59 (7.6)	26 (9.8)	15 (25.4)
Non-randomised controlled study	271 (18.0)[b]	102 (22.7)	153 (19.9)	38 (14.3)	15 (25.4)
Uncontrolled study	1095 (72.7)[b]	306 (68.2)	558 (72.5)	202 (75.9)	29 (49.2)
Ongoing	68	24	19	19	9
Total	1574	473	789	285	65

a Restrictive procedures are those that result in a reduction in size or volume of the stomach and the category includes sutured, stapled and revisional procedures and combinations of these.
b *n* (%) of 1506 published articles.

Note
Values are number of articles including conference abstracts *n (%)*. Articles reporting a study with multiple endoscopic intervention arms may have been counted in up to four intervention categories. Assigning an article to a study design category was mutually exclusive.

Details of the population given in the abstract usually included one or more of obesity class, BMI or a description of obesity (e.g. morbidly obese) and comorbidities. Comorbidity was often associated with the intervention being investigated, for example studies involving malabsorption devices or procedures generally enrolled participants with T2D. Eight per cent of all published articles had a very small sample size of 10 or fewer participants. All of these articles were reporting uncontrolled studies. Nearly half of published articles enrolled 11–50 participants (45%). Eighteen and 19% of articles reported studies with a sample size of 51–100 and 101–500, respectively. Only 5% of articles recruited over 500 participants, none of which were RCTs.

Most studies were carried out in adults; however, 10 studies (reported in 12 articles) were undertaken in children and/or adolescents. Nine of these were uncontrolled studies and can be found in the evidence map by searching for children/adolescents under the population descriptor. One was a non-randomised controlled study comparing DJBL to conservative treatment in 45 participants over 24-month follow-up (Klemencic 2021, 264637195).

One hundred and seventeen articles reported studies enrolling participants specifically for WL prior to surgery including bariatric surgery. There were 115 articles reporting a study enrolling participants for WL intervention due to weight regain or plateau following previous obesity treatment(s). Most of these articles reported a study involving restrictive procedures.

Restrictive procedures were included in a study arm in 29% of RCTs, 38% of non-randomised studies and as the intervention in 28% of uncontrolled studies. Space-occupying devices featured in 42% of articles of RCTs, 57% of non-randomised studies and 51% of uncontrolled studies. Articles reporting studies investigating malabsorption devices accounted for 19% of RCTs, 14% of non-randomised controlled studies and 18% of uncontrolled studies. Other endoscopic treatments included aspiration and gastric injection of botulinum toxin which accounted for 11% of articles of RCTs, 6% of articles reporting non-randomised controlled studies and 3% of uncontrolled studies.

Table 3 shows a breakdown of available evidence for each comparison.

Seventy-one articles reported studies with comparator arms involving bariatric surgery. Some of these did not report any details of the surgery involved but where mentioned, LSG was the most common comparator (32 articles). Nineteen articles compared gastric bypass, 16 articles involved surgical gastric plication and 12 articles compared outcomes from laparoscopic gastric band.

TABLE 3 Summary of evidence for intervention by comparator

Endoscopic interventions	Comparator						Uncontrolled studies
	Bariatric surgery	Sham procedure	LSI	Endoscopic interventions	Pharmacotherapy	Other combinations	
ESG	0/22	0/1	4/6	10/35	0/2	3/8	151
POSE	0/1	7/0	13/3	1/9	0/0	0/0	31
TORe	0/1	1/0	0/0	0/17	0/1	0/0	27
Other restrictive procedures	0/8	2/0	2/0	1/7	0/0	0/0	100
Endoscopic IGB	0/21	17/3	17/24	4/32 (other IGB) 0/32 (other endo) 1/2 (non-endo) 0/13 (no treatment)	4/2	2/19	486
Swallowable IGB	0/2	3/0	0/0	0/6	0/0	3/0	71
Other space-occupying devices	0/0	2/0	0/0	0/0	0/0	1/1	1
DJBL	0/12	4/1	4/2	0/3	1/0	8/20	188
Other malabsorption devices or procedures	0/0	1/0	0/0	0/0	0/0	0/0	15
Aspiration	0/3	0/1	7/1	0/1	0/0	0/0	13
Botox	0/1	6/2	0/4	1/4	0/0	0/0	12

Note
Numbers of articles reporting RCTs/non-randomised controlled studies. Uncontrolled studies are also shown for completeness.

A sham endoscopic comparator was reported in 26 articles. Seventy-eight articles reported a study which compared an endoscopic intervention to LSI alone. One hundred and fifty-five articles involved a comparison to a variation of the same endoscopic intervention (e.g. a different suture pattern, location, or generation of device) or a different endoscopic treatment. Nineteen articles reported eight studies involving obesity pharmacotherapy alone in the comparator arm.

Some articles reported studies with multiple treatment arms which could include various combinations of comparators, for example bariatric surgery, LSI and a different endoscopic intervention.

Most LSIs were diet and exercise related but could also include behavioural interventions such as one-to-one or group counselling, advice, or cognitive–behavioural therapy (CBT) sessions. Where details were given in the abstract, diets were low-calorie, low-carbohydrate, specific calorie counts per day (e.g. 1500 kcal), 'American diet' or branded diets such as the Atkins diet among others. Regimens varied from intensive programmes with frequent sessions with a dietitian or trainer to a single visit with a counsellor. Details of LSI were frequently not reported in the abstract.

Most studies reported WL and/or safety outcomes but could also include changes in body composition, satiety and gastric emptying, and biomarkers of metabolic and glycaemic control. Where follow-up was short term (e.g. 30 days or less). Outcomes were less likely to include WL and more likely to focus on AEs. Pilot studies in small numbers of participants were more likely to report outcomes related to procedural safety.

Duration of follow-up varied from 1 week to 5 years with over half of all articles following participants for 6–12 months but was often unclear or not reported in the abstract.

The following sections consider the evidence for each category of endoscopic intervention focusing on RCTs and non-randomised controlled studies (411 articles). The number of uncontrolled studies is given at the end of each category.

Restrictive endoscopic procedures

A breakdown of the number of articles for the main restrictive endoscopic procedures by study design is shown in *Table 4*.

Endoscopic sleeve gastroplasty

Details of the 84 articles involving studies reporting ESG are outlined in the following section by comparator and study design.

Endoscopic sleeve gastroplasty versus bariatric surgery

Randomised controlled trials There were no published RCTs identified comparing ESG with LSG or any other form of bariatric surgery.

Non-randomised controlled studies Twenty-two articles were identified which reported 17 non-randomised controlled studies comparing ESG with bariatric surgery.

TABLE 4 Summary of restrictive procedures by study design

Number of articles	ESG	POSE	TORe	Other
RCTs	16	25	1	4
Non-randomised controlled studies	68	16	18	11
Uncontrolled studies	151	31	27	100

Other includes aspiration and botox.

Sixteen of these articles reported a two-arm comparison of ESG versus LSG. Four articles reported short-term outcomes. Short-term WL and safety outcomes were reported by two studies where follow-up was for 1 month (*n* = 180) (Hadi 2022, 930783341) and 3 months (*n* = 37) (Alghafees 2020, 264633638) post intervention, respectively. Gudur *et al*. reported AE-related outcomes in over 600,000 patients in the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) database in the 30 days following ESG or sleeve gastrectomy (Gudur 2023, 930783331) and a small formative study followed 50 participants up for just 2 weeks (Marshall 2022, 930783505).

Ten articles reported a follow-up of 6 months and recruited between 24 and 137 patients (Fayad 2019, 264635611; Fiorillo 2019, 264635681; Fiorillo 2020, 264635682; Lopez-Nava 2020a, 264637780; Lopez-Nava 2020b, 264637781; Marshall 2019, 264638002; Sadek 2017, 264639748; Schweitzer 2018, 264639983). A longer follow-up of 12 months was reported for 61 participants (Marshall 2021, 264638001; Carr 2022, 930783188), 24 months (*n* = 25) (Benias 2020, 264634169) and 36 months (Alqahtani 2022, 930783077), with the latter study also enrolling the largest number of patients in this set of studies (*n* = 6036).

Three articles reported two studies comparing ESG with laparoscopic gastric plication (LGP). The study reported by Abu Dayyeh and El Mohsen compared ESG with laparoscopic greater curvature plication (LGCP) and included a third arm of intensive LSI (Abu Dayyeh 2017, 264633324; El Mohsen 2017, 264633325). The sample size was small (*n* = 29) with follow-up for 6 months. A second larger study (*n* = 296) compared ESG with LSG or LGP and followed participants for 24 months (Lopez-Nava and Asokkumar 2021, 264637741).

The study by Novikov *et al.* compared ESG with LSG or laparoscopic gastric band. They recruited 278 participants and followed them for 12 months (Novikov 2017, 264638859; Novikov 2018, 264638858).

One small study (*n* = 18) compared endoscopic re-sleeve (sleeve-in-sleeve) with surgical re-sleeve over 12-month follow-up in participants with weight regain following a primary sleeve gastrectomy (Bazarbashi 2020, 264634096).

Endoscopic sleeve gastroplasty versus sham procedures

Randomised controlled trials There were no published RCTs comparing ESG with a sham form of ESG.

Non-randomised controlled studies One article was identified that reported a non-randomised controlled study involving an ESG (*n* = 4) versus sham (*n* = 15) comparison. The study focused on the influence of gastric emptying caused by endoscopic treatments on WL. The abstract did not give details of the sham procedure. This multi-intervention study included botox (*n* = 45), duodenal–jejunal bypass sleeve (DJBS; *n* = 25) and endoscopic IGB (*n* = 15) and LSI alone (*n* = 14). Follow-up was over a 6 months (Abu Dayyeh 2016, 264633434).

Endoscopic sleeve gastroplasty versus lifestyle interventions

Randomised controlled trials Four articles were identified reporting RCTs comparing ESG with LSI. Three of these articles were from the same group and reported the MERIT trial. This RCT compared ESG in combination with LSI to LSIs alone in 209 participants over a 52-week follow-up. All participants in the lifestyle group were offered ESG after 1 year and those in the intervention arm were offered retightening of ESG. Participants in the primary ESG group were followed up for a further 52 weeks. LSI included a low-calorie diet and physical activity (Abu Dayyeh 2022, 930783047; Abu Dayyeh 2022, 930783049). A smaller study (*n* = 36) related to the MERIT RCT reported outcomes of gastric emptying, gastric motility, hormones and eating behaviours after ESG with an 18-month follow-up (Vargas 2022, 930783790).

The fourth article reported an ESG versus lifestyle comparison as part of a four arm RCT which included the distal-POSE procedure or endoluminal vertical gastroplasty (EVG). Follow-up was for 6 months with a sample size of 120 (di Prampero 2022, 930783780). This RCT is mentioned elsewhere but without the lifestyle comparator arm.

Non-randomised controlled studies Six articles report four non-randomised controlled studies involving a comparison of ESG with LSIs. A large study (*n* = 386) reported ESG in combination with low-intensity diet and LSI compared with matched patients undergoing a high-intensity diet lifestyle therapy over 12-month follow-up (Cheskin 2020, 264634754). A second large study (*n* = 521) evaluated ESG as part of a mixed group with POSE 2.0 versus IGB versus LSI alone over 12 months. Results were not reported separately for ESG and POSE 2.0 in the two conference abstracts which focused on WL outcomes and surrogate markers for inflammation, and markers of metabolic disease and hepatic steatosis, respectively (Rapaka 2022a, 930783650; Rapaka 2022b, 930783648). Two studies involving an ESG versus lifestyle comparison were noted under the section Endoscopic sleeve gastroplasty versus bariatric surgery (LGP) (Abu Dayyeh 2017, 264633324; El Mohsen 2017, 264633325) and ESG versus Sham (and other endoscopic interventions) (Abu Dayyeh 2016, 264633434) sections.

Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.)

Randomised controlled trials Ten articles report three RCTs comparing ESG to other endoscopic interventions or a variation in the type of ESG. Five of these conference abstract articles describe one RCT comparing ESG using the Apollo OverStitch to distal-POSE or EVG. It was noted that a sixth article by the same authors reported the same RCT but with the addition of a LSI comparator arm (a low-calorie Mediterranean diet) (di Prampero 2022, 930783780). The largest sample size reported for this RCT was 90 participants (di Prampero 2022, 930783781) but other articles reported enrolment of 54 participants presumably at an earlier stage of the study (di Prampero 2022, 930783247, 930783782, 930783783, 930783784). The primary end point was to assess the technical success rate and the occurrence of serious adverse events (SAEs). Efficacy of the three endoscopic procedures at inducing WL, improving obesity-related comorbidities and QoL was also assessed after 6-month follow-up.

Three articles reported one RCT comparing three different suturing patterns for ESG using the Endomina device in combination with LSI. The suture patterns aimed to modify gastric accommodation by increasing the fundus distention ability (Group A), to reduce gastric volume (Group B) or to interrupt gastric emptying (Group C). A small number of patients (*n* = 48) were followed up over 12 months (Gkolfakis 2022, 930783315, 930783316; Huberty 2021, 264636575).

The 10th article reported a RCT which compared reinforcement of the ESG procedure with a control arm in which ESG was not reinforced. One hundred and twenty-six patients, who appeared to be part of a larger ongoing study, were followed up for 18 months (Sander 2019, 264639842).

Non-randomised controlled studies Thirty-five articles report non-randomised controlled studies involving ESG in a comparison with other endoscopic interventions or a variation in the type of ESG. ESG was compared to endoscopic IGB in a 2-arm study design in 14 articles. A large sample (*n* = 168) was recruited and followed up over 1 month in one study (Hadi 2022, 930783340). A second large study which identified 5209 ESG and endoscopic IGB cases from the MBSAQIP registry investigated trends and outcomes in minority populations (Ouni 2022, 930783607; Ouni 2022, 930783608).

Two studies followed up patients for 3 months with enrolment of 13 and 88 patients, respectively (Gew 2109, 264636004; Vargas 2019, 264640916). A fourth study prospectively enrolled 41 patients to receive ESG or the Orbera endoscopic IGB with a 6-monthfollow-up (Rapaka 2022, 930783647; Rapaka 2022, 930783649). Lopez-Nava *et al.* reported an ESG versus endoscopic IGB comparison in 160 participants with a follow-up of 9 months post procedure. Total study duration was unclear (Lopez-Nava 2020, 264637743). Fayad reported a study comparing ESG to a 6-month placement of endoscopic balloon with a 12-month follow-up. This study appears to have been reported in 2 articles with 88 participants and a larger recruitment of 137 patients (Fayad 2018, 264635610; Fayad 2019, 264635612). Lopez-Nava also report a study with a 12-month follow-up (*n* = 107) (Lopez-Nava 2017, 264637759; Lopez-Nava 2018, 264637750).

Badurdeen *et al.* reported 1-year WL outcomes following ESG and endoscopic IGB (Orbera and ReShape Duo) as part of building an endobariatric programme (Badurdeen 2020, 264633976). Only one study comparing ESG to endoscopic IGB (6-month placement) continued follow-up for 24 months. Fifteen patients with non-alcoholic fatty liver disease (NAFLD) were enrolled (Bhakta 2019, 264634217).

One study reported in three conference abstracts by Lopez-Nava *et al.* compared ESG with TORe for weight regain. Patients were recruited to form a large European prospective data registry to monitor outcomes including practice patterns of suturing, WL, and AEs after ESG and TORe. At the time of reporting, recruitment had reached a large sample size of 800. Follow-up was over 12 months but will continue until all patients reach 2-year follow-up (Lopez-Nava 2019, 264637768; Lopez-Nava 2019, 264637769; Lopez-Nava 2020 264637757).

Four articles reported two studies comparing different types of suturing of ESG. ESG with or without longitudinal compression suturing was compared in 32 patients with a 6-month follow-up (Glaysher 2019, 264636053, 264636052). ESG with or without fundal suturing was compared in 247 patients who were followed up for 12 months (Farha 2021, 264635591; Farha 2020, 264635590).

Fourteen articles involved a comparison of ESG with more than one other endoscopic intervention. One article reported a comparison of ESG to 6-month or 12-month balloon placement in a three-arm study with all arms in combination with LSI. Follow-up was 12 months in 227 participants, although this sample size was a little unclear (Kozlowska-Petriczko 2022, 930783454).

Lopez-Nava *et al.* published five articles covering a multiarm study comparing ESG (Apollo OverStitch) to the endoscopic IGB Orbera or ReShape Duo, and to POSE. A large number of patients were recruited (*n* = 1020) (Lopez-Nava 2018, 264637776) and WL outcomes were compared after 1 year. The other articles reported slightly smaller sample sizes (*n* = 717) (Lopez-Nava 2017, 264637760) (*n* = 962) (Lopez-Nava 2019, 264637747; Lopez-Nava 2019, 264637753; Lopez-Nava 2019, 264637751).

Two conference abstracts described a study comparing ESG with endoscopic IGB or TORe. Two hundred and six patients were enrolled and followed up over 6 months (Vargas 2020, 264640924; Vargas 2021, 264640923). Two articles reported ESG compared with two weight regain procedures (TORe and endoscopic re-sleeve of surgical sleeve gastrectomy). The larger of the studies enrolled 71 patients receiving TORe (*n* = 71 out of 95). The primary outcome was to determine predictive factors of same-day discharge and AEs rather than WL and duration of follow-up was unclear (Kozan 2021, 264637298). The aim of the smaller study was to assess antibiotic administration and AEs over the 30 days following ESG, TORe, endoscopic revision of surgical sleeve and TORe-gastroplasty (Kozan 2021, 264637299).

Two conference abstracts reported a retrospective study of three intervention arms comparing single endoscopic therapy with IGB or ESG versus obesity pharmacotherapy versus combination therapy consisting of serial endoscopic therapies with or without obesity pharmacotherapy. All interventions were in combination with LSI. One article reported a sample size of 38 participants (Young 2021, 264641384) and the second article recruited 128 patients (Young 2022, 930783847). All participants were followed up over 2 years.

Endoscopic sleeve gastroplasty (Apollo OverStitch), endoscopic IGB Orbera and ReShape Duo, the swallowable IGB Obalon and aspiration using AspireAssist were compared in a retrospective cohort study. Ninety-eight patients were enrolled and follow-up of WL and AEs was for 6 months (Almuhaidb 2019, 264633686). The last article in this section describes a four-arm study comparing ESG to endoscopic IGB, POSE or DJBL. Follow-up was unclear as was the sample size, although 6771 procedures were reported (Espinet Coll 2017, 264635512).

Endoscopic sleeve gastroplasty versus pharmacotherapy

Randomised controlled trials There were no RCTs identified that compared ESG to obesity pharmacotherapy.

Non-randomised controlled studies Two conference abstract articles reporting one non-randomised controlled study were identified and were described above (Young 2021, 264641384; Young 2022, 930783847).

Endoscopic sleeve gastroplasty in other combinations

Randomised controlled trials Three articles were identified. One article reported a RCT comparing ESG performed under two different forms of ventilation (traditional vs. modified) combined with high thoracic epidural analgesia in 37 patients (Nevmark 2017, 264638768). In a small study (*n* = 55) with unclear follow-up, ESG with LSI with semaglutide was compared to ESG with LSI with a sham form of semaglutide (Hoff 2021, 264634581). In the second study by Hoff, ESG with LSI was compared to ESG with LSI with liraglutide in 30 patients over 12 months (Hoff 2020, 264636464).

Non-randomised controlled studies Eight articles were identified which reported four non-randomised controlled studies involving ESG that was the same in both study arms. ESG was compared to ESG with liraglutide in 52 patients (*n* = 66 in an earlier conference abstract) over 12 months (Badurdeen 2020, 264633979; Badurdeen 2021, 264633978). ESG was compared with or without multidisciplinary evaluation in a study that enrolled 31 participants (Boskoski 2019, 264634369; Boskoski 2019, 264634370) and continued to recruit 89 patients (Boskoski 2019, 264634368; 264634372) and followed them over 1 year. Gudur identified over 6000 matched cases from the MBSAQIP database involving ESG carried out by either bariatric surgeons or gastroenterologists. AEs and early WL outcomes were reported from the first 30 days follow-up (Gudur 2022, 930783330). A study comparing three different types of anaesthesia used to carry out ESG was conducted in 128 patients and evaluated outcomes during the first month of follow-up (Jirapinyo 2022, 930783403).

Uncontrolled studies

There were 151 articles identified that reported uncontrolled studies involving ESG as the intervention. Thirteen of these articles report studies using ESG as a method to treat weight regain following a primary obesity intervention. Four of these articles report studies using ESG specifically to aid WL prior to surgery, including bariatric surgery.

Primary Obesity Surgery Endoluminal

Details of the 41 articles involving studies reporting POSE are outlined in the following section by comparator and study design.

Primary Obesity Surgery Endoluminal versus bariatric surgery

Randomised controlled trials No RCTs were identified comparing POSE with any surgical bariatric procedure.

Non-randomised controlled studies A single article was identified reporting a non-randomised controlled study. This conference abstract described a small study (*n* = 16) comparing POSE to RYGB with a short-term follow-up of 2 months (Al Rasheid 2014, 264633553).

Primary Obesity Surgery Endoluminal versus sham procedures

Randomised controlled trials Seven articles were identified relating to one multicentre RCT, the ESSENTIAL trial, which compared POSE to a sham procedure. Full text was reported by Sullivan in 2017 (264640449) with a further six conference abstract articles, some of which report results from a single centre with smaller sample sizes (De La Cruz-Munoz 2016, 264635109; Boyer 2016, 264634396). POSE was carried out using an IOP. All 332 participants also received low-intensity lifestyle therapy with a blinded study dietitian who assessed changes in eating behaviours and diet compliance. WL and safety outcomes were reported after a 2-year follow-up with the sham group being offered cross-over to receive POSE after 12 months (Lavin 2016, 264637473). The remaining articles report outcomes after12-month follow-up (Lavin 2015, 264637472; Lavin 2016, 264637474; Sullivan 2017, 264640449; Sullivan 2016, 264640450).

Non-randomised controlled studies No non-randomised studies comparing POSE to a sham procedure were identified.

Primary Obesity Surgery Endoluminal versus lifestyle interventions

Randomised controlled trials Thirteen articles reported two RCTs involving POSE and LSI comparisons. Twelve of these articles related to the MILEPOST trial, a multicentre RCT comparing a combination or POSE and LSIs with LSIs alone. All articles were conference abstract reports except for one full-text publication (Miller 2017, 264638211). WL and satiety outcomes were measured along with safety at 6- and 12-month follow-up in the 44 participants (34 POSE: 10 lifestyle). The control group were offered cross-over to POSE at 12 months. Two-year follow-up data were also reported (Miller 2019, 264638213; Miller 2018, 264638205).

The second RCT had four study arms. Distal-POSE, ESG, EVG and LSIs were compared in 120 participants with 6-month follow-up (di Prampero 2022, 930783780).

Non-randomised controlled studies Three conference abstract articles were identified reporting two non-randomised controlled studies of POSE compared to LSIs. The second-generation POSE procedure in combination with LSIs was compared to LSI alone in 42 participants. Outcomes were measured over a 1-year follow-up (Alkhatry 2022, 930783072). The second study was larger (*n* = 521) and also used the POSE 2.0 procedure. POSE 2.0 and ESG outcomes were not reported separately in these conference abstracts but were compared as a group to IGB or LSIs after a 1-year follow-up. This study was mentioned previously in section ESG versus LSIs (Rapaka 2022a, 930783650; Rapaka 2022b, 930783648).

Primary Obesity Surgery Endoluminal versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.)

Randomised controlled trials One RCT reported in five conference abstracts was identified in which POSE was compared to other endoscopic interventions. There were three arms in this RCT comparing distal-POSE with ESG and EVG in a maximum of 90 participants over a 6-month follow-up. This study was described in section Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.) (di Prampero 2022, 930783781, 930783247, 930783782, 930783783, 930783784).

Non-randomised controlled studies Nine articles reporting six non-randomised controlled studies were identified. There was 1 two-arm study in which POSE was compared to endoscopic IGB in a large sample of 463 participants with a12-month follow-up (Miranda-Penarroya 2022, 264638247).

One study compared POSE to two types of endoscopic IGB (Orbera and ReShape Duo) and to ESG and measured WL outcomes after 1-year follow-up in a large sample reported in three conference abstracts and one full publication (Lopez-Nava 2017, 264637760; Lopez-Nava 2019, 264637747, 264637753; Lopez-Nava 2018, 264637776). A third study compared POSE to ESG or endoscopic IGB or DJBL. Follow-up was unclear as was the sample size, although 6771 procedures were reported (Espinet Coll 2017, 264635512). These articles were described in Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.).

The other three studies all compare two versions of the POSE procedure. POSE was compared with or without reinforcement in two different groups of participants dependent on BMI with follow-up for 3 months (Garcia 2019, 264635893; Garcia 2019, 264635897). A small study in 33 participants followed up over 6 months compared first- and second-generation POSE procedures (Maselli 2022, 264638042). WL and safety outcomes from single- and double-helix approaches to distal POSE were compared in 110 participants after follow up for 12 months in the study reported by Jirapinyo (Jirapinyo 2022, 930783409; Jirapinyo 2022, 930783405).

Primary Obesity Surgery Endoluminal versus pharmacotherapy

Randomised controlled trials There were no articles identified reporting RCTs.

Non-randomised controlled studies There were no non-randomised studies in which POSE was compared to obesity pharmacotherapy.

Primary Obesity Surgery Endoluminal in other combinations
There were no other comparative articles identified.

Uncontrolled studies
There were 31 articles identified reporting uncontrolled studies for the POSE procedure. One article reported the intervention as redoing POSE for POSE failure. Three articles reported using the POSE 2.0 procedure.

Transoral outlet reduction by endoscopy
Details of the 19 articles involving studies reporting TORe are outlined in the following section by comparator and study design. The population undergoing the TORe procedure was usually those with weight regain or plateau.

Transoral outlet reduction by endoscopy versus bariatric surgery
Randomised controlled trials No RCTs were identified comparing TORe with any form of bariatric surgery.

Non-randomised controlled studies One non-randomised study from one conference abstract was identified in which TORe was compared to surgical revision of the gastro-jejunal anastomosis. The study included two further intervention arms, one in which pharmacotherapy was used in combination with TORe and another in which participants were treated with pharmacotherapy alone. One hundred and twenty-six RYGB patients with weight regain were enrolled and followed up over 12 months (Jirapinyo 2022, 930783408).

Transoral outlet reduction by endoscopy versus sham procedures
Randomised controlled trials One RCT was identified comparing TORe with a sham procedure. This multicentre, blinded study combined both intervention arms with a healthy lifestyle eating programme and followed patients with weight regain (*n* = 77) for 6 months to assess WL, safety and clinical outcomes (Thompson 2013, 264640660).

Non-randomised controlled studies No non-randomised studies comparing TORe to a sham procedure were identified.

Transoral outlet reduction by endoscopy versus lifestyle interventions
Randomised controlled trials There were no articles identified reporting any RCTs comparing TORe to LSIs.

Non-randomised controlled studies No non-randomised controlled studies were identified.

Transoral outlet reduction by endoscopy versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.)
Randomised controlled trials No articles reporting a RCT comparing TORe to other endoscopic interventions were identified.

Non-randomised controlled studies Seventeen articles were identified reporting non-randomised studies. One study reported in three conference abstracts by Lopez-Nava *et al.* compared ESG with TORe for weight regain and were described in section Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.) (Lopez-Nava 2019, 264637768; Lopez-Nava 2019, 264637769; Lopez-Nava 2020, 264637757).

Nine further articles report two-arm comparisons of variations in TORe and have not been mentioned elsewhere in this chapter. TORe with argon plasma coagulation (APC) was compared to TORe with endoscopic submucosal dissection (ESD) in 2 studies of 41 patients (Hollenbach 2019, 264636485) and 76 patients (Jirapinyo 2020, 264636816) both over a 1-year follow-up. Standard TORe was compared to tubular transoral pouchplasty in 131 participants over an18-month follow-up (Ghazi 2021, 264636013).

Outcomes from TORe full-thickness sutures were compared with TORe superficial sutures in 118 patients that were followed up for 6 months (Kumar 2013, 264637342; Kumar 2014, 264637348). TORe with APC was compared to the second-generation TORe procedure in 30 participants (Schulman 2016, 264639967), and TORe with suturing in 175 patients (Schulman 2016, 264639966). Both studies followed patients up for 6 months.

Two forms of TORe (purse-string and interrupted sutures) were compared in 241 patients that were followed up over 1 year (Schulman 2018, 264639970). Purse-string TORe was compared to TORe without purse-string sutures in 51 participants over 12-month follow-up (Meyers 2022, 930783530).

Transoral outlet reduction by endoscopy was compared with endoscopic IGB or ESG in a study reported in two conference abstracts (Vargas 2020, 264640924; Vargas 2021, 264640923). One study reported in a conference abstract compared TORe with two other intervention arms of endoscopic revision of surgical sleeve gastrectomy or ESG (Kozan 2021, 264637298). A second similar study by the same authors included a fourth intervention arm in which the TORe-gastroplasty procedure was carried out (Kozan 2021, 264637299). These four articles were previously described in section Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.).

One study reported in a conference abstract compared WL outcomes for a combination of TORe and injection of botulinum toxin versus botox alone in 10 patients with weight regain following RYGB. Preliminary results were reported for 1-month follow-up with a planned 12-month completion (Vargas 2017, 264640921).

Transoral outlet reduction by endoscopy versus pharmacotherapy

Randomised controlled trials There were no articles reporting RCTs.

Non-randomised controlled studies There was one non-randomised study in which TORe was compared to obesity pharmacotherapy. TORe was compared to pharmacotherapy alone or to TORe with pharmacotherapy or to surgical revision of gastro jejunal anastomosis (GJA). Prescribed medications included topiramate, phentermine/topiramate, phentermine, liraglutide, bupropion/naltrexone and lorcaserin. One hundred and twenty-six participants were followed up for 12 months (Jirapinyo 2022, 930783408).

Transoral outlet reduction by endoscopy in other combinations

There were no further articles identified.

Uncontrolled studies

There were 27 articles reporting uncontrolled studies using interventions involving TORe or variations of TORe.

Other restrictive endoscopic treatments

Details of the 15 articles involving studies reporting other forms of restrictive endoscopic treatment are outlined in the following section by comparator and study design.

Other restrictive endoscopic procedures versus bariatric surgery

Randomised controlled trials No RCTs were identified in which other forms of restrictive endoscopic procedure were compared to bariatric surgery.

Non-randomised controlled studies Eight articles were identified which reported six non-randomised studies. Two studies reported in three conference abstract articles compared endoscopic gastric plication to LSG or RYGB with 92 patients enrolled (Cerri 2021, 264634645) and LSG or LGCP with 357 patients enrolled (Ruiz 2016, 264639669; Ruiz 2017, 264639670). Maximum length of follow-up was 24 months for both studies. The TOGA procedure was used in a three-arm comparative study versus RYGB or biliopancreatic diversion (BPD). Eighty-nine patients were followed up over 24 months (Nanni 2011, 264638499; Nanni 2012, 264638498). Endoscopic gastric pouch reduction using the Stomaphyx device was compared to RYGB in 37 patients who needed revision for weight regain. WL and safety outcomes were measured but follow-up period was unclear (Bolton 2013, 264634309). 'Endoscopic gastroplasty' was compared to LGP in 40 participants over a 6-month follow-up in a single conference abstract. No specific details for 'endoscopic gastroplasty' were given in the abstract (Buzga 2017, 264634515). A large study (*n* = 11,177) using the MBSAQIP database compared 30-day postoperative AEs and related outcomes of primary endoscopic interventions (IGB were excluded) with laparoscopic therapies. Results were not reported separately for specific interventions (Fayad 2020, 264635613).

Other restrictive endoscopic procedures versus sham procedures

Randomised controlled trials Two RCTs reported in two articles were identified that compared an endoscopic intervention with a sham procedure. Endoscopic full-thickness gastric plication using the Stomaphyx device was compared to a sham procedure in 74 patients who had regained weight after RYGB. Enrolment closed early but 1-year follow-up was completed by 74 patients (Eid 2014, 264635398). Results from three of a multicentre blinded RCT comparing TOGA with a sham procedure in 83 participants who were followed up for 1 year were presented in a conference abstract article (Jonnalagadda 2012, 264636863).

Non-randomised controlled studies No non-randomised controlled studies were identified.

Other restrictive endoscopic procedures versus lifestyle interventions

Randomised controlled trials Two RCTs involving endoscopic interventions in comparison with LSIs were reported in two articles. Endoscopic sutured gastroplasty using the Endomina system combined with LSI was compared to LSI alone in 71 participants with WL outcomes reported after a 12-month follow-up (Huberty 2021, 264636580). EVG was compared with ESG, POSE and LSI alone in 120 participants over a 6-month follow-up. This study was also reported in conference abstracts without the lifestyle comparator arm in a smaller cohort (*n* = 54 and 90) (di Prampero 2022, 930783780). This was described in earlier section.

Non-randomised controlled studies No non-randomised controlled studies were identified.

Other restrictive endoscopic procedures versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.)

Randomised controlled trials One RCT (two articles) involving other forms of restrictive endoscopic interventions was identified. Endoscopic full-thickness suturing to reduce the stoma with or without the gastric pouch with APC was compared to APC alone in 40 patients who had regained weight after RYGB and were followed up for 12 months (Brunaldi 2019, 264634463; Brunaldi 2020, 264634464).

Non-randomised controlled studies Seven articles reporting non-randomised controlled studies were identified. In some articles, specific details of the intervention were not given. Endoscopic suturing was compared to sclerotherapy (*n* = 37) over 3-month follow-up (Abu Dayyeh 2012, 264633424) to ROSE in combination with APC (*n* = 42) over a 3-month follow-up (Jirapinyo 2018, 264636830) or endoscopic suturing with reinforcement (*n* = 31) with 18-month follow-up (Sander 2019, 264639853). Endoscopic sutured gastroplasty was compared to endoscopic balloon in 30 participants with NAFLD over a 12-month follow-up (Espinet Coll 2019, 264635515; Espinet Coll 2019, 264635516). The TERIS implant was investigated in two articles. Both compared the first generation of the device to the second with a 6-month follow-up in 18 participants (Verlaan 2011, 264640972) and 12-month follow-up in 22 participants (Hould 2011, 264636522).

Other restrictive endoscopic procedures versus pharmacotherapy

Randomised controlled trials There were no articles reporting RCTs.

Non-randomised controlled studies There were no non-randomised studies in which other forms of restrictive procedure were compared to obesity pharmacotherapy.

Other restrictive endoscopic procedures in other combinations

There were no other articles identified that reported comparative studies.

Uncontrolled studies

One hundred articles which reported uncontrolled studies with other forms of endoscopic procedure were identified. The majority of these (59 articles) mentioned 'endoscopic suturing' in the abstract. A form of 'endoscopic plication' was described by nearly a third of articles. The OverStitch device manufactured by Apollo Endosurgery accounted for 23 articles where a brand name was recorded in the abstract.

Space-occupying devices

Table 5 shows a summary of the number of articles mapped as reporting space-occupying interventions broken down by study design.

Endoscopic intragastric balloons

Details of the 200 articles involving studies reporting endoscopic balloons are outlined in the following section by comparator and study design.

Due to the volume of evidence identified involving endoscopic balloons, this section has been divided into extra comparisons (endoscopic balloon vs. endoscopic balloon, endoscopic balloon vs. non-endoscopic interventions, endoscopic balloon vs. no treatment).

Endoscopic intragastric balloons versus bariatric surgery

Randomised controlled trials No RCTs were identified in which endoscopic IGB was compared to any form of bariatric surgery.

Non-randomised controlled studies There were 21 articles identified reporting non-randomised studies comparing endoscopic balloons to bariatric surgery. Many of these studies used endoscopic balloon placement as a bridge to bariatric surgery and the comparison often involved comparing WL in the intervention and comparator arms at different time points in the patient treatment pathway. A study design involving endoscopic IGB followed by bariatric surgery versus no endoscopic balloon followed by bariatric surgery was commonly used and outcomes could be reported at various follow-up times.

Four studies compared endoscopic balloon to LSG with sample sizes ranging from 16 to 120. Follow-up was 6 months (Milone 2005, 264638219), 1 year (Genco 2019, 264635967; Plua Marcillo 2019, 264639270) and 2 years (Jearapongpakorn 2019, 264636786).

In four studies, the comparator was laparoscopic gastric band in a two-arm design. One study enrolled 86 participants with a 6-month follow-up (Busetto 2004, 264634166). Twelve-month follow-up was used in a smaller study (n = 47) (Tayyem 2011, 264640603, 264640601). The smallest of these studies enrolled 32 participants and used two sequential balloon placements with a follow-up of 18 months (Peker 2011, 264639166). Endoscopic IGB was compared to LGP over a 6-month follow-up in 95 participants (Solmaz 2015, 264640274).

TABLE 5 Summary of space-occupying devices by study design

Number of articles	Endoscopic balloon	Swallowable balloon	Other space-occupying devices
RCTs	50	6	3
Non-randomised controlled studies	150	9	1
Uncontrolled studies	486	71	1

Seven studies involved endoscopic balloon compared to more than one comparator arm. These included LSG, LAGB and laparoscopic gastric bypass with some specifying RYGB. The largest studies were retrospective comparisons using registry databases where the proportion of balloons was far less than bariatric surgery.

Endoscopic balloon was compared to LSG and LAGB in 88 participants with a 12-month follow-up (Nikolic 2015, 264638812). Thirty-two patients with an endoscopic IGB prior to bariatric surgery were compared to 901 patients without a balloon prior to LSG or RYGB. Follow-up duration was unclear (Rzepa 2019, 264639725).

A large UK study aimed to evaluate differences in WL following endoscopic balloons and bariatric surgery and the association with deprivation. WL outcomes were given up to 1-year follow-up in 983 patients (LAGB *n* = 533, gastric bypass *n* = 362, gastric balloons *n* = 88) (Alfa Wali 2014, 264633630).

Four studies recruited several hundred participants with follow-up of 6 months (Musella 2014, 264638462; Ng 2009, 264638777; Kolesnikov 2015, 264637246) or unclear follow up (Musella 2012, 264638461).

Five studies compared an endoscopic balloon to non-specified bariatric surgery. Sample size varied from 12 patients to 134 with a follow-up of 1 year where specified (De Stefano 2012, 264635171; Banks 2021, 264634022; Kirby 1990, 264637175). Two of these studies used analysis of the use of balloons recorded in the MBSAQIP Registry to make a comparison of balloons versus bariatric surgery (Dang 2018, 264635035; Chow 2022, 930783210).

Endoscopic intragastric balloons versus sham procedures

Randomised controlled trials Seventeen articles were identified reporting RCTs comparing endoscopic IGB with a sham procedure. The largest RCT (*n* = 326) was the multicentre REDUCE pivotal trial which aimed to evaluate the safety and effectiveness of the ReShape Duo balloon system in combination with diet and exercise compared to a sham endoscopy with diet and exercise alone. The balloon was in place for 24 weeks and participants in the lifestyle arm were offered the balloon at week 24. Safety was monitored through to 12-month follow-up (Ponce 2015, 264639289).

A series of seven articles published by Mathus-Vliegen *et al.* report RCTs comparing endoscopic IGB with a sham treatment in a maximum reported sample of 43 participants. The earliest publication was a cross-over RCT in which a balloon in combination with LSI was compared with sham combined with LSI for 17- and 18-week treatment periods. Participants were super morbidly obese, but the sample size was unclear (Mathus-Vliegen 1990, 264638077). A similar study design was reported in the remaining articles, although the combination with LSI was not mentioned. The balloon was in place for 13 weeks before all participants were offered the balloon for a second 13-week period with a follow-up of 6 months (Mathus-Vliegen 2013, 264638072; Mathus-Vliegen 2014, 264638073; Mathus-Vliegen 2021, 264638059). The same study was also reported with a balloon placement period of 4 months and further 4 months in all 32 participants with a total follow-up of 8 months (Mathus-Vliegen 2003, 264638078). These studies focused on effects of the balloon on satiety, fasting and related hormone secretion, gastro-oesophageal reflux and a possible mechanism of action for balloon-induced WL. One of the articles described the study continuing for a 52-week balloon placement in all participants after the initial 13-week comparative study to evaluate long term effects on gastro-oesophageal reflux (Mathus-Vliegen 2002, 264638074). A report with a similar design allowed participants to continue with a balloon in place for a total of 12 months if WL targets were met after the initial comparative 3 months study. Total study follow-up was longer at 24 months (Mathus-Vliegen 2005, 264638076).

Eight further RCTs involving endoscopic IGB versus sham comparisons are reported in nine articles. The largest sample size was 59 participants (Hogan 1989, 264636472) and the longest placement of a balloon was for 6 months (Lee 2012, 264637552; Lee 2009, 264637553; Hollenbach 2022, 930783369). Duration of follow-up was up to 12 months but unclear in one study (Martinez-Brocca 2007, 264638021). LSI was specifically mentioned as part of the intervention in both arms in four studies (Hogan 1989, 264636472; Lee 2012, 264637552; Lee 2009, 264637553; Ramhamadany 1989, 264639437; Rigaud 1995, 264639555). In one study, the sham procedure was in combination with 'conventional medical therapy', but no further details were given in the abstract (Lindor 1987, 264637671). Morbidly or severely obese patients were enrolled in two studies (Genco 2006, 264635964; Rigaud 1995, 264639555) and a third study evaluated the efficacy of IGB in improving histology of non-alcoholic steatohepatitis (NASH) in obese patients

(Lee 2012, 264637552; Lee 2009, 264637553). The Weight-Loss Endoscopy Trial (WET) trial compared 6 months endoscopic IGB to 12 months DJBL and to a sham procedure in a three-arm RCT in 33 participants over a 12-month follow-up (Hollenbach 2022, 930783369).

Non-randomised controlled studies Only three non-randomised controlled studies were identified that compared endoscopic balloon placement to a sham procedure. Eighty-seven participants were followed up for 12 months in a balloon versus sham comparison (Hoff 2020, 264633347). A four-group comparison of 6 months balloon placement with intensive or limited diet advice, sham procedure with intensive diet therapy or no treatment with limited advice was described in a total of 40 participants with up to 18-month follow-up (Krakamp 1997, 264637567). The third study included several intervention and comparator arms which included ESG, DJBS, botox and lifestyle in addition to balloon and sham (Abu Dayyeh 2016, 264633434). This study has been described in a previous section Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.).

Endoscopic intragastric balloons versus lifestyle interventions

Randomised controlled trials Seventeen articles were identified that reported eight RCTs comparing endoscopic IGB to various LSIs. Seven articles were published by Abu Dayyeh *et al.* A conference abstract (Abu Dayyeh 2019, 264633428) and associated full text (Abu Dayyeh 2021, 264633426) reported the pivotal multicentre RCT comparing the Spatz3 adjustable balloon in place for 8 months in combination with diet and exercise for 12 months with diet and exercise alone in 288 participants. Safety and effectiveness outcomes were reported for a 56-week follow-up. Two smaller studies in which some of the same participants were also enrolled evaluated the microbiome, gastric emptying and hormonal changes associated with IGB interventions (Hussan 2022, 930783380; Vargas 2019, 264640927). The safety and efficacy of the Orbera balloon were evaluated in a very similar study design reported in a conference abstract (Abu Dayyeh 2015, 264633421) and full text (Courcoulas 2017, 264634955). The balloon was removed after 6 months but LSI continued for 12 months (n = 255). Another small study from the same research group evaluated the effects of balloon treatment on gastric emptying (Gomez 2016, 264636090).

Two articles report a RCT of endoscopic balloon versus LSI in a small cohort (n = 30) of obese adolescents. The control group undertook a 1-year lifestyle programme consisting of a 3-month intensive phase followed by a 9-month maintenance phase. The intervention group followed the lifestyle programme in addition to 6 months balloon placement. Outcomes were measured at 6- and 18-month follow-up (Curran 2011, 264635003; Curran 2015, 264635004).

Another study was reported by 2 articles in which 66 obese participants with metabolic syndrome were randomised to receive the Orbera balloon for 6 months with 12 months diet and exercise or 12 months diet and exercise alone. Six-month safety and efficacy data were presented (Fuller 2010, 264635817) and hormone changes associated with balloon-induced WL (Fuller 2013, 264635819). Two RCTs reporting balloon intervention for 6 months compared with LSI over a 6-month follow-up enrolled 68 (Kashani 2022, 930783425) and 128 participants, respectively (Mohammed 2014, 264638303). The larger study aimed to evaluate the effects of the interventions on hormone levels. Six-month BioEnterics balloon placement was compared with a hypocaloric diet in 66 patients scheduled for bariatric surgery. Outcomes were reported after a 6-month follow-up (Vicente 2020, 264640984; Rabago 2018, 264639397; Vicente 2017, 264640982). A small RCT (n = 30) compared a 24-week placement of the ReShape Duo balloon in combination with diet and exercise to diet and exercise alone. Safety, efficacy and QoL outcomes were reported over a48-week follow-up (Ponce 2013, 264639288).

Non-randomised controlled studies Twenty-four articles reported 21 non-randomised controlled studies comparing endoscopic balloon to LSI. The majority of these compared endoscopic balloon to LSI as part of a two-arm design. In these studies, follow-up was 4 months (Doldi 2002, 264635278), 6 months (Takihata 2014, 264640533; Leeman 2013, 264637560; Mariani 2016, 264637973; Sanchez-Santos 2011, 264639845), 8 months (Hussan 2019, 264636599), 9 months (Konopko-Zubrzycka 2009, 264637259, 264637260, 264637261), 12 months (Fuller 2013, 264635820; Oster 2021, 264638993; Oster 2022, 930783605), 18 months (Ahmed 2019, 264633518) and 24 months (Shchukina 2014; 264640132). Sample sizes ranged from 12 to 281 participants.

One study enrolled 10 patients with Prader–Willi syndrome who were followed up for 6 months (Ashem 2013, 264633911). In three studies, endoscopic balloon was described as being in combination with LSI compared to LSI alone with follow-up of 4 months (Tosetti 1996, 264640736), 24 months (Genco 2008, 264635961) or of unclear duration (Vicente 2017, 264640983). Two studies involved three intervention arms. These compared endoscopic balloon to either two forms of diet (Balejko 2018, 264634001) or endoscopic balloon with LSI to sham with LSI or no treatment with LSI (Krakamp 1997, 264637567). A study compared endoscopic balloon alone to endoscopic balloon with LSI to LSI alone or no treatment in 86 participants. Follow-up was 3 months duration (Geliebter 1991, 264635950).

In two studies, endoscopic balloon was compared to ESG, POSE 2.0, botox, DJBS, sham, no treatment or LSI (Rapaka 2022, 930783648; 930783650; Abu Dayyeh 2016, 264633434). These were mentioned earlier in section Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.).

Endoscopic intragastric balloons versus endoscopic intragastric balloons

Randomised controlled trials Four articles reporting four RCTs were identified in which endoscopic balloons were compared with other endoscopic balloons. Two RCTs were identified comparing the saline-filled Bioenterics balloon with the air-filled Heliosphere balloon. Outcomes focused on efficacy, safety and tolerance. In one of these studies, the sample size was 33 participants and follow-up was over 6 months with 6 months balloon placement (De Castro 2010, 264635081). Duration of balloon placement and follow-up was unclear in the larger (n = 60) study (Giardiello 2012, 264636025). The other two RCTs compared variation in volume of the adjustable Spatz3 balloon. A standard volume was compared to a greater volume in 180 participants in one study (Fittipaldi-Fernandez 2021, 264635714). In the second study, all participants (n = 87) started with a standard volume saline-filled Spatz3 balloon and were then either given an increased volume using air or a sham form of volume increase (Hoff 2020, 264636465). Follow-up duration was not clear in either study.

Non-randomised controlled studies Thirty-two articles reporting non-randomised controlled studies were identified in which two or more study arms contained an endoscopic balloon. A brief summary is given here.

Six articles compared a liquid-filled balloon to a gas-filled balloon. Sample sizes ranged from 49 to 123 with follow-up from 6 months (Billing 2018, 264634250; Bonfante 2011, 264634317), 12 months (de Castro 2013, 264635082), 18 months (Poliwoda 2011, 264639281) and 36 months (Mylytsya 2014, 264638471). Follow-up was not reported by one study (Erdogan 2013, 264635490).

Fourteen articles described brand-specific comparisons in as few as 12 to as many as 202 participants. Follow-up was 3 months (Siardi 1990, 264640181; 264640182), 4 months (Reed 1988, 264639497), 6 months (Caglar 2013, 264634533; Bozkurt 2011, 264634402; Curry 2017, 264635007; Sartoretto 2018, 264633337; Abeid 2020, 264633376; Hein 2022, 930783356) and 12 months (Genco 2013, 264635968; Dellepiane 2013, 264635195). In one study, follow-up was probably 9 months but was unclear (Sivero 2017, 264640243). Another brand comparison study did not report follow-up (Russo 2017, 264639695).

Five articles investigated two different balloon volumes or reported adjustable versus non-adjustable comparisons with follow-up from 6 to 12 months (Pezzo 2019, 264639223; Wahlen 2009, 264641059; Kola 2017, 264637243; Schwaab 2020, 264639978) or was not reported (Barrichello 2018, 264634067).

The remaining eight articles have been mentioned elsewhere [section Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.)]. Briefly, one article reported a comparison between 6 months and 12 months balloon placement and to ESG in a three-arm study with all arms in combination with LSI (Kozlowska-Petriczko 2022, 930783454). Seven articles reported studies evaluating the Orbera and ReShape Duo balloons compared to ESG (Badurdeen 2020, 264633976) or compared to ESG or POSE (Lopez-Nava 2017, 264637760; Lopez-Nava 2019, 264637747; Lopez-Nava 2019, 264637753; Lopez-Nava 2019, 264637751; Lopez-Nava 2018, 264637776), or compared to swallowable balloon, ESG or aspiration (Almuhaidb 2019, 264633686).

Endoscopic intragastric balloons versus other endoscopic interventions

Randomised controlled trials No RCTs comparing endoscopic balloon to any other endoscopic intervention were identified.

Non-randomised controlled studies There were 32 articles reporting non-randomised controlled studies in which endoscopic balloon was compared to other endoscopic interventions. The majority of these studies were of a 2-arm study design in which endoscopic balloon was compared to ESG (13 articles), POSE (1 article) or endoscopic sutured gastroplasty (2 articles), and multiarm studies comparing endoscopic balloon to ESG and other endoscopic interventions (12 articles). These 28 articles were all mentioned previously in section Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.) and section Primary Obesity Surgery Endoluminal versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.).

There were four studies that have not been previously mentioned. One retrospective matched study compared safety and efficacy of endoscopic IGB to DJBL in 140 participants over a 12-month follow-up (Theodoridou 2022, 930783760).

The safety and efficacy of botox injection in comparison to endoscopic balloon were investigated in a large case matched cohort (n = 176) over a follow-up of 6 months. The main measured outcomes were WL, procedure duration, complications, early satiety and QoL (Tayyem 2022, 930783755). In a smaller study involving comparison of endoscopic balloon to botox, both study arms were also given LSI. Follow-up for the 52 participants was over 3 months (Durmus 2019, 264635353). A study enrolling 121 participants compared endoscopic balloon to botox or endoscopic balloon combined with botox in a three-arm study design following participants up for 6 months (Kanlioz 2020, 264636939).

Endoscopic intragastric balloons versus pharmacotherapy

Randomised controlled trials Four RCTs were identified in five articles that compared endoscopic balloon to pharmacotherapy. Ng *et al.* published three articles comparing endoscopic balloon to sibutramine. Randomisation took place at the point of endoscopy and follow-up continued for 6 months (Ng 2009, 264638776) with a longer follow-up of 10 years also reported (Chan 2021, 264634664; Cruz 2017, 264634977). The fourth study compared endoscopic balloon to sibutramine with LSI in both study arms with a 6-month follow-up (n = 50) (Farina 2012, 264635595). In all studies, balloon placement appears to have been for 6 months. Pharmacotherapy was in the form of hyaluronic acid injections in 1 study which enrolled 101 participants randomised to endoscopic IGB alone or endoscopic balloon with hyaluronic acid injections or hyaluronic acid injections alone and followed them up for 24 months (Dargent 2015, 264635051).

Non-randomised controlled studies Two non-randomised studies (three articles) investigated WL and glycaemic control in a comparison of GLP-1 analogue to endoscopic balloon. Liraglutide was specified in the publication by Stier *et al.* in 46 participants over 6-month follow-up (Stier 2015, 264640366; 264640370). A smaller study enrolled 28 participants and used the Medsil balloon over 6 months, but the GLP 1 analogue was not given in the abstract (Melnikova 2016, 264638165).

Endoscopic intragastric balloons versus non-endoscopic interventions

Randomised controlled trials One RCT reported in four articles was identified involving a comparison between 6-month endoscopic balloon placement and another non-endoscopic intervention. Coffin *et al.* enrolled 115 super obese patients to receive either balloon or 'standard medical care' with a 6-month follow-up. It was not clear what 'standard medical care' included but could include LSI and pharmacotherapy (Coffin 2017, 264634868; Coffin 2016, 264634869; Coffin 2014, 264634870; Coffin 2014, 264634871).

Non-randomised controlled studies There were two non-randomised controlled studies comparing endoscopic balloon to other non-endoscopic forms of treatment for obesity. Anthropometric, biochemical and blood pressure measurements were evaluated in a study comparing endoscopic balloon to CBT in 114 participants over a 6-month follow-up (Majanovic 2014, 264637911). The second study involved an endoscopic balloon versus liposuction comparison with a third study arm of a combination of the two interventions. Follow-up was over 4 months with an unclear number of participants (Tramontano 2010, 264640741).

Endoscopic intragastric balloons versus no treatment comparisons

Randomised controlled trials No RCTs were identified.

Non-randomised controlled studies Thirteen articles reporting 10 non-randomised controlled studies involved a comparison of endoscopic balloon to no endoscopic balloon (no treatment). The majority of these studies aimed to compare the effects of balloon placement prior to bariatric surgery to controls without a balloon prior to bariatric surgery on a range of outcomes including WL, surgical complications, surgery time, hospital stay and AEs. Sample sizes ranged from 18 to 144 participants. Follow-up was 6 months (Chan 2008, 264634662), 39 weeks (Gostout 2015, 264636114), 12 months (Zerrweck 2009, 264641449; Zerrweck 2011, 264641448, 264641447; Zerrweck 2012, 264641451; Platt 2022, 930783633), 24 months (Veloso 2013, 264640956), or over 24 months (Hering 2022, 930783357; Mocanu 2017, 264638291). Duration of follow-up was not reported for two studies (Rzepa 2022, 930783675; Rabago 2014, 264639396). One study with a follow-up of 3 months enrolled 86 participants into 1 of 4 arms (endoscopic balloon alone vs. endoscopic balloon with LSI; LSI alone or no treatment) (Geliebter 1991, 264635950). It is likely that participants in the 'no treatment' arm received some form of LSI.

Endoscopic intragastric balloons in other combinations

Randomised controlled trials There were two RCTs reported in three articles. The Orbera balloon was compared to Orbera with liraglutide in 90 participants over a period over 6 months (Fittipaldi-Fernandez 2018, 264635708; Fittipaldi-Fernandez 2018, 264635707). In the second RCT, 6 months of the Orbera balloon combined with a very-low-calorie ketogenic diet was compared to 6 months of the Orbera balloon combined with a low-calorie diet in 80 participants (Genco 2018, 264635971).

Non-randomised controlled studies Nineteen articles were identified reporting non-randomised studies involving endoscopic balloon in other combinations. Five articles reported a two-arm study in which the intervention group comprised those receiving either endoscopic balloon or a laparoscopic gastric band versus a comparator of LSI. WL and metabolic outcomes related to liver steatosis in patients with morbid obesity (n = 31) were followed up for 6 months (Benetti 2011, 264634166; Folini 2011, 264635738; Folini 2014, 264635739; Garbossa 2011, 264635891; Pontiroli 2012, 264639295).

Fourteen additional articles were identified. A range of comparator combinations included diet (Maekawa 2020, 264637870; 264637871), pharmacotherapy (Kolli 2020, 264637251; Mehta 2021, 264638149; Coskun 2010, 264634934; Mosli 2017, 264638391), psychological treatment (Reid 2017, 264639502), multidisciplinary team involvement (Mazure 2009, 264638098), sedation and anaesthesia (Milone 2011, 264638220), bariatric surgery follow-up (Angrisani 2006, 264633769) and fluoroscopic guidance instead of endoscopic placement (Mathus-Vliegen 2018, 264638070).

Three articles involved a comparison of endoscopic balloon in different patient groups. One small study enrolled obese participants with or without lymphoedema (Khan 2012, 264637079). Two studies enrolled obese participants compared to healthy volunteers (Blus 2015, 264634286) or non-obese controls (Busetto 2005, 264634498).

Uncontrolled studies

There were 486 articles identified that involved an endoscopic balloon in an uncontrolled study.

Swallowable intragastric balloons

Details of the 15 articles involving studies reporting swallowable balloons are outlined in the following section by comparator and study design.

Swallowable intragastric balloon versus bariatric surgery

Randomised controlled trials There were no RCTs identified that compared a swallowable IGB to bariatric surgery.

Non-randomised controlled studies Two articles were identified that reported comparing a swallowable balloon to bariatric surgery. Scopinaro BPD was used as the bariatric comparator in the larger study (*n* = 143). Follow-up was 2 years to evaluate basal BMI (Kotelnikova 2015, 264637277). The Elipse balloon was compared to bariatric surgery or 'non-surgical weight loss' in 77 participants in a study designed to investigate remote follow-up using the patient's smartphone to provide body composition analysis versus biweekly office follow-up over 1 year. No further details of the interventions were given in this conference abstract (Raftopoulos 2019, 264639407).

Swallowable intragastric balloons versus sham procedures

Randomised controlled trials Three articles reporting one RCT were identified in which the Obalon swallowable balloon was compared with a sham procedure. LSI was in combination with both interventions. A large number of participants (*n* = 387) in this multicentre study swallowed at least one capsule over the randomised 6-month period before all patients in the sham plus lifestyle arm were offered the swallowable balloon. Efficacy and safety were evaluated after 6- and 12-month follow-up (Sullivan 2018, 264640448; Pryor 2016, 264639351; Sullivan 2016, 264640451).

Non-randomised controlled studies There were no non-randomised controlled studies identified comparing swallowable balloon with a sham procedure.

Swallowable intragastric balloons versus lifestyle interventions

Randomised controlled trials There were no RCTs identified that involved a comparison between any swallowable balloon versus LSI alone.

Non-randomised controlled studies There were no non-randomised controlled studies identified.

Swallowable intragastric balloons versus endoscopic interventions

Randomised controlled trials There were no RCTs identified in which a swallowable balloon was compared to any other endoscopic treatment for obesity.

Non-randomised controlled studies Six articles were identified reporting five non-randomised controlled studies. All studies involved comparison of swallowable versus endoscopic balloons. The efficacy, tolerance and safety of the Obalon swallowable and Orbera endoscopically placed balloons were compared at 6 months in patients (*n* = 87) who completed more than 20 weeks of therapy (Swei 2022, 930783750; Almuhaidb 2020, 264633685). The same research group reported a similar study involving additional comparator arms of endoscopic IGB (ReShape Duo), aspiration (AspireAssist) and ESG in 98 participants over 6 months (Almuhaidb 2019, 264633686). An intervention arm of two swallowable Obalon balloons over 3 months was compared with the swallowable Elipse balloon over 4 months in 75 participants as a way of evaluating air versus fluid-filled swallowable balloons (Alasfar 2019, 264633593). The efficacy and safety of the swallowable Obalon balloon were compared to the endoscopic Orbera balloon in another study in 143 participants with a 3-month follow-up (Al Sharqawi 2016, 264633556). Safety outcomes were evaluated in a large cohort of patients (773 cases) undergoing swallowable (Obalon) and endoscopic (Orbera and ReShape Duo) balloons taken from post-marketing surveillance data. Duration of follow-up was not clear (Ramai 2021, 264639430).

Swallowable intragastric balloons versus pharmacotherapy

Randomised controlled trials No RCTs were identified in which a swallowable balloon was compared to obesity pharmacotherapy.

Non-randomised controlled studies There were no non-randomised studies.

Swallowable intragastric balloons in other combinations

Randomised controlled trials There were three RCTs identified. All three studies involved the Elipse swallowable balloon in both the intervention and comparator arms. A small study investigated using Bluetooth connected collection of anthropometric measurements and delivery of an exercise and eating plan compared to those without during an 8-month follow-up (Ienca 2018, 264636637). A study was carried out in 24 participants who were given a very-low-calorie ketogenic diet in addition to the Elipse balloon for a period of 1 month compared to 4 months (Ienca 2018, 264636633). Schiavo *et al.* evaluated the Elipse balloon in combination with a ketogenic diet versus a standard low-calorie diet in 48 participants over a 4-month follow-up (Schiavo 2021, 264639940).

Non-randomised controlled studies No non-randomised controlled studies were identified.

Uncontrolled studies

There were 71 articles reporting uncontrolled studies investigating swallowable balloons. Forty-one of these employed the Elipse balloon and 22 articles involved studies using the Obalon balloon.

Other forms of endoscopic space-occupying devices

Details of the four articles involving studies reporting other forms of space-occupying devices are outlined in the following section by comparator and study design.

Other endoscopic space-occupying devices (e.g. TransPyloric Shuttle, SatiSphere) versus bariatric surgery

Randomised controlled trials No RCTs were identified involving other forms of space-occupying endoscopic device compared to bariatric surgery.

Non-randomised controlled studies There were no non-randomised controlled studies.

Other endoscopic space-occupying devices (e.g. TransPyloric Shuttle, SatiSphere) versus sham procedures

Randomised controlled trials Two conference abstract articles reporting two RCTs were identified comparing transpyloric shuttle (TPS) with a sham procedure. The largest study (n = 270), the ENDObesity II study, evaluated WL, cardiometabolic risk factors and QoL outcomes following 12 months device placement (Rothstein 2019, 264639642). A small number of patients (n = 44) were followed up for up to 4 years in a substudy of the ENDObesity II study (Puri 2021, 264639368). There were no other RCTs identified.

Non-randomised controlled studies No non-randomised controlled studies comparing other forms of space-occupying device with a sham procedure were identified.

Other endoscopic space-occupying devices (e.g. TransPyloric Shuttle, SatiSphere) versus lifestyle interventions

Randomised controlled trials No RCTs were identified involving other forms of space-occupying device compared to any form of LSI.

Non-randomised controlled studies There were no non-randomised controlled studies.

Other endoscopic space-occupying devices (e.g. TransPyloric Shuttle, SatiSphere) versus endoscopic interventions

Randomised controlled trials No RCTs were identified that compared other space-occupying devices with any other endoscopic treatments.

Non-randomised controlled studies There were no non-randomised controlled studies.

Other endoscopic space-occupying devices (e.g. TransPyloric Shuttle, SatiSphere) versus pharmacotherapy

Randomised controlled trials No RCTs were identified in which any other form of space-occupying device was compared to obesity pharmacotherapy.

Non-randomised controlled studies There were no non-randomised controlled studies.

Other endoscopic space-occupying devices (e.g. TransPyloric Shuttle, SatiSphere) in other combinations

Randomised controlled trials One small RCT (n = 31) was identified which compared the safety and efficacy of the SatiSphere device with a control group who did not receive the implant (no treatment). Participants were followed up for 3 months (Sauer 2013, 264639905).

Non-randomised controlled studies One non-randomised study was identified which compared TPS in place for 3 months with a 6-month placement. This feasibility study evaluated the safety and efficacy of the clinical procedure and device in 20 participants who were followed up for 6 months (Marinos 2014, 264637977).

Uncontrolled studies

One uncontrolled study was identified involving the use of the TPS device. No other uncontrolled studies were identified that used other forms of space-occupying device.

Malabsorption devices and procedures

A summary of the number of articles identified reporting studies of malabsorption devices and procedures broken down by study design is shown in *Table 6*.

Duodenal–jejunal bypass liner

Details of the 63 articles involving studies reporting DJBL are outlined in the following section by comparator and study design.

Duodenal–jejunal bypass liner versus bariatric surgery

Randomised controlled trials There were no RCTs identified that compared DJBL with any form of bariatric surgery.

Non-randomised controlled studies Twelve articles were identified that reported two non-randomised controlled studies. DJBL was compared to surgical gastric plication in a series of reports evaluating anthropometric, biochemical and hormonal outcomes during a 10-month follow-up. The largest sample size reported was 59 participants, the majority of whom were T2D patients with some reports including a lean healthy control group (Cinkajzlova 2017, 264634838; Cinkajzlova 2017, 264634839; Cinkajzlova 2015, 264634840; Cinkajzlova 2015, 264634841; Klouckova 2015, 264637199; Mraz 2018, 264638408; Kratochvilova 2019, 264637309). Guenthert *et al.* published a series of reports which aimed to compare outcomes focused on glycaemic control, WL and BMI in obese T2D patients (n = 46) receiving either DJBL or RYGB. Follow-up was 9 months (Guenthert 2015, 264636203; Guenthert 2016, 264636201) or up to 12 months (Guenthert 2017, 264636202; Stier 2017, 264640369; Guenthert 2022, 930783334).

Duodenal–jejunal bypass liner versus sham procedures

Randomised controlled trials Four articles were identified reporting four RCTs comparing DJBL to a sham procedure. A small (n = 18) study compared DJBL to sham over a 12-month follow-up (Rodriguez 2009, 264639585). One study was large with 325 participants and a follow-up over 12 months. Sham was in combination with LSI (Thompson 2022, 930783761). One study followed 47 participants for 3 months and included LSI in both arms (Gersin 2010, 264636000). The WET compared 12 months implanted DJBL to 6 months endoscopic IGB or a sham with a post removal follow-up of a further 12 months. Outcomes evaluated were WL, changes in comorbidities, QoL and complications (Hollenbach 2022, 930783369).

Non-randomised controlled studies One non-randomised controlled study was identified which compared multiple endoscopic therapies including the DJBS, botox, endoscopic IGB and ESG compared to LSI or a sham procedure. One

TABLE 6 Summary of malabsorption devices and procedures by study design

Number of articles	DJBL (or DJBS)	DMR
RCTs	25	1
Non-randomised controlled studies	38	0
Uncontrolled studies	188	15

DJBL, duodenal jejunal bypass liner or sleeve; DMR, duodenal mucosal resurfacing.

hundred and eighteen participants were followed up for 6 months (Abu Dayyeh 2016, 264633434). This study has been mentioned previously in other endoscopic intervention sections.

Duodenal–jejunal bypass liner versus lifestyle interventions

Randomised controlled trials Four articles were identified comparing DJBL to LSI. Two small studies (*n* = 41 and 39) implanted the DJBL for 3 months in combination with a low-calorie diet compared to a low-calorie diet alone and followed participants for 3 months to evaluate efficacy and safety outcomes (Schouten 2010, 264639658; Tarnof 2009, 264640577). Greve *et al.* carried out the largest study comparing DJBL (EndoBarrier) to LSI in a multicentre study in the Netherlands. The device was implanted in combination with dietary intervention for 6 months in 77 patients with obesity and T2D. Follow-up continued for a total of 12 months (Koehestanie 2014, 264637222; Koehestanie 2012, 264637224).

Non-randomised controlled studies Two non-randomised articles were identified. A large study compared the safety and efficacy of DJBL to LSI in a matched controlled study of 333 obese T2D patients but duration of follow-up was not clear (Laubner 2018, 264637462). The study by Abu Dayyeh *et al.*, which included many endoscopic invention groups, including DJBL, has been mentioned in previous sections (AbuDayyeh 2016, 264633434).

Duodenal–jejunal bypass liner versus endoscopic interventions

Randomised controlled trials No RCTs were identified.

Non-randomised controlled studies Three non-randomised controlled studies were identified that compared DJBL to other endoscopic interventions. These were previously described in section Endoscopic intragastric balloons versus other endoscopic interventions (Theodoridou 2022, 930783760) and Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.) (Espinet Coll 2017, 264635512; Abu Dayyeh 2016, 264633434).

Duodenal–jejunal bypass liner versus pharmacotherapy

Randomised controlled trials One RCT comparing DJBL to obesity pharmacotherapy was identified in a series of nine articles reporting the efficacy, safety and tolerability outcomes of EndoBarrier as an adjunct to glucagon-like peptide therapy in suboptimally controlled T2D. Three treatment groups received either the DJBL alone for 12 months or DJBL in combination with 1.2 mg Liraglutide or an increased dose of 1.8 mg Liraglutide. Participants (*n* = 70) were followed for up to 2 years. Preliminary results were published with smaller numbers of participants or shorter follow-up (Johal 2016, 264636844; Sen Gupta 2016, 264640036; Sen Gupta 2015, 264640034) and a UK CEA was also presented (Armstrong 2018, 264633877; Gupta 2018, 264636237; Gupta 2018, 264636237). Ten-year CVD risk was estimated following 12 months of DJBL placement (Ryder 2016, 264639705) and the effect of the DJBL on NAFLD was evaluated using the same study design with a 3- (Hayee 2016, 264636366) and 12-month follow-up (Sen Gupta 2015, 264640035).

Non-randomised controlled studies There were no non-randomised controlled studies identified comparing DJBL to pharmacotherapy.

Duodenal–jejunal bypass liner in other combinations

Randomised controlled trials Eight articles reported two RCTs involving DJBL in a comparison with ‘conventional medical therapy or care’ or ‘intensive medical care’. It was not clear what these comparators entailed.

Ruban *et al.* published seven articles that appear to report aspects of the same study which was a UK-based two-centre EndoBarrier RCT. In this study, 12 months implant of the DJBL was compared to ‘conventional medical therapy’ in combination with diet and exercise in 170 participants with obesity and T2D. Outcomes including glycaemic control, WL and cardiometabolic risk factors were evaluated at 12 and 24 months. Safety profile (Ruban 2021, 264639656), plasma metabolic profile (Ruban 2021, 264639652) and liver function tests for NAFLD (Ruban 2020, 264639657) were reported. Two articles likely report the same study, but the population is described as ‘inadequately controlled T2D patients’ and the DJBL is described as being in combination with ‘intensive medical care’ compared to ‘intensive medical care’ alone (Ruban 2021, 264639658; Ruban 2022, 930783667). No further details were given in the abstracts as to what constituted 'conventional medical therapy' and 'intensive medical care'. Plasma fatty acids were investigated in 140 participants (Glaysher 2021, 264636055) and assessments of food intake, food preference and taste function in a small group (*n* = 47) (Aldhwayan 2022, 930783069). It was not clear whether the participants enrolled were those also included in the main study.

In the second RCT, the efficacy and safety of 12-month implantation of DJBL were compared to 'conventional medical care' in 82 patients with metabolic syndrome over a 24-month follow-up (Caiazzo 2020, 264634536).

Non-randomised controlled studies Twenty articles for four non-randomised controlled studies were identified. The majority of these (14 conference abstracts) were published by Benes *et al.*, who carried out a multicentre comparison of the EndoBarrier DJBL implanted for 10 months versus controls who did not receive the implant. All 70 participants were obese with T2D, and study follow-up was 10 months. Safety and effectiveness were reported as preliminary results (Benes 2015, 264634151; 264633320; 264634162), interim results (Benes 2014, 264634157; Benes 2015, 264634163) or final results (Benes 2016, 264634164, 264634158; Benes 2017, 264634153; Benes 2018, 264634154), and identification of factors associated with a suboptimal outcome of the EndoBarrier (Benes 2018, 264634155, 264634152, 264634159, 264634160; Benes 2019, 264634161).

A study comparing 12 months DJBL to 'conservative treatment' was carried out in 45 severely obese adolescents over a 2-year follow-up. The aim was to evaluate emotional and behavioural factors in addition to WL and metabolic outcomes (Klemencic 2021, 264637195; Bujisic 2017, 264634489).

Three articles were reported for a study in which EndoBarrier was implanted for 1 year in 11 patients prior to bariatric surgery and compared to 11 participants who underwent primary bariatric surgery. The aim was to evaluate morbidity, complications and length of stay post bariatric surgery (Younus 2015, 264641385; Younus 2017, 264641386; Younus 2018, 264641387).

One non-randomised controlled study was reported in which the DJBL was the same in both intervention and comparator arms. The DJBL was implanted either using conscious sedation or with a general anaesthetic in 56 patients. Follow-up was short term to assess safety, efficacy and feasibility outcomes (Betzel 2013, 264634206; Koehestanie 2014, 264637220).

Uncontrolled studies
There were 188 articles reporting uncontrolled studies involving a DJBL or DJBS.

Other forms of malabsorption devices and procedures
Details of the one article involving a study reporting other forms of malabsorption device are outlined in the following section.

Only one comparative study was identified that investigated the use of duodenal mucosal resurfacing (DMR) as an endoscopic treatment for obesity. This RCT compared DMR to a sham procedure in 32 insulin-resistant women with polycystic ovary syndrome and obesity. Follow-up was 6 months for outcomes relating to glycaemic control (Kaur 2021, 264637007).

Uncontrolled studies
Fifteen articles were identified that investigated DMR in an uncontrolled study.

Other endoscopic procedures
A summary of the number of articles mapped as reporting aspiration or botox procedures broken down by study design is shown in *Table 7*.

Aspiration
Details of the 13 articles involving studies reporting aspiration are outlined in the following section by comparator and study design.

TABLE 7 Summary of other endoscopic procedures by study design

Number of articles	Aspiration	Botox
RCTs	7	7
Non-randomised controlled studies	6	8
Uncontrolled studies	13	12

Aspiration versus bariatric surgery

Randomised controlled trials There were no RCTs identified that compared aspiration to any form of bariatric surgery.

Non-randomised controlled studies Three articles were identified reporting two non-randomised controlled studies. Aspiration was compared to RYGB with respect to weight reduction, QoL, cardiometabolic parameters, complications, mortality and health economics in a sample of 106 participants and an initial follow-up period of 12 months (Wilson 2017, 264641182) and a later publication reporting 3-year follow-up (Wilson 2018, 264641183). A second study aimed to evaluate methods to reliably predict response to obesity therapies. AspireAssist was compared to several arms including sleeve, band, bypass, stimulator and LSI. Thirty patients were followed up for up to 5 years for WL outcomes (Mathur 2021, 264638056). No further details were given in this conference abstract.

Aspiration versus sham procedures

Randomised controlled trials There were no RCTs identified that reported aspiration compared to a sham procedure.

Non-randomised controlled studies One non-randomised controlled study was identified. The acute effects of aspiration on postprandial glucose tolerance, hormone responses, appetite sensations and food intake were evaluated in seven participants in cross-over between aspiration and sham, and seven no treatment controls (Gether 2022, 930783309; Gether 2021, 264636003).

Aspiration versus lifestyle interventions

Randomised controlled trials Seven articles were identified reporting two RCTs comparing aspiration to LSI. The first RCT was a pilot trial of aspiration therapy in 18 obese participants over 1 year in combination with a 15-session diet and behavioural education programme compared to the lifestyle programme alone (Klein 2012, 264637193). Follow-up continued for a further 12 months in a proportion of participants (Sullivan 2012, 264640444; Sullivan 2012, 264640444).

The second RCT was the Pathway trial, a 52-week multicentre RCT that was published in four articles. Up to 207 participants were treated with AspireAssist plus lifestyle counselling or lifestyle counselling alone to investigate WL outcomes (Thompson 2017, 264640656; Thompson 2016, 264640657). Up to 5-year long-term follow-up of a smaller cohort of participants was also reported (Thompson 2018, 264640661; Thompson 2019, 264640658).

Non-randomised controlled studies There was one non-randomised controlled study comparing aspiration to bariatric surgery or LSI alone (Mathur 2021, 264638056). This was also noted in section Aspiration versus bariatric surgery.

Aspiration versus endoscopic interventions

Randomised controlled trials There were no RCTs identified that compared aspiration to other forms of endoscopic intervention.

Non-randomised controlled studies One non-randomised controlled study was identified in which aspiration was compared to three interventions (endoscopic balloon, swallowable balloon and ESG) (Almuhaidb 2019, 264633686). This was noted in section Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.).

Aspiration versus pharmacotherapy

Randomised controlled trials There were no RCTs identified that compared aspiration to obesity pharmacotherapy.

Non-randomised controlled studies No non-randomised controlled studies were identified.

Aspiration other combinations

There were no other comparative studies involving aspiration.

Uncontrolled studies

Thirteen articles report aspiration as the intervention in an uncontrolled study.

Gastric botulinum toxin injection

Details of the 15 articles involving studies reporting botox are outlined in the following section by comparator and study design.

Botox versus bariatric surgery

Randomised controlled trials No RCTs were identified.

Non-randomised controlled studies One non-randomised controlled study comparing endoscopic botox A injection to bariatric surgery was identified. LSI was also compared in a third arm of this study. WL outcomes were compared after 6-month follow-up in 72 participants (Ozdil 2022, 930783609).

Botox versus sham procedures

Randomised controlled trials Six articles were identified that reported five RCTs of endoscopic botox injection compared to endoscopic saline injection (placebo sham). The IntraTox study enrolled the largest sample (*n* = 52) and followed participants up for 6 months to determine the effect of one-time botox injection on WL, satiety, biomarkers, and QoL of obese patients prior bariatric surgery (Sanchez-Torralvo 2021, 264639822). A follow-up analysis was also reported (Sanchez-Torralvo 2022, 930783689). Four further articles evaluated botox injection versus placebo sham injection in small numbers of participants. Two articles reported 6-month follow-up (de Moura 2019, 264635151; Mittermair 2007, 264638276). Two pilot studies followed up participants for 8 weeks (Foschi 2007, hand search) or 5 weeks using two different doses of botox (Gui 2006, 264636211).

Non-randomised controlled studies Two non-randomised controlled studies were identified. An extension to the RCT reported by Foschi *et al.* employed a second injection site to that used in the original study (Foschi 2008, 264635760). The second study comparing botox to a sham procedure, ESG, endoscopic IGB, DJBS and lifestyle has been previously noted in earlier section Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.) (Abu Dayyeh 2016, 264633434).

Botox versus lifestyle interventions

Randomised controlled trials There were no RCTs identified in which botox injections were compared to LSI alone.

Non-randomised controlled studies Four non-randomised controlled studies were reported. One study delivered a botox injection in combination with low-calorie high-protein diet or a low-calorie high-protein diet alone. Seventy-one participants were followed up for 4 months (Hsu 2022, 930783376). A study enrolled 87 participants to three different treatment arms to evaluate the effect of botox with a low-calorie high-protein diet (botox vs. botox in combination with LSI vs. LSI alone). Length of follow-up was unclear from the abstract (Ferhatoglu 2020, 264635638). Two studies also involved a LSI comparator arm. In both studies, follow-up was for 6 months and sample size was 72 (Ozdil 2022, 930783609) and 118 participants (Abu Dayyeh 2016, 264633434). See section Botox versus bariatric surgery and Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.).

Botox versus endoscopic interventions

Randomised controlled trials One RCT was identified which aimed to investigate the effect of two different doses of botox on WL and peripheral appetite-related hormones in 20 patients. Safety outcomes were also evaluated after a 3-month follow-up (Li 2012, 264637608; Li 2012, 264637600).

Non-randomised controlled studies Four non-randomised studies were identified and have all been noted in previous sections. Three articles were noted in section Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.). The safety and efficacy of botox injection in comparison to endoscopic balloon were investigated in a large case-matched cohort (*n* = 176) over a follow-up of 6 months. The main measured outcomes were WL, procedure duration, complications, early satiety and QoL (Tayyem 2022, 930783755). A second study also compared botox injection to endoscopic balloon, but in this study both arms were given LSI. Follow-up for the 52 participants was over 3 months (Durmus 2019, 264635353). The larger study (*n* = 121) compared endoscopic balloon to botox or endoscopic balloon combined with botox in a three-arm study design following participants up for 6 months (Kanlioz 2020, 264636939). The study reported by Abu Dayyeh mentioned in earlier sections [Endoscopic sleeve gastroplasty versus endoscopic interventions (including variations in suturing patterns or location of stitching or stapling, next generation of procedure, addition of reinforcement, etc.)] also compared botox injection to endoscopic balloon as well as DJBS, ESG, sham injection and LSI (Abu Dayyeh 2016, 264633434).

Botox versus pharmacotherapy

Randomised controlled trials There were no RCTs identified that compared botox to obesity pharmacotherapy.

Non-randomised controlled studies There were no non-randomised controlled studies.

Botox in other combinations

There were no other comparative studies identified involving endoscopic gastric botox injection.

Uncontrolled studies

Twelve articles reported investigating botox as an intervention in an uncontrolled study.

Discussion

Summary of findings

The evidence base identified was considerably larger than expected and included many more interventions (and variations) as well as a wide range of comparators and different populations. An overarching approach was required to categorise the evidence, and an evidence map (Excel spreadsheet) was produced for this purpose. This includes 1574 records on endoscopic therapies.

The map provides a repository of all evidence on endoscopic therapies which can be filtered by population (e.g. general obesity, bridge to bariatric surgery), study design (RCT, non-randomised controlled study and uncontrolled study), intervention, comparator (if applicable), sample size and length of follow-up to identify the evidence on any combination of these. Details of the RCTs and non-randomised controlled studies have further been summarised in tables, and brief descriptions of all studies have been provided earlier under the categories of restrictive procedures, space-occupying devices, malabsorption devices and procedures and other endoscopic procedures.

Around 9% (*n* = 140) of records related to RCTs, 18% (*n* = 271) to non-randomised controlled trials and 73% (*n* = 1095) to single-arm studies. The vast majority of articles report observational studies, usually retrospective, analysing data in registries. In terms of interventions, most of the evidence relates to space-occupying devices (mostly IGB) and restrictive procedures (mostly different types of ESG), with less evidence available for malabsorption procedures or other types of endoscopic treatment. Other than IGB and ESG, the main interventions were POSE, TORe and DJBL, with only a small proportion of studies reporting on aspiration therapy, botox injections or other procedures. The main comparators were bariatric surgery, LSIs, sham procedures or other endoscopic interventions (including variations of the same intervention, e.g. comparison of two different types of ESG).

Focusing on the comparative evidence only, most of the records on RCTs related to comparisons between IGB and a sham procedure or LSI; POSE versus LSI; and ESG versus a different endoscopic treatment. Most of the records on non-randomised controlled studies related to comparisons between ESG and bariatric surgery or another endoscopic intervention; TORe versus another endoscopic intervention; IGB versus bariatric surgery or another endoscopic intervention; or DJBL versus other treatment combinations.

There was a notable lack of evidence on some endoscopic treatments and/or study designs. For example, there were no RCTs comparing any endoscopic treatment to bariatric surgery; and there were very few RCTs or non-randomised controlled studies that included pharmacotherapy as a comparator. This is important considering the rapidly expanding options of pharmacotherapy for obesity management including the impact on a wide range of obesity-related complications. Hence, there is a real need for RCTs directly comparing endoscopic obesity treatments with obesity pharmacotherapy including longer-term data. This is particularly important as some of the agents that might become available in the future have greater efficacy on WL and complications than currently available treatments.

Most studies looked at WL outcomes and/or safety, with fewer also reporting on other outcomes such as satiety, gastric emptying or indices of glycaemic control. Very short-term studies (e.g. up to 1 month) tended to focus on procedural safety and complications, with longer-term studies (6–12 months) reporting weight changes and metabolic outcomes. Over half the articles reported studies with follow-up of 6–12 months.

In addition, data on treatment options are needed to guide patients, clinicians and payers considering that the characteristics of the population that are eligible for these treatments are similar (e.g. certain BMI levels or the presence of obesity-related complications). This also highlights the need for better phenotyping of obesity to be able to use precision medicine approaches. Another important aspect of the evidence is to consider the treatment of obesity as a chronic disease. Many patients require different treatments at different stages of their lives and some patients might require combination therapy either consecutively or simultaneously. Hence, future evidence needs to consider these possibilities to guide the decision-making process of the stakeholders.

Strengths/weaknesses of evidence map

The evidence map is based on comprehensive searches (to January 2023) with no restrictions by study design, date, language or publication type. More than 9000 records were screened independently by at least two reviewers. Data extraction was based on the abstract and details were extracted on population, intervention, comparator (if applicable), study design, sample size and length of follow-up, and records can be filtered according to any combination of these categories.

As data extraction was based on title and abstract, this meant relying on sometimes limited descriptions of studies. This in turn may have led to some inconsistencies in how studies were mapped and described due to variation in the type and detail of information reported in abstracts. Examples include a procedure described only as 'endoscopic gastroplasty' with no details given on the device used, or the positioning of sutures or staples, which meant this study could not be grouped with studies that had a more definitive description, for example ESG. Another example is a comparator described in the abstract as 'no treatment', which may have included LSI; this study would then not have been grouped with other studies with a LSI comparator. LSI is an assumed component of any obesity management but may be under-represented in the evidence map. Lack of detail reported in the abstract may also have led to under-representation of populations having weight regain or needing WL as a bridge to surgery.

Multiple reporting of the same study (e.g. in conference abstracts, at different time points, for different outcomes or subgroups) was common and not always easy to identify. A consequence is that the map might suggest there is more evidence than actually exists for some intervention–comparator combinations; however, the details in the map would facilitate assigning records to individual studies in such cases.

Study features were highlighted where these were deemed noteworthy, for example a population that differed from a 'standard' obese population (e.g. where all had a specific comorbidity) or an outcome that was not commonly reported.

Strengths/weaknesses of studies included in the evidence map

Most studies (73%) were single-arm studies which are not useful for establishing relative effectiveness of different interventions. However, there were also 140 records of RCTs and 271 records of studies with a comparator arm, which could potentially provide more robust evidence.

Implications for stakeholders (clinicians, policy-makers, patient and public involvement)

The evidence map is a repository of endoscopic studies that can be searched according to population, intervention, comparators, sample size and length of follow-up. The evidence map could be used for the scoping part of any planned research and is a starting point for any stakeholders wishing to use this information to undertake further evaluations of the evidence. The map can also be searched to find evidence to inform model parameters of any future models on any endoscopic treatments.

Unanswered questions and future research

The evidence map has notable value in determining where evidence gaps exist with regard to primary studies and also to determine the feasibility for and resource allocation to future evidence synthesis. As already mentioned above, for some endoscopic treatments there was a lack of evidence and/or the need for more robust study designs. Despite the large volume of RCTs identified, there were none directly comparing the interventions evaluated in the economic modelling (see *Chapter 5*).

Furthermore, one of the issues identified was the far more extensive and diverse volume of evidence than expected by all parties to this project, which made untenable the originally proposed evidence synthesis plans. This indicates that there is a need and scope for prioritisation of targeted evidence syntheses to inform defined use of specific interventions in delineated obese populations.

Chapter 4 A review of cost-effectiveness evidence for the management of obesity using endoscopic therapy

Introduction

People with obesity have an increased incidence of stroke, respiratory disease, CVD and T2D, among many others. This not only strains healthcare systems but also reduces the quality and length of life.[73,74] The latest clinical guideline[36] from the NICE underscores the use of semaglutide for weight management, specifically recommending it for a maximum of 2 years in adults with a BMI of at least 35.0 kg/m^2 and at least one weight-related comorbidity or adults with a BMI of between 30 and 34.9 kg/m^2 and who meet the criteria for referral to weight management services.[36]

For adults with a BMI of 40, or between 35 and 39.9 with a significant health condition, bariatric surgical assessment is recommended but access to surgery in the UK is limited by healthcare capacity constraints and associated obesity stigma.[75] Recently, endoscopic therapies have been considered as an alternative treatment option, as they offer the benefits of being minimally invasive, less expensive and involve a lot less time in hospital.[76] However, there is a lack of robust evidence on the cost-effectiveness of endoscopic therapy, compared to the alternative options for obesity treatment.

In this chapter, a review of the existing health economics literature on the use of endoscopic therapy for adults with obesity is presented. The aim of the systematic review was to identify and narratively synthesise existing economic evidence for endoscopic therapy for the management of patients with obesity and to assess the methodological quality of this evidence.

Methods

The protocol is registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (reference number: CRD 42022302942).[70]

Search strategies

The broad searches used to identify effectiveness studies for the evidence map (see *Chapter 3*) were also used to identify the model-based economic evaluations for this review. This was possible as the searches only used terms for obesity and endoscopic interventions and searched MEDLINE and EMBASE.

The reference lists of key articles were checked to identify additional studies.

Inclusion and exclusion criteria and screening

During screening of titles and abstracts for the evidence map, records were tagged if they contained any reference to economic aspects of endoscopic therapies, for example mention of costs, economic evaluation, analysis or modelling, or economic-related outcomes [e.g. quality-adjusted life-years (QALYs) or disability-adjusted life-years (DALYs)].

Full text of relevant tagged articles was obtained and assessed for inclusion according to the following criteria:

Population – Individuals of any age living with obesity, and with or without obesity-related comorbidities.
Intervention – Any endoscopic therapy for the management of obesity.
Comparator – any.
Outcomes – Any economic-related outcome, for example QoL, QALYs, DALYs, cost or incremental cost-effectiveness ratios (ICERs) and net monetary benefit.
Study *design*: trial-based or model-based economic evaluations comparing the costs and outcomes gained from two or more obesity treatments where at least one was an endoscopic therapy; *Publication status* – fully published.

All stages of study selection were undertaken independently by two reviewers with any disagreements resolved by consensus and, if required, involvement of a third reviewer.

Quality criteria

The quality of the included economic evaluations was assessed using the Philips checklist for model-based studies,[77] and the Consensus on Health Economic Criteria tool was applied to any included trial-based studies.[78]

Data extraction

For all included studies, data were extracted by a single reviewer into a pre-specified data extraction form and independently checked for completeness and accuracy by a second reviewer. The information extracted on the study context included the authors, year of publication, country and setting, study population, interventions and comparators, the methods for economic evaluation CEA, cost–utility analysis (CUA), cost–benefit analysis (CBA) or cost–consequence analysis, and, where relevant, methodological detail on the type of model design used (model structure), range of health states, time horizon, study perspective, currency/price year and sources for the model inputs relating to treatment efficacy, patient transition parameters, resource use, outcome measures [QALYs, life-years gained (LYG)] and details of uncertainty analysis undertaken.

Analysis

A narrative synthesis of the included studies was carried out to assess the purpose, perspective, approach, methods (including types of costs and resources incorporated) and outcomes, applied within the economic evaluation, and if relevant an analysis of model structures, time horizons, cycle lengths and parameter inputs.

Results

From the search results for the evidence map, 112 potentially relevant records were identified by title and abstract screening.

Ten articles were identified as relevant and full text was retrieved. Eight studies were excluded as these either were available only as conference abstracts or were commentary articles (see *Appendix 3*, *Table 103*). One additional relevant study was identified through hand-searching reference lists. The selection process is outlined in *Figure 3*.

Full review of included studies

The characteristics of the three included studies are summarised in *Table 8*. One study was conducted in the UK,[79] and the remaining two studies conducted by the same authors were carried out in the USA[80] and Canada,[81] respectively.

Modelling methods and parameters

Model structure

Kelly *et al.*[79] used a state transition (Markov) model, while Mital and Nguyen[81] used a Markov model with a cohort simulation. In contrast, Mital and Nguyen[80] used a Markov model with individual-level microsimulation. All the Markov models used a lifetime horizon as the base case with shorter time horizons explored as part of the sensitivity analyses.

The models by Mital and Nguyen included four BMI health states: no obesity (BMI ≤ 30 kg/m^2), class 1 obesity (BMI 30–34.9 kg/m^2), class 2 obesity (BMI 35–39.9 kg/m^2) and class 3 obesity (BMI ≥ 40 kg/m^2).[80,81] Kelly *et al.*[79] used similar BMI health states with an additional health state specified as 'no obesity' comprising overweight (BMI 25.0–29.9 kg/m^2) and healthy weight (BMI 18.5–24.9 kg/m^2).

The cycle lengths in the models varied based on the treatment options under comparison. Mital and Nguyen[80] utilised a 4-month cycle to align with the duration of a swallowable IGB treatment episode, while Mital and Nguyen[81] used a 12-month cycle length for aspiration therapy. For ESG, Kelly *et al.*[79] used a 6-month cycle length for the first year, reflecting the immediate WL associated with ESG, and switched to a 12-month cycle thereafter.

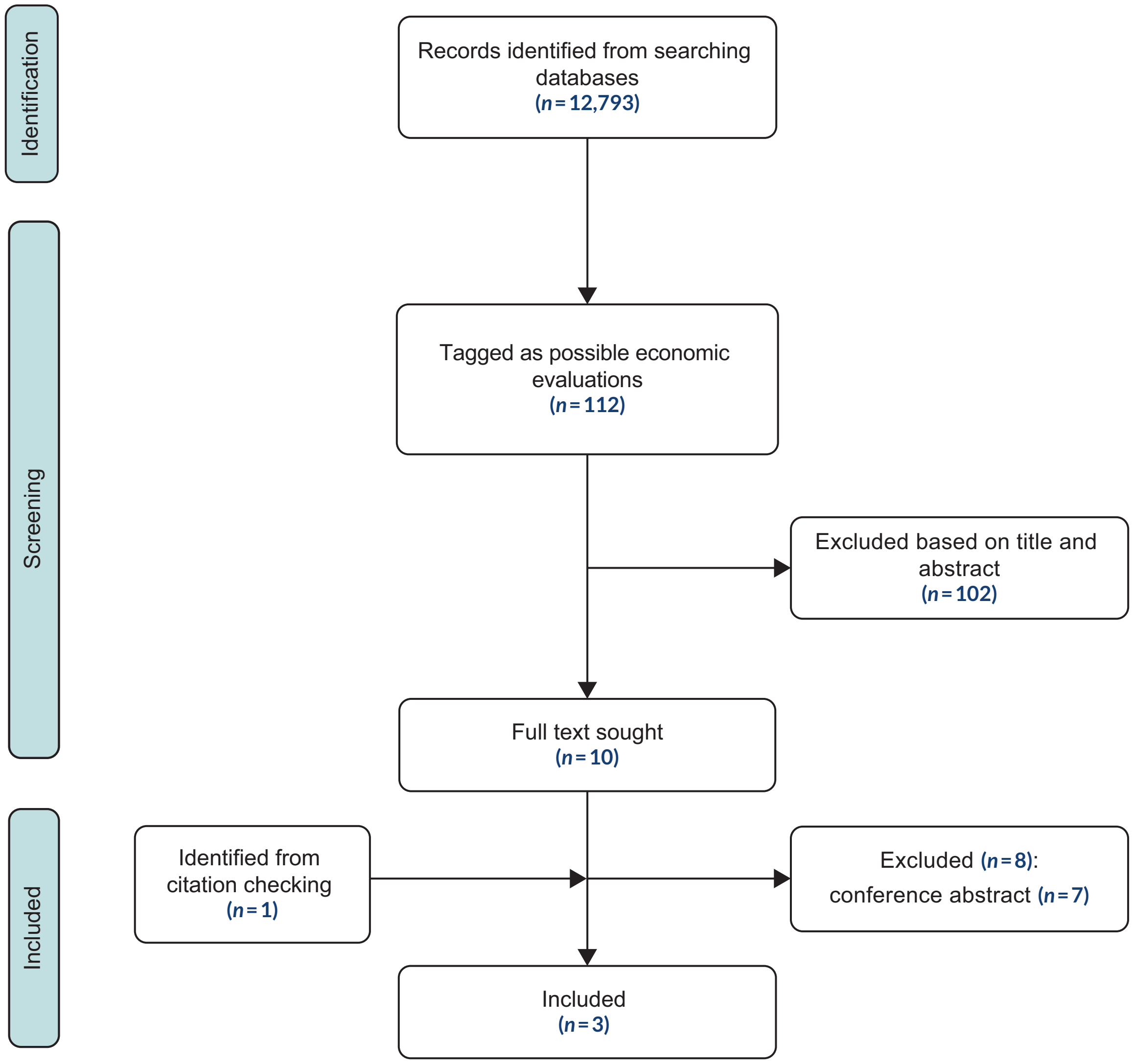

FIGURE 3 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for review of cost-effectiveness.

Resource use and costs

All the studies reported direct medical costs such as the intervention/device cost, follow-up visits and medications (*Table 9*). Across all three studies, a standard discount rate of 3.5% was applied to costs.

In Kelly *et al.*'s[79] analysis, intervention costs for ESG, management of AEs and treatment of obesity-related comorbidities were considered. In their model,[79] the ESG costs were estimated based on the device and hospital costs associated with the delivery of the procedure. Costs related to lifestyle management were applied to both treatment arms.

Within the Mital and Nguyen[80] swallowable IGB model, the costs covered the intervention, follow-up care, general BMI-specific health care and treatment of complications. Swallowable IGB costs were assumed to include the device, six physician visits, an abdominal X-ray for balloon placement confirmation, and medications.[83]

The Mital and Nguyen (2019)[81] model incorporated both short-term and long-term procedure-specific costs for each comparator, along with annual general healthcare costs specific to BMI health states. Procedure-related costs included initial surgery, follow-up visits, device replacement (for aspiration therapy), management of complications and treatment discontinuation (if applicable). For patients discontinuing aspiration therapy, additional costs for the reversal procedure were considered.

TABLE 8 Characteristics of included studies for review of cost-effectiveness

#	Author, year, country	Study population (obesity definition/eligibility)	Interventions	Health states/ diseases modelled	EE type/model type	Time horizon	Cycle length	Perspective	Benefit measure
1	Mital and Nguyen, 2019,[81] Canada	Adults aged 22–74 years with a BMI of 35–55 kg/m^2	Aspiration therapy vs. bariatric surgery (gastric bypass and sleeve gastrectomy) and no treatment	4 BMI health states; no obesity, obesity 1, obesity 2, obesity 3	CUA/Markov	Lifetime	12 months	Health system	QALY
2	Mital and Nguyen, 2021,[80] USA	10,000 adults aged 18–64 years with Class 2 or Class 3 (i.e. BMI ≥ 35 kg/m^2) and no contraindications for swallowable IGB	Swallowable IGB, gastric bypass, sleeve gastrectomy as stand-alone treatment; swallowable IGB as a bridge to gastric bypass, swallowable IGB as a bridge to sleeve gastrectomy vs. no WL treatment	4 BMI health states: no obesity (BMI ≤ 30 kg/m^2), class, 1 obesity (BMI 30–34.9 kg/m^2), class 2 obesity (BMI 35–39.9 kg/m^2), class 3 obesity (BMI ≥ 40 kg/m^2)	CUA/individual Markov microsimulation model	Lifetime	4 months	Health system	QALY
3	Kelly *et al.*, 2023,[79] UK	Adults with class 2 obesity aged 20–64 years	ESG vs. LSI	5 BMI health states: states: health weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25.0–29.9 kg/m^2), class, 1 obesity (BMI 30–34.9 kg/m^2), class 2 obesity (BMI 35–39.9 kg/m^2), class 3 obesity (BMI≥ 40 kg/m^2)	CUA/Markov	Lifetime	6 months for the first year, 12 months thereafter	NHS and NHS/PSS	QALY

DOI: 10.3310/PWKQ2310

TABLE 9 Costs from the included studies

#	Study	Cost category	Resource use	Source	Assumptions
1	Kelly 2023[79]	Direct Medical	ESG Device Hospital costs associated with the delivery of the procedure. LM Healthcare professional visits (general practitioner, nurse, dietitian, specialist, clinical psychologist and blood count) Management of AEs, Treatment of obesity-related comorbidities	Personal Social Services Research Unit 2021-unit costs NHS England 2020–1 reference costs	'*As the model does not capture subsequent obesity treatment costs (e.g. bariatric procedures for eligible patients in whom treatment does not result in adequate or durable weight loss), LM costs were assumed to be incurred in both treatment groups for the duration of the model horizon* *Although it is expected that a proportion of patients will not be compliant with LM medical advice about lifestyle and dietary changes throughout the intervention, a 100% compliance rate was assumed in the absence of robust data* ...' (Kelly *et al.*, 2023, p. 1166)[82]
2	Mital and Nguyen 2021[80]	Direct Medical	Swallowable IGB: Device, 6 physician visits, abdominal X-ray and medications Bariatric surgery: Procedure, Follow-up visits (5 visits in year 1, 3 visits in year 2 and 2 visits year 3 onwards for gastric bypass and 5 visits in year 1, 2 visits in year 2 and 1 visit year 3 onwards for sleeve gastrectomy[25]), dietary supplementation General BMI-specific health care Treatment of complications	Published literature	No cost assumptions
3	Mital and Nguyen 2019[81]	Direct Medical	Initial procedure Procedure reversal (for patients who discontinue aspiration therapy) Device Follow-up Dietary supplements Complications Annual BMI-specific health care	Published literature	The assumed cost of managing complications linked to sleeve gastrectomy aligns with that of gastric bypass. Minor complications resulting from aspiration therapy were addressed using oral antibiotics or analgesics, and the associated drug cost was estimated at US$50. Individuals discontinuing aspiration therapy incurred additional expenses for the reversal procedure. Lastly, each patient encountered average annual healthcare costs tailored to their specific BMI category

Note
Exchange rate of 1 US$ = 0.75 GBP, as of 25 April 2025.

Kelly *et al.*[79] compared ESG with LSI. Mital and Nguyen[81] focused their study on aspiration therapy compared to bariatric surgery and Mital and Nguyen[80] assessed swallowable IGB as a stand-alone, and as a bridge to bariatric surgery, specifically gastric bypass and sleeve gastrectomy.

All three studies modelled adult patients aged between 18 and 75 years. In their baseline population, Kelly *et al*.[79] focused on individuals with class 2 obesity (defined as BMI 35–39.9 kg/m^2). The models by Mital and Nguyen[80,81] used a starting population of patients with a BMI of ≥ 35 kg/m^2, and up to 55 kg/m^2 when the comparator arm was aspiration therapy as this is only approved for patients with a BMI within this range. All three studies conducted a CUA and adopted a health service perspective.

In general, different treatment options were assessed, using a range of methodologies, which reduce the level of comparability across the studies. The following sections describe the findings and provide a summary of the methods used.

Health outcomes

Kelly *et al*.[79] used EuroQol-5 Dimensions (EQ-5D) data to measure health-related quality of life. For the class II obesity state, the EQ-5D data were mapped using a published algorithm[84] from 36-Item Short Form Survey (SF-36) data obtained from the MERIT study.[85] For the other obesity health states within the model (obesity I and obesity III), these utility values were informed by a large UK population-based cohort study;[82] thereby a linear mixed-effect model was used to derive the incremental disutility associated with increasing BMI, applied to the overweight health state utility value, to derive the utility values for the obesity I and obesity III health states. Disutilities were also incorporated for ESG-related AEs, such as abdominal abscesses, upper gastrointestinal bleeds and malnutrition. Since the procedure was one-off, these disutilities were applied only in the first cycle of the model. To prevent double counting, comorbidity-associated disutility was assumed to be already encompassed in the BMI-based health state utility values.

The model by Mital and Nguyen[80] used age and BMI-specific utility values obtained from a published study[86] that estimated EQ-5D scores using data from the US Medical Expenditure Panel Survey. These utility values were combined with decrements related to the intervention and its complications. Following existing literature, it was assumed that bariatric surgery and its major complications resulted in a utility decrement lasting for 6 weeks, while minor complications led to a 4-week decrement.[87] Considering the less invasive nature of swallowable IGB and its milder complications compared to bariatric surgery, the authors assumed that the utility decrement from balloon placement was half that of bariatric surgery, lasting only 1 week. Additionally, utility decrements from complications of swallowable IGB were assumed to be half those of bariatric surgery, with a major complication causing a decrement lasting 4 weeks and a minor complication causing a decrement lasting 1 week.

Mital and Nguyen[81] applied the same age and BMI-specific utility values used by Alsumali *et al*,.[86] Disutility resulting from the procedures and their complications was also considered, although limited detail was provided within the paper on how this was done.

Measures of effectiveness and sources of clinical evidence

With respect to the effectiveness measures (*Table 10*), Kelly *et al.*[79] used a change in BMI as the main effect outcome. Patients transitioned within the model depending on changes to weight measured using BMI. To calculate the transition probabilities, the authors used patient-level data from the MERIT study[85] for the first 2 years of the model time horizon, and then applied assumptions to extrapolate transition probabilities for beyond 2 years. The authors assumed that the WL would plateau after 2 years for 80% of the patients receiving ESG and for the remaining 20%, they assumed weight regain returning to baseline BMI after 5 years.[79] That assumption was informed by a published review for weight regain following bariatric surgery.[88] For all patients on lifestyle management, weight regain was assumed to return to baseline BMI by 5 years.

Mital and Nguyen[81] used the total percentage WL, and Mital and Nguyen[80] used the percentage of EWL. These effectiveness measures were drawn from various sources. For Mital and Nguyen,[80] WL data for swallowable IGB treatment were derived from a global multicentre study involving 1770 patients.[83] Additionally, information on WL after bariatric surgery was obtained from a published CEA.[86] In the case of Mital and Nguyen's[81] model on aspiration therapy,

DOI: 10.3310/PWKQ2310

TABLE 10 Additional information on selected studies

#	Author, year, country	Primary clinical treatment effects modelled/assessed	Level and source of effectiveness evidence	Uncertainty	Model validation	Currency base	Discount rate	ICER/QALY	WTP threshold
1	Kelly *et al.*, 2023,[79] UK	Change in BMI	RCT	One-way DSA and PSA	Structural validation	2020–1 GBP	3.50%	ESG is highly cost-effective, compared with LM alone for treating adults with class II obesity. The base-case ICER was £2453/QALY gained	£20,000/QALY
2	Mital and Nguyen, 2021,[80] USA	% Total WL	A multicentre study of 1770 patients; and previous CE studies	DSA and PSA	No formal validation reported	2020 US$	3.50%	Of the six strategies, swallowable IGB as a bridge to sleeve gastrectomy most cost-effective with an ICER of $3781 per QALY gained. Swallowable IGB alone vs. no treatment: $21,711 per QALY gained	$100,000/QALY
3	Mital and Nguyen, 2019,[81] Canada	% Excess WL	A multicentre study and meta-analysis	DSA and PSA	No formal validation reported	2017 US$	3.5%	Aspiration therapy vs. no treatment: ICER of US$17,532 per QALY gained	$100,000/QALY

WTP, willingness to pay.

Note
Exchange rate of 1 US$ = 0.75 GBP, as of 25 April 2025.

WL effects were available for the initial 4 years post treatment from a multicentre European registry study involving 200 patients,[89] and annual WL estimates for the comparators (gastric bypass and sleeve gastrectomy) were sourced from a meta-analysis.[90]

Adverse events, complications and risk of mortality

The three studies included AEs[79] or complications[80,81] and all included mortality risks.

In Kelly *et al.*'s[79] study, three AEs associated with ESG were incorporated: abdominal abscess, upper gastrointestinal bleed and malnutrition. The frequency of SAEs reported in the MERIT study[85] informed these considerations. Mortality risk was calculated by applying BMI-specific hazard ratios obtained from the literature[15] applied to all-cause mortality rates from the UK general population data provided by the Office for National Statistics (ONS).[91]

For the Mital and Nguyen[80] model, patients treated with swallowable IGB faced the risk of treatment complications (early deflation/expulsion, major and minor complications), and patients who underwent bariatric surgery faced a risk of surgery-related mortality as well as short- and long-term complications.

In the aspiration therapy model by Mital and Nguyen,[81] both short- and long-term complications were considered using information obtained from the literature. Furthermore, patients undergoing bariatric surgery faced a risk of perioperative and postoperative mortality;[90] no treatment-related risk of mortality was applied to aspiration therapy.

Both the swallowable IGB model in Mital and Nguyen[80] and the aspiration therapy model in Mital and Nguyen[81] incorporated age and BMI-specific mortality risks. These risks were derived by inflating age-specific mortality risks from US life tables with BMI-specific hazard ratios that varied by age.[92]

Main findings of the studies

The three studies assessed cost-effectiveness using QALYs gained, as outlined in *Table 10*. Cost-effectiveness was measured using different willingness-to-pay (WTP) thresholds. Kelly *et al.*[79] applied the UK WTP threshold of £20,000/QALY and Mital and Nguyen[80,81] used WTP values for the US health system by applying the 'conventional' WTP threshold of $100,000 per QALY.

In the ESG model, Kelly *et al.*[79] found that ESG was £3024 more costly when compared to lifestyle management and resulted in an additional LYG of 0.31 and a gain of 1.23 QALYs. The reported ICER for ESG versus lifestyle management was £2453 per QALY gained and the authors concluded that ESG is a highly cost-effective option when compared to lifestyle management for patients with class II obesity in England.

For the swallowable IGB model, Mital and Nguyen[80] identified that, among the six strategies evaluated, swallowable IGB as a bridge to sleeve gastrectomy was the most cost-effective, with an ICER of $3781 per QALY gained. While swallowable IGB alone was not cost-effective compared to bariatric surgery, it proved cost-effective compared to no treatment, with an ICER reported at US$21,711 (£16,283.25) (exchange rate of 1 US$ = 0.75 GBP, as of 25 April 2025) per QALY gained.

In the aspiration therapy model, Mital and Nguyen[81] found that despite being a cheaper procedure than bariatric surgery, aspiration therapy incurred higher long-term costs due to maintenance expenses (periodic replacement of device parts), with an additional cost of $5318. Aspiration therapy also resulted in lower QALYs compared to bariatric surgery due to its smaller WL effects, reporting 1.31 fewer QALYs. Consequently, aspiration therapy was dominated by bariatric surgery. However, when compared to no treatment, aspiration therapy was considered cost-effective, with an ICER reported at US$17,532 (£13,149) (exchange rate of 1 US$ = 0.75 GBP, as of 25 April 2025) per QALY gained.

Uncertainty

Sensitivity analyses were conducted to address the uncertainty around the model parameters and examine the robustness of results to changes in parameters. The three studies conducted a series of deterministic sensitivity analyses (DSAs) on costs and duration of benefits and probabilistic sensitivity analyses. For all three studies, the results of the sensitivity analyses showed that the base-case analysis was largely insensitive to changes in the model parameters considered.

Risk-of-bias assessment

The assessment of the quality of the model-based economic evaluations was conducted using the Philips Criteria,[77] detailed in *Appendix 3*, *Table 104*. In general, the studies met most of the criteria, although some notable issues were identified. Firstly, none of the studies adequately stated or justified the scope of their models. Some model parameters lacked sufficient explanation for the applied assumptions. Additionally, when selecting data sources for specific model parameters, the rationale for the choices made was not appropriately justified. Furthermore, none of the studies addressed heterogeneity by running the model separately for different subgroups. It is worth noting that Kelly *et al.*[79] in the ESG model, justified the inability to perform subgroup analyses due to the small sample size.

Limitations of the included studies

The included studies acknowledged various limitations, primarily related to the absence of long-term WL data, the reliance on separate studies for intervention comparison due to a lack of data on direct comparison, the use of non-RCT data for WL effects, and the exclusion of some (dis-)utilities.

In the UK study by Kelly *et al.*[79] which conducted a cost–utility analyses based on data from the MERIT study, the extrapolation of long-term health effects beyond the trial duration introduced uncertainty. The authors addressed the lack of data on weight regain after ESG by assuming that 20% of patients returned to baseline weight after 5 years. Additionally, there were insufficient data from the MERIT study for estimating the utility values associated with both the healthy weight and overweight health state, and these had to be informed by an external study and generated using a mixed-effects model. The authors also noted insufficient data from the MERIT study for estimating obesity-related comorbidities and mortality rates.

Mital and Nguyen[80] reported limitations related to the availability of WL data specific to morbid obesity for swallowable IGB beyond a 4-month duration. Data reliance on a meta-analysis that included patients with mild to moderate obesity further contributed to model uncertainty. Mital and Nguyen[81] addressed the lack of long-term WL data for aspiration therapy by using 4- to 5-year post-treatment data for both aspiration therapy and bariatric surgeries in the base-case analysis and assumed that the BMI category remained constant thereafter.

In both the Mital and Nguyen studies (2021 and 2019),[80,81] non-RCT data were applied to estimate WL effects, as RCT data were either unavailable or limited in duration. Furthermore, according to Mital and Nguyen,[80] there was a lack of information from studies that directly compared swallowable IGB and bariatric surgery with respect to WL which meant these data had to be obtained from separate studies, introducing an additional layer of uncertainty. Finally, Mital and Nguyen[81] also noted a limitation in failing to capture any potential utility gain from aspiration therapy allowing patients to continue eating as before, although they note this would have been unlikely to affect their overall findings.

Discussion

Summary of findings

This chapter has presented a focused systematic review on the cost-effectiveness of endoscopic therapy for patients with obesity. The primary objective of the review was to identify and synthesise published evidence concerning the cost-effectiveness of endoscopic therapies for obesity. The overarching aim was to inform the development of an economic model that would assess the cost-effectiveness of endoscopic therapy in comparison to alternative obesity treatments, reported in *Chapter 5*.

Following the application of eligibility and screening criteria, only three studies were identified that were conducted within a UK, USA, or Canadian setting. All three studies were full economic evaluations conducted as cost–utility analyses, with primary outcomes reported in terms of costs per QALYs. The studies explored three endoscopic therapies, including ESG, swallowable IGB and aspiration therapy. These treatments were compared against LSI or bariatric surgery.

The collective findings of the studies suggest that endoscopic therapies were cost-effective when compared to lifestyle management or no treatment but were dominated when compared to bariatric surgery. However, a common and significant limitation across all the studies was the scarcity of long-term data on the effectiveness of endoscopic therapies, highlighting the need for further research in this area.

Strengths and weaknesses of the review

The review was carried out in accordance with a registered protocol (CRD42022302942) and adhered to reporting guidelines, for example PRISMA.[72] The comprehensiveness of the review is highlighted by the absence of restrictions on the database searches in terms of dates or languages. Two independent reviewers carried out the screening and study selection. Full publication of a study was required for it to be included as details on the methods, models, parameters and outcomes were required in order to be fully informative. Six records were excluded as these were only reported in brief abstracts. Two of these (which may be reporting the same trial-based evaluation) appeared undertaken in the UK and therefore may have a UK perspective (see *Appendix 3*, *Table 103*).

Strengths and weaknesses of the evidence

The three models identified were the first published papers to present evidence on the cost-effectiveness of different types of endoscopic therapy. Given the diversity of these endoscopic therapies, the heterogeneity of methods, and the variation in adopted WTP thresholds, it would be inappropriate to directly compare the cost-effectiveness outcomes. However, notable consistency emerged when comparing the interventions to no treatment in the USA and Canadian studies. The reported ICERs were US$21,711 (£16,283.25) (exchange rate of 1 US$ = 0.75 GBP, as of 25 April 2025) per QALY gained for swallowable IGB, and US$17,532 (£13149) (exchange rate of 1 US$ = 0.75 GBP, as of 25 April 2025) per QALY gained for aspiration therapy, whereas in the UK study, ESG compared to LSI yielded a much lower ICER of £2453 per QALY gained.

All identified studies noted several limitations, mainly associated with the lack of long-term WL data, the necessity to rely on separate studies for comparing interventions due to the absence of data for direct comparison, the utilisation of RCT data with limited follow-up for assessing WL effects, and the omission of certain utilities/QoL effects from the analysis.

Evidence in context

In the context of the decision problem for the models within this report, which involves assessing the cost-effectiveness of endoscopic therapies compared to other weight management interventions from the UK NHS perspective, the three identified papers proved valuable, offering insights into the model structure, health states, effectiveness and costs. Critical considerations included the model structures, health system settings, the type of endoscopic therapy assessed and the characteristics of the baseline model populations.

Given these aspects, the UK paper[79] was considered the most useful to inform the development of a new model because of the relevance of the setting and patient population. The other two papers[80,81] conducted within either a USA or Canadian healthcare setting, combined with the endoscopic therapies assessed (swallowable IGB and aspiration therapy), were deemed less relevant but still contained potentially useful data for the new economic model. Overall, the included studies demonstrate limited coverage of the available endoscopic therapies with economic analyses. Novel models to explore the cost-effectiveness of prioritised endoscopic therapies against current alternative therapies from the UK healthcare perspective are required to aid appropriate service-level decision-making on their use.

Implications for stakeholders/future research

The absence of long-term effectiveness data, as identified in this review, underscores the need for future studies to evaluate the cost-effectiveness of endoscopic therapies as more long-term WL data become available. This can be achieved through the conduct of longer-term, large-scale studies (randomised trials in the mid-term and cohort approaches beyond the feasible time from for the former), offering valuable insights into BMI-based health state transition probabilities, comorbidity rates, and potentially, mortality rates, which can be used to inform model parameters. Furthermore, across the included studies, none of the models considered pharmacotherapy as a WL treatment and given the recent recommendation by the UK NICE for semaglutide in obesity management.[36,93] there is a pressing need for cost-effectiveness evidence comparing endoscopic therapies with this new therapy.

Chapter 5 Economic model: assessment of the cost-effectiveness of endoscopic therapy compared to alternative weight management interventions

Introduction

The previous chapter presented a systematic review of the cost-effectiveness evidence available for endoscopic therapy for obesity and highlighted the limitations of the existing evidence base. The review concluded that due to the limited coverage of endoscopic therapies and comparator treatments, relevant to a UK setting, a new economic model was needed.

This chapter describes the development of three separate economic models designed to estimate the cost-effectiveness of endoscopic therapies compared to alternative weight management interventions for adult patients with obesity (BMI of > 30 kg/m^2). Given the number of endoscopic interventions potentially available (see *Chapter 3*) and the recent emergence of pharmacotherapy as an important category of WL therapy alongside bariatric surgery, it was considered that a single economic model would not be sufficiently informative as it could only consider a single intervention–comparator dyad. In consultation with the advisory group, it was decided that three separate models would be developed to encapsulate what were considered to be the three major decision problems relevant to a UK setting. These were to estimate the cost-effectiveness of:

model 1: ESG compared to LSG
model 2: ESG compared to semaglutide (Wegovy)
model 3: IGB compared to semaglutide (Wegovy).

The chapter first describes a purposive review to identify further data to inform the development of the models. It then describes why these treatments were chosen, the various stages of developing the models, along with the results of the base-case analyses and sensitivity analyses for each intervention.

Purposive literature review to inform the development of the model

Following on from the previous chapter, targeted literature searches were pragmatically undertaken to encompass treatments for obesity beyond endoscopic procedures, exploring options such as bariatric surgery and pharmacotherapy therapies that could serve as potential comparator treatments.

The additional searches aimed to identify relevant model structures that could be adapted to the decision problem, and to identify further sources for model parameters. These additional searches were undertaken up to September 2022 using economics databases, including EconLit (via EBSCOhost), CEA registry (via Tufts Medical Center website), and the NHS Economic Evaluation Database (NHS EED) (via CRD website) as well as MEDLINE. The search used terms related to costs, cost analysis, cost-effectiveness models, pharmacoeconomic or economic or price or cost, CBA or CEA or CUA or health utilities, Markov or Monte Carlo method. For practical reasons, and considering a similar search was conducted in a previous *Health Technology Assessment* report,[94] the search was restricted to studies published from 2010. For each relevant study, details were extracted on model types (model structure), the range of health states, time horizon, perspective, and sources for the model inputs related to treatment efficacy, patient transitions, resource use and outcome measures. Information on methods for the uncertainty analysis and model validation was also gathered.

After eliminating papers from non-Organisation for Economic Co-operation and Development countries and those focusing on patient populations with underlying illnesses such as liver disease and kidney disease, 20 studies were considered potentially suitable for supporting the development of the economic model, and these are summarised in *Appendix 4*, *Tables 105* and *106*.

Fifteen studies explored various aspects related to bariatric surgery, three focused on pharmacotherapy, and the remainder comprised a combination of both. State transition (Markov) models were predominately used across the studies, with cohort Markov models being the most common choice, while a few studies utilised individual-level microsimulation models. Despite the noted advantages of microsimulation models with being able to consider previous obesity-related disease history and related impact of comorbidities, the identified studies had adapted these models initially intended for diabetes, and therefore did not align with the focus of our model.

The time horizon across the studies ranged from 12 months to a lifetime, with bariatric surgery models extending towards the upper end of this range and pharmaceutical interventions towards the lower end – due to the scarcity of long-term data.

Development of the models

Model overview

State transition cohort Markov models were designed in Microsoft Excel 2018 to estimate the cost-effectiveness of endoscopic therapies compared to alternative weight management interventions for adult patients with obesity (BMI of > 30 kg/m^2). CUA was conducted based on the outcome of cost per QALY. The base-case analysis was from the perspective of the NHS and PSS over a 5-year time horizon. Costs and benefits were subjected to an annual discount rate of 3.5%, following the recommendation of NICE.[95] The methods and reporting of the economic evaluations are in keeping with the recommended guidelines.[96]

Methods

Selection of intervention and comparator treatments

The models conducted a comparison between endoscopic therapies and two alternative interventions, namely bariatric surgery and pharmacotherapy. Specifically, the endoscopic therapies considered in the models were ESG and IGB, chosen: (1) due to their prevalence in current endoscopic practices,[97,98] (2) on the level of evidence that exists for these procedures and (3) on advisory group input. For ESG versus IGB, no specific type of balloon was specified, instead the model assumed a generic type, that was assumed to be in place for 6 months.

Bariatric surgery was identified as a cost-effective treatment comparator and LSG as the most common type in current clinical practice[99] The UK NICE recommends bariatric surgery for patients with class III or severe obesity (BMI ≥ 40 kg/m^2 or BMI ≥ 35 kg/m^2 and one major medical comorbidity).[8]

Semaglutide was chosen as a comparator as it was recently approved by NICE, as a pharmacotherapeutic option for individuals with at least one weight-related comorbidity and a BMI of 35 kg/m^2, or a BMI ranging from 30.0 to 34.9 kg/m^2, provided they meet the criteria for referral to a specialist weight management service.[36] The recommended duration for this medication is a maximum of 2 years.

Based on the above, and after discussion with the advisory group, the three decision models included treatment comparisons using the BMI eligibility criteria as follows:

- *model 1*: For obesity class II and class III: ESG versus LSG
- *model 2*: For obesity class I and class II: ESG versus semaglutide (Wegovy)
- *model 3*: For obesity class I and class II: IGB versus semaglutide (Wegovy).

Model structure

For each model, a Markov model was chosen for its ability to simulate recurring outcomes over time, ideal for capturing the cyclical weight fluctuations inherent in patients with obesity. This model type also enables the projected impacts of weight regain following interventions. Furthermore, given that the benefits of WL manifest over several years, the Markov model was considered suitable for evaluating the long-term intervention costs and effects, ensuring the comprehensive capture of all associated benefits.

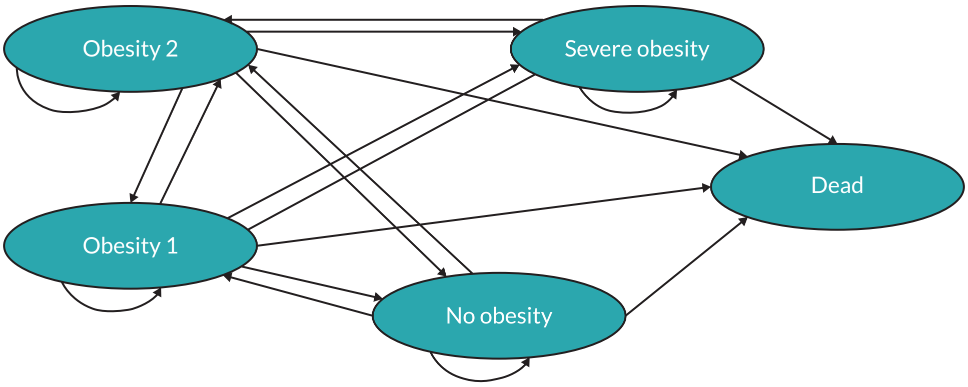

FIGURE 4 Model structure.

The Markov model (*Figure 4*) replicates the progression of patients living with obesity, with obesity categories reflective of their initial BMI, across mutually exclusive obesity-related health states following the interventions. The model is designed to capture health economic impacts of shifts in BMI, influenced by the percentage TBWL, and considers BMI-related comorbidities, costs and well-being impacts.

The model structure remained consistent across all interventions – ESG, IGB, LSG and semaglutide. Arrows indicate possible transitions between states. Patients can transition to 'dead' from any of the states. Following the intervention, the patients progress to one of four obesity health states:

- obesity class III (BMI ≥ 40 kg/m^2)
- obesity class II (BMI 35–39.9 kg/m^2) but without comorbidity
- obesity class I (BMI 30–34.9 kg/m^2)
- no obesity (BMI ≤ 30 kg/m^2).

Health states were linked to distinct treatment costs, utilities and mortality risks. A cycle length of 6 months was adopted for the first year, as it was deemed sufficient for patients to transition between health states. Thereafter, annual cycles were employed. Half-cycle corrections were applied to estimate state transitions occurring midway through each cycle. The model's time horizon was set at 5 years to adequately balance capturing variances in costs and effects among the four treatment options while reflecting widespread uncertainty on the WL trajectories beyond 5 years.

Model input data

Model parameters such as transition probabilities, utilities and resource use were informed by studies from within the evidence map, additional targeted searches for relevant studies and supplemented by clinical advice sought from our advisory group. All model parameters are summarised in *Table 11*.

Baseline population

As stated above, based on clinical advice and NICE guidance, the eligibility criteria for each treatment option were determined as follows:

- *model 1 (ESG vs. LSG)* – adults with obesity II and obesity III.[8]
- *model 2 (ESG vs. semaglutide) and model 3 (IGB vs. semaglutide)* – adults with obesity I and II, as per the NICE guidelines for semaglutide.[36]

Patients were allocated to baseline health states based on the BMI distribution of 35,000 randomly sampled patients extracted from data sourced from the Clinical Practice Research Datalink (CPRD) database as of July 2023.[108] The CPRD is an ongoing collection of anonymised electronic healthcare records from general practices in the UK, providing comprehensive information on patient demographics, symptoms, laboratory test results, diagnoses, treatments, health-related behaviours, and referrals to secondary care.[109] Individuals in the CPRD database are considered

TABLE 11 Model parameters and distributions

Parameter	Mean %	SE	Distribution	Source
Baseline characteristics	Mean	SE		
Age at the time of intervention	44	N/A	N/A	Review/clinical advice
% of females	87			Beran, 2022[100]
% of males	13			Beran, 2022[100]
Time horizon	5 years/lifetime	N/A	N/A	Review/clinical advice
Total number of cycles	6	N/A	N/A	Clinical advice
Discount rate costs	3.50%	N/A	N/A	NICE
Discount rate outcomes	3.50%	N/A	N/A	NICE
Baseline distribution (ESG vs. LSG)				
% with obesity III	0.3854	N/A	N/A	CPRD
% with obesity II	0.6146	N/A	N/A	CPRD
Baseline distribution (ESG vs. semaglutide, IGB vs. semaglutide)				
% with obesity II	0.2829	N/A	N/A	CPRD
% with obesity I	0.7069	N/A	N/A	CPRD

Parameter	Mean %	SE	Distribution	Source
Prevalence of comorbidities (rate)				
CHD (unstable angina/myocardial infarction): severe obesity	0.023	0.001	Beta (390.777, 16,599.527)	Haase *et al.*, 2020[101]
CHD: obesity 2	0.032	0.002	Beta (387.168, 11,711.832)	
CHD: obesity 1	0.040	0.002	Beta (383.960, 9215.040)	
CHD: no obesity	0.034	0.002	Beta (386.194, 10831.327)	
T2D: severe obesity	0.139	0.007	Beta (344.261, 2132.437)	
T2D: obesity 2	0.099	0.005	Beta (360.301, 3279.103)	
T2D: obesity 1	0.080	0.004	Beta (367.920, 4231.080)	
T2D: no obesity	0.038	0.002	Beta (384.635, 9653.680)	
Sleep apnoea: severe obesity	0.018	0.001	Beta (392.782, 21,428.440)	
Sleep apnoea: obesity 2	0.010	0.001	Beta (395.990, 39,203.010)	
Sleep apnoea: obesity 1	0.005	0.000	Beta (397.995, 79,201.005)	
Sleep apnoea: no obesity	0.005	0.000	Beta (397.995, 79,201.005)	
CVD (stroke/TIA): severe obesity	0.018	0.001	Beta (392.782, 21,428.440)	
CVD (stroke/TIA): obesity 2	0.020	0.001	Beta (391.980, 19,207.020)	
CVD (stroke/TIA): obesity 1	0.026	0.001	Beta (389.574, 14,594.041)	
CVD (stroke/TIA): no obesity	0.023	0.001	Beta (390.588, 16,249.830)	
Osteoarthritis: severe obesity	0.141	0.007	Beta (343.459, 2092.420)	
Osteoarthritis: obesity 2	0.131	0.007	Beta (347.469, 2304.966)	
Osteoarthritis: obesity 1	0.130	0.007	Beta (347.870, 2328.053)	
Osteoarthritis: no obesity	0.090	0.005	Beta (363.796, 3665.699)	
Mortality risks				
BMI-specific Mortality Hazard ratios (ONS)				
Severe obesity	1.880	0.030	Lognormal (0.631, 0.016)	Bhaskaran *et al.*, 2018[15]
Obesity 2	1.360	0.010	Lognormal (0.307, 0.007)	
Obesity 1	1.120	0.010	Lognormal (0.113, 0.009)	

continued

TABLE 11 Model parameters and distributions (*continued*)

Parameter	Mean %	SE	Distribution	Source
Utilities				
BMI specific utilities				
Severe obesity	0.610	0.040	Beta (90.089, 57.598)	Kelly *et al.*, 2023[79]
Obesity 2	0.700	0.030	Beta (162.633, 69.70)	
Obesity 1	0.780	0.030	Beta (147.940, 41.727)	
No obesity	0.827	0.020	Beta (295.271, 61.897)	
Intervention disutilities				
ESG	0.138	0.028	Beta (21.412, 133.747)	Based on the assumption that the surgical impact of ESG is 25% less severe than LSG
LSG	0.184	0.037	Beta (20.216, 89.654)	Sandhuet *al.*, 2023[102] and NICE semaglutide model 2023[36]
Semaglutide	0.037	0.013	Beta (7.801, 203.033)	Abramson *et al.*, 2019[103]
IGB	0.138	0.028	Beta (21.412, 133.747)	Assumed same as ESG
AEs disutilities				
ESG	0.140	0.028	Beta (21.360, 131.211)	Kelly *et al.*, 2023[79]
LSG	0.140	0.028	Beta (21.360, 131.211)	Assumed same as ESG
IGB	0.140	0.028	Beta (21.360, 131.211)	Assumed same as ESG
Semaglutide	0.050	0.010	Beta (23.700, 450.300)	NICE semaglutide model 2023[36]
SAEs incidence				
ESG	0.020	0.004	Beta (24.480, 1199.520)	Docimo *et al.*, 2023[104] (pooled estimate)
LSG	0.040	0.008	Beta (23.960, 575.040)	Beran *et al.*, 2022[100]
Semaglutide	0.049	0.010	Beta (23.726, 460.478)	NICE semaglutide model, 2022[36]
IGB	0.006	0.001	Beta (24.844, 4115.823)	Review and clinical advice
IGB mortality	0.001	0.0002	Beta (24.974, 24,949.026)	Singh, 2020[105]

Parameter	Mean %	SE	Distribution	Source
Costs				
Intervention costs				
ESG				
ESG procedure	4409	440.9	Normal (4409, 440.9)	Clinical advice
Total cost baseline-Y1	98.860	10	Normal (98.860, 10)	Clinical advice
Total cost Y1–Y2	45.240	4.524	Normal (45.240, 4.524)	Clinical advice
LSG				
LSG surgery	6963	696.3	Normal (6963,696.3)	NHS Cost Schedule 2021–2
Total cost baseline Y1	98.860	10	Normal (98.860, 10)	Clinical advice
Total cost Y1–Y2	45.240	4.524	Normal (45.240,4.524)	Clinical advice
Semaglutide				
Cost of semaglutide Y1	1926.480	192.648	Normal (1926.480, 192.648)	NICE semaglutide model[36]
Cost of semaglutide Y2	2285.4	228.540	Normal (2285.4, 228.540)	NICE semaglutide model[36]
IGB				
IGB procedure	4500	450	Normal (4500,450)	Clinical advice
Follow-up costY1–Y2 (4 visits to dietician)	45.240	4.524	Normal (45.240,4.524)	Clinical advice
Annual disease management costs				
T2DM	2290	458	Gamma (25,91.6)	Wang *et al.*, 2022[106]
CHD (MI and unstable angina)	1827.531	365.506	Gamma (25,73.101)	NHS cost 2021–2
Stroke/TIA	4094.229	818.846	Gamma (25,163.769)	NHS cost 2021–2
Sleep apnoea	717	143.4	Gamma (25,28.68)	NHS cost 2021–2
Osteoarthritis	1006.631	201.326	Gamma (25,40.265)	Galvain *et al.*, 2021[107]
AE cost				
ESG	1403	280.520	Gamma (25.014,56.088)	NHS cost 2021–2
LSG	1403	280.520	Gamma (25.014,56.088)	Assumed same as ESG
Semaglutide	154.888	30.978	Gamma (25,6.196)	NICE semaglutide model[36]
IGB	1403	280.6	Gamma (25,56.120)	Assumed same as ESG

CHD, coronary heart disease; SE, standard error; TIA, transient ischaemic attack.

DOI: 10.3310/PWKQ2310

representative of the general adult population of the UK in terms of age, sex and ethnicity.[101] It was assumed that the BMI distributions in the data align with the typical population eligible for endoscopic therapies for obesity, as outlined in the NICE guidelines.[8]

Data extracted from the CPRD[108] comprised individuals with a minimum of two out of three measurements – weight, height and BMI – extracted from the period between January 2017 and December 2019. In the base case, purposive sampling of eligible patients was performed such that 87% of the sampled individuals were female and the mean age was 44 years.[100] Samples were selected from CPRD data based upon the eligibility criteria for each treatment option. Average BMI for the baseline cohort was 40.3 (ranging from 35 to 87) for model 1, and 33.52 (ranging from 30 to 39.99) for models 2 and 3.

Transition probabilities

Appendix 4, *Table 108* presents the transition probabilities employed in each model. These probabilities were simulated semi-annually for the initial year (at 6 months and 12 months) and subsequently on an annual basis up to 5 years. To accurately capture the dynamics of WL and regain, the model required distinct transition probabilities for each intervention across different time periods. Given that the efficacy data from clinical studies often presented percentage WL or EWL, innovative approaches were used to convert the extracted efficacy data into transitions between BMI categories. The entire baseline population, sourced from the CPRD data, were simulated depending upon their eligibility for each intervention. Four separate simulations were undertaken, one for each of the interventions (ESG and IGB) and comparators (LSG and semaglutide). In each simulation, a distribution was placed around the efficacy parameters for WL and subsequent regain, and then randomly sampled for each eligible individual from the baseline population using Monte Carlo simulation. Due to likely individual correlation between WL and regain, each individual was assigned one random number for simulation over all time periods. Each sampled individual underwent a unique weight trajectory over time based on their initial height and weight, as well as the Monte Carlo simulated intervention efficacy, with the model continuously tracking their BMI category at each time point. The movement of these sampled patients between BMI categories in this manner provided the transition probabilities for each intervention and comparator in the model, effectively addressing the challenge of obtaining transition probabilities for BMI categories from WL data.

Effectiveness data

Data on effectiveness were acquired in terms of percentage total body weight loss (%TBWL) where available (shown in *Table 12*). Data on the effectiveness of ESG versus LSG up to 2 years was available from the evidence map (seven non-randomised controlled studies). Data on the effectiveness of ESG versus semaglutide and IGB versus semaglutide up to 12 months were generated from indirect comparison analysis (see *Appendix 2*, *Table 97*). Longer-term effectiveness data for all comparisons were sought from searching the evidence map for single-arm studies and additional targeted searches for relevant studies. For models 2 and 3, it was assumed that WL estimates derived in studies from all obesity classes (I–III) would be applicable to obesity I and II patients within the models. Where no relevant data could be found assumptions were based on clinical advice.

For ESG, in the absence of evidence on ESG versus LSG beyond 2 years, it was assumed that the rate of regain in years 2–3 found in a propensity score matched study of LSG patients[110] could be applied. The rate of change in weight regain from years 1 to 3 was then extrapolated into years 4 and 5.

For LSG, an analysis of one clinical trial with 5-year follow-up[111] was used to estimate the rates of long-term weight regain from years 2 to 5, this rate was then applied to the WL obtained from the clinical systematic review at the 2-year time point.

As the indirect comparison data for semaglutide and IGB only spanned 1 year, it was assumed for semaglutide that WL continued for the duration of treatment following Wilding *et al.*[112] and Lincoff *et al.*[114] Given the lack of evidence beyond the treatment duration of 2 years for semaglutide, expert clinical opinion obtained from the advisory group suggested that weight regain is likely to be rapid, occurring within the duration of the model time horizon. Accordingly, the model assumes that all previous weight is regained by 5 years. Given the critical absence of evidence, this assumption is rigorously tested within a sensitivity analysis.

TABLE 12 Effectiveness parameters for treatment options

Model time point (months)	Treatments			
	ESG (%)	LSG (%)	Semaglutide (%)	IGB (%)
6	15.2*	18.8*	13.05[a]	13.42[a]
12	19.1*	28.9*	18.56[a]	10.65[a]
24	16.4*	22.3*	19.06[b]	5.58[d]
36	14[+]	22.11[^]	12.71[c]	4.05[d]
48	11.9[~]	21.80[^]	6.35[c]	3.65[d]
60	9.97[~]	21.50[^]	0[c]	3.23[d]
	*Beran *et al.*, 2022[100]		[a]Indirect comparison with ESG	[a]Indirect comparison with ESG
	[+]Rate of regain years 2–3 taken from Alqhatani *et al.*, 2022[110]		[b]Assumed another 0.5% WL in second year, as Wilding *et al.*, 2022[112] showed increased WL from 52 to 68 weeks	[d]Kotzampassi, *et al.*, 2012 –Scaled their rate of weight regain years 1–5 to the weight lost at 12 months from indirect comparison[113]
	[~]Rate of change in regain years 1–3 assumed to continue years 3–5		[c]Rapid weight regain after ceasing treatment based upon clinical assumption	
	[^] Rate of regain years 2–5 taken from Wölnerhanssen *et al.*, 2021[111]			

For IGB, a 5-year cohort study followed up patients who had IGB, and percentage weight lost was obtained at 12, 24, and 60 months[113] and converted into percentage total weight lost for the purposes of our model. The annual rates of weight regain from the Kotzampassi study for years 1–5 were then scaled to the estimate of weight lost at 12 months from the indirect comparison from our clinical review.

Mortality risks

Mortality was estimated by applying BMI-specific mortality risks[15] to age- and sex-matched general population mortality rates for 2023, obtained from the ONS.[91] The assumption was made that these mortality risk ratios encompassed mortality attributable to BMI-related comorbidities, thereby negating the need to apply disease-specific mortality.

Comorbidities

The model only considered comorbidities associated with obesity that were deemed to have significant implications for healthcare costs and QoL, as identified by the WHO.[115] Focusing on comorbidities included within published obesity models,[36,79,102,107] and combined with expert clinical opinion, we selected five specific conditions: T2D, coronary heart disease (CHD) encompassing unstable angina and myocardial infarction, CVD including stroke and transient ischaemic attack, sleep apnoea and knee osteoarthritis.

The prevalence of these obesity-related comorbidities were derived from a previous study which explored the association between BMI and the risk of conditions related to obesity.[101] This study involved a cohort of 2.9 million individuals, sourced from a UK primary care database, specifically the CPRD.[101] The assumed prevalence rates of these comorbidities are shown in *Table 13*.

Adverse events

Adverse events were based on the most SAEs associated with each intervention. Following clinical advice, SAEs were defined as AEs that require hospitalisation. Due to lack of consistent data, and the minimal overall effect of cost and disutility of individual AEs, an aggregated approach was adopted to model the incidence rate, costs and disutilities associated with SAEs.

TABLE 13 Health state costs

Comorbidity (prevalence)	Comorbidity cost/year[a]	Total cost (£)
Severe obesity		588.85
T2DM (0.139)	318.28	
CHD (0.023)	42.03	
CVD (0.018)	73.70	
Sleep apnoea (0.018)	12.91	
Osteoarthritis (0.141)	141.94	
Obesity 2		506.10
T2DM (0.099)	226.69	
CHD (0.032)	58.48	
CVD (0.02)	81.88	
Sleep apnoea (0.01)	7.17	
Osteoarthritis (0.13)	131.87	
Obesity 1		497.18
T2DM (0.08)	183.19	
CHD (0.04)	73.10	
CVD (0.026)	106.45	
Sleep apnoea (0.005)	3.59	
Osteoarthritis (0.13)	130.86	
No obesity		341.32
T2DM (0.0383)	87.70	
CHD (0.0344)	62.92	
CVD (0.0235)	96.21	
Sleep apnoea (0.005)	3.59	
Osteoarthritis (0.0903)	90.90	

T2DM, type 2 diabetes mellitus.
a Annual management costs were estimated at £2290 for T2DM (Wang *et al.*, 2022),[106] £1828 for CHD (NHS cost 2021–2), £4094 for CVD (NHS cost 2021–2), £717 for Sleep Apnoea (NHS cost 2021–2), and £1007 for Osteoarthritis (Galvain *et al.*, 2021).[107]

Serious adverse event-related incidence rates are reported in *Table 11*. Model parameters and distributions. For ESG, the SAE incidence rates were derived from a previous review by Docimo *et al.*[104] and a pooled estimate of 2% was integrated into the model. Due to lack of consistent evidence, the SAE incidence rate for LSG was estimated using findings from a previous systematic review, which indicated a 0.51 lower risk of overall AEs (including non-severe) for ESG compared to LSG (Beran *et al.*, 2022).[100] Consequently, a SAE rate of 4% for LSG was incorporated into the model, with a much higher rate of SAEs tested in DSA (24% based upon clinical expert opinion).

The SAE rate of 0.6% for IGB was determined through a review of previous studies, including those conducted by Wiggins,[116] Ulgur,[117] Singh,[105] Saber[118] and Yorke,[119] and further informed by clinical advice.

As semaglutide is a pharmacological treatment it is expected that it would follow a different AE profile. Indeed, none of the studies on semaglutide defined any SAEs as requiring hospitalisation. Therefore, we followed the approach of the NICE model whereby SAEs were defined as gastrointestinal events and having an annual incidence of 4.9% (with accompanying lower disutility and costs than the SAEs for the surgical treatments).[36] This simplifying assumption was tested in DSA.

Intervention-related mortality rates were minimal for ESG, LSG and semaglutide; hence, they were assumed to be zero. In the case of IGB, a mortality rate of 0.1% was applied based on a systematic review by Singh *et al.* (2020).[105]

Utilities

Utilities corresponding to each BMI health state were obtained from the recent study conducted in the UK identified in *Chapter 4*, which examined the cost-effectiveness of ESG compared to LSIs.[79] In line with NICE technical guidance,[95] the study utilises a linear mixed-effects model to calculate the incremental disutility associated with increasing BMI health states for obesity I, II and III. These disutilities were then applied to BMI-specific utility values obtained from a previous study[82] to derive obesity health state utility values (see *Table 11*).

While the referenced paper[79] presented separate utilities for overweight and healthy weight BMI categories, our model included both utilities within the 'no obesity' health state. To address this distinction, we estimated weighted averages based on the distribution of patients in the CPRD who were either overweight or had a healthy weight. This approach was used to calculate the health state utility values for the 'no obesity' category at various time points. Consequently, for all interventions, patients in obesity I–III maintained their initial utility levels for the model's duration, whereas patients in the 'no obesity' category exhibited different utilities up to year 5.

As the Kelly *et al.*[79] study did not control for the independent impact of BMI-related comorbidities upon utility, to avoid double counting, it was assumed the disutility associated with each comorbidity was already captured within the BMI–health state utility values.

Utility decrements

The disutilities applied in the model represent the decrease in QoL associated with (1) the treatment, and (2) SAEs. The assumption was made that surgical interventions and SAEs would lead to a reduction in utility only during the first cycle (6 months), while semaglutide would cause a sustained utility loss throughout the treatment duration (2 years) but not after treatment is discontinued.

Treatment-related disutility

The disutility of LSG was −0.184, as obtained from previous studies.[36,102] The disutility associated with ESG was assumed to be slightly less (−0.138), based on the clinical assumption that the severity of the surgical effect from ESG is 25% less severe than that of LSG. The same disutility was also assumed for IGB. The treatment-related disutility applied to semaglutide was −0.037 as obtained from a previous CEA[103] with a higher value from Sandhu *et al.*,[102] tested in deterministic analysis.

Serious adverse event-related disutility

A uniform SAE-related disutility of 0.14 was applied to all surgical interventions. This disutility was determined by calculating the average of disutility values associated with the most common AEs, abdominal abscess and gastrointestinal bleeding resulting from these procedures. In the case of semaglutide, a disutility of −0.05, specifically related to gastrointestinal events, was applied throughout the entire treatment period in the model.[36]

Resource use and costs

The models incorporated the costs associated with the interventions (ESG and IGB), bariatric surgery, and semaglutide as well as the cost associated with each health state. SAE-related costs were also included in the model independent of the interventions. These costs were obtained from a variety of sources. All reported costs are in GBP prices for the year 2022–3, and a discount rate of 3.5% was applied to future costs and benefits.

ESG – The costs of ESG were assumed to be the cost of the device along with staff fees and follow-up costs. The total cost of ESG was assessed at £4409, guided by input from clinical experts within the study team. This cost includes the cost of the device (£2209 – inclusive of the device, suture, suture cinch, tissue helix and flexible endoscopic scissors) and the procedural cost (£2000 – covering fees for the surgeon, nurses and anaesthesia). Follow-up after an ESG procedure included a review by a specialist nurse (after 1 week), two visits to a surgeon (at 6 weeks and 1 year), and six visits to the dietitian (four in year 1 and two in year 2). These follow-up costs were applied to model 2 only. Within model 1, LSG was assumed to have the same follow-up protocol and so there would be no different in follow-up costs.

IGB – The cost of IGB includes the cost of the device, insertion, removal and surgeon/gastroenterologist fees estimated at £4500, plus the follow-up cost which included four visits to the dietician.

LSG – The cost of LSG was obtained from the NHS cost schedule as £6963 and included the cost of the device, preoperative assessment, surgeon/assistant time and anaesthetic. The follow-up costs of LSG were assumed to be the same as ESG.

Semaglutide – Semaglutide, marketed as Wegovy in the UK, is administered once weekly through subcutaneous injection using pre-filled pens. It is available in five different dose strengths. The recommended dosing regimen involves initiating the drug at 0.25 mg once a week and increasing the dose every 4 weeks until the maintenance dose of 2.4 mg is reached at 16 weeks. The breakdown of the dosing schedule and associated cost is as follows:

- Week 1–4: 0.25 mg per week – £73.25 for a pack of four pre-filled pens.
- Week 5–8: 0.5 mg per week – £73.25 for a pack of four pre-filled pens.
- Week 9–12: 1.0 mg per week – £73.25 for a pack of four pre-filled pens.
- Week 13–16: 1.7 mg per week – £124.53 for a pack of four pre-filled.
- Week 17–104: 2.4 mg per week (90 weeks) based on clinical advice, with a monthly cost of £175.

Health state costs

The cost of each health state was calculated as the product of the annual management cost of each comorbidity and the prevalence of the comorbidity (see *Table 13*).

Model assumptions

A range of assumptions were necessary for the model due to the limitations associated with available data and practical computational considerations. These assumptions include:

- Adverse events included in the model were assumed to be intervention-related one-off events likely to occur once following the intervention, hence the costs and disutility relating to the AEs were applied in the first model cycle (the first 6 months) only.
- However, for semaglutide (which involves continuous treatment for 2 years), it was assumed that any SAEs could occur more than once; therefore, the relevant disutility and associated costs were applied per cycle up to 2 years after which treatment was withdrawn (as per NICE guidelines).[36]
- For models 1 and 2 (ESG vs. LSG and ESG vs. semaglutide), it was assumed that rates of weight regain for patients who had ESG occurred at the same rate for years 4 and 5 as in years 2 and 3.
- For model 2 (ESG vs. semaglutide), mean %TBWL differences were obtained for ESG compared to semaglutide at 6 months and 12 months, from an indirect comparison of studies conducted by the team.
- Beyond 12 months, based on existing literature and clinical expert validation, it was assumed that following semaglutide treatment, patients maintained their WL until the end of the second year. Following expert advice, it was then assumed that all weight was regained in a linear fashion from the end of year 2 until year 5.
- Due to scarcity and inconsistencies in the existing data, coupled with the minimal sensitivity of the model to SAEs, an aggregate approach was followed to model SAEs. Using this approach, estimates for incident rates, and utilities, related to all SAEs were averaged and incorporated into the model.
- SAE-related disutilities were assumed to be the same for all surgical interventions, namely, ESG, LSG and IGB. This assumption was tested independently for each intervention in the sensitivity analyses.
- Health state utilities were assumed to be dependent on BMI. Consequently, it was assumed that utilities remained constant for each health state over time, aside from age adjustment.
- To avoid double counting, it was assumed that the disutility associated with each comorbidity was already captured in the BMI-related health-state utilities.

- Adverse events were assumed to incur disutility in the model.
- In addition, it was assumed that each intervention incurred treatment-related disutility for one cycle in the model, aside from semaglutide which occurred throughout the duration of treatment.
- The disutility of LSG was obtained from a previous study[36,102] as −0.184. Based on expert clinical advice that the surgical effect of ESG is 25% less severe than that of LSG, the disutility associated with ESG was assumed to be slightly less at −0.138.
- Comorbidity costs: Given the chronicity of the comorbidities, patients were assumed to incur literature-derived annual morbidity-specific treatment costs.
- Adverse event costs: Given the acuity of the AEs, patients with AEs were assumed to incur literature-derived one-off disease treatment costs per AE.
- Treatment-related mortality was assumed to be zero for ESG, LSG and semaglutide. For IGB, a mortality rate of 0.1% was applied.
- Mortality hazard risk ratios were calculated by applying BMI-specific all-cause mortality risks. It was assumed that these mortality risk ratios captured the mortality attributable to comorbidities; hence, we did not apply disease-specific mortality.

Outcomes and analyses

An incremental CUA provides information on the difference in costs and QALYs between the endoscopic interventions, bariatric surgery and pharmacological therapy in the models. The main outcomes are reported as cost per QALY gained as an ICER calculated as follows:

$$\textit{Incremental}\ \cos t\ \textit{per QALY} = \frac{\text{Cos}\,\textit{ts}\,(\textit{Endoscopictherapy}) - \text{Cos}\,\textit{ts}\,(\textit{Comparator})}{\textit{QALYs}\,(\textit{Endospcopic therapy}) - \textit{QALYs}\,(\textit{Comparator})}$$

According to NICE guidelines, an ICER below the threshold of £20,000 and £30,000 per QALY indicates that the health intervention is considered cost-effective in the UK. If an intervention is less costly and generates a higher number of QALYs, the intervention is dominant. All analyses were undertaken from the NHS/PSS perspective over a base-case time horizon of 5 years.

Sensitivity analyses

Uncertainty in the model parameters was explored by conducting probabilistic and various DSAs. Population heterogeneity was considered in relation to the severity of disease at baseline and was explored in a sensitivity analysis.

Probabilistic sensitivity analysis

A PSA assesses the parameter uncertainty by randomly varying the model parameters around pre-defined distributions.[120] The assigned distributions depend on the nature of the parameter, with the gamma (γ) distribution commonly used for costs, and the beta (β) distribution used for utilities and most other parameters, and the log-normal distributions used for ratio measures.[120] For the three models, the PSA involved running numerous simulations to recalculate the incremental costs and incremental QALYs, thereby generating a distribution around the estimated ICER. The distribution parameters that were used are shown in *Table 11*. Model parameters and distributions, and the distributions for the transitions between obesity states are given in *Appendix 4*, *Table 108*. Standard errors (SEs) were taken from original sources where possible; alphas and betas reflected original study sample sizes where possible. Where no measure of variance was provided by the original source, standard errors were commonly assumed to be 20% of the mean (aside from the costs of treatments which were set at 10% of the mean to reflect lower uncertainty regarding their cost).

In the models, the PSA comprised 10,000 simulations and results are presented using cost-effectiveness acceptability curves (CEAC) and cost-effectiveness planes. The CEACs were used to estimate the Bayesian probability of the intervention being cost-effective at various WTP thresholds. A PSA robustness check was performed to understand the potential impact of parameter uncertainty regarding WL estimates upon the cost-effectiveness probabilities. In this robustness check, confidence intervals for WL on each intervention were doubled and resulting beta distribution parameters halved to accentuate uncertainty. This was judged appropriate on the basis that the studies were not direct comparisons.

Deterministic sensitivity analysis

Due to the significant uncertainty in the published evidence, substantial DSAs were conducted to explore the sensitivity of the cost-effectiveness results to variations in specific input parameters and to identify the parameters with the greatest impact. Where evidence was available, input parameter values were varied based on upper and lower bounds from the literature or clinical advice. For all other variables, a variation of ± 20% and ± 10% were applied to the base-case value. The long-term transition probabilities were varied based on a pessimistic and an optimistic scenario informed by clinical advice. *Table 14* provides a list of the scenarios and model inputs explored within the DSAs.

The SAE rates for ESG and IGB were based on published studies indicating a 0–8% rate for ESG and 0.17–12.50% rate for IGB. Adjusting the base-case SAE rates according to these values enabled the uncertainty associated with the assumption of using pooled incidence estimates for various SAEs to be explored.

The sensitivity of the model results to the assumed utility decrements associated with the interventions, and the SAEs, was tested by varying the respective disutility values by 20% and 10% for each intervention. For semaglutide, a higher disutility value was used in the sensitivity analysis taken from Sandhu *et al.*[102]

The uncertainty associated with the cost parameters was explored in separate DSAs for each intervention, SAE-related and comorbidity costs. The base-case values for these costs were varied by 20% and 10%.

Regarding the model assumptions on long-term effects, a pessimistic and optimistic scenario was adopted in the sensitivity analysis based on clinical advice. The optimistic scenarios assumed a 50% lower rate of weight regain than in the base-case scenario. Pessimistic scenarios for ESG and LSG were based upon a linear rate of weight regain such that 0%TBWL was achieved at 5 years. As very little WL was sustained for IGB and semaglutide in the later years of the base-case model, when 5% less TBWL was assumed at years 3, 4 and 5 (compared to the base-case model), this led to some patients reaching a higher weight than baseline for both treatments at 5 years.

Other parameters explored in the DSA included the health-state utilities, CHD prevalence, and the class of obesity assumed for the starting/baseline population.

Following expert advice that semaglutide could be administered for 5 years in certain jurisdictions, a scenario analysis was performed where patients took semaglutide across the entire model time horizon. In this analysis, it was assumed that the WL at 2 years in *Table 12* (19.06%) was sustained to year 5, with the associated treatment-related costs, disutilities, and AEs also being applied throughout the 5-year model time horizon.

Results

The results of the CEA are presented separately for the base-case and the sensitivity analyses.

Base-case results

Base-case results are summarised in *Table 15*.

Model 1: Endoscopic sleeve gastroplasty versus laparoscopic sleeve gastrectomy

The base-case results for model 1 showed that LSG was more expensive than ESG at 5 years by £2400. The mean cost for LSG was approximately £8900 while for ESG was £6400. However, LSG also generated 0.230 more QALYs than ESG (3.50 QALYs compared to 3.27 QALYs from ESG) indicating that it is more effective.

The base-case ICER for model 1 showed that LSG had a cost of £10,593 per additional QALY when compared with ESG.

Model 2: Endoscopic sleeve gastroplasty versus semaglutide

The model 2 results showed that, compared to semaglutide, ESG was more expensive by £394 but also more effective as it generated 0.05 more QALYs than semaglutide.

The ICER indicates that ESG, when compared to semaglutide, is associated with £7267 per QALY gained.

DOI: 10.3310/PWKQ2310

TABLE 14 Deterministic (one-way) sensitivity analysis scenarios and inputs

Scenario	Parameter	Base case	Variation		Value source
			Lower value	Upper value	
1. Varying SAE incidence rates based on evidence and clinical advice					
	ESG-SAE rate	2%	0%	8%	Literature
	LSG-SAE rate	4%	0%	24%	Clinical advice
	IGB-SAE rate	0.6%	0.17%	12.50%	Literature
	Semaglutide- SAE rate	5%	4%	6%	Authors' approach (± 20%)
2a. Increasing/decreasing surgery disutilities by 20%					
	ESG disutility	−0.138	−0.166	−0.110	Authors' approach (± 20%)
	LSG disutility	−0.184	−0.221	−0.147	
	IGB disutility	−0.138	−0.166	−0.110	
2b. Increasing/decreasing surgery disutilities by 10%					
	ESG disutility	−0.138	−0.152	−0.124	Authors' approach (± 10%)
	LSG disutility	−0.184	−0.202	−0.166	
	IGB disutility	−0.138	−0.152	−0.124	
3. Applying a higher semaglutide disutility based on evidence					
	Semaglutide disutility	−0.037	−0.069	N/A	Sandhu *et al.*[102]
4a. Increasing/decreasing SAE disutilities by 20%					
	ESG/LSG/IGB- SAE disutility	−0.14	−0.168	−0.112	Authors' approach (± 20%)
	Semaglutide-SAE disutility	−0.05	−0.0600	−0.0400	
4b. Increasing/decreasing SAE disutilities by 10%					
	ESG/LSG/IGB- SAE disutility	−0.14	−0.154	−0.126	Authors' approach (± 10%)
	Semaglutide-SAE disutility	−0.05	−0.0550	−0.0450	
5a. Increasing/decreasing SAE costs by 20%					
	ESG/LSG/IGB- SAE costs	1403	1122.40	1683.60	Authors' approach (± 20%)
	Semaglutide- SAE costs	155	124.00	186.00	

continued

TABLE 14 Deterministic (one-way) sensitivity analysis scenarios and inputs (*continued*)

Scenario	Parameter	Base case	Variation		Value source
			Lower value	Upper value	
5b. Increasing/decreasing SAE costs by 10%					
	ESG/LSG/IGB- SAE costs	1403	1262.70	1543.30	Authors' approach (± 10%)
	Semaglutide- SAE costs	155	139.5	170.5	
6. Aligning CHD prevalence rate with disease severity to account for mortality bias in the literature					
	Disease-specific CHD rate	CHD-Ob III = 0.023; CHD-Ob II = 0.032	CHD-Ob III = 0.032; CHD-Ob II = 0.023		Literature
7a. Increasing/decreasing intervention costs by 20%					
	ESG cost	4409	3527.20	5290.80	Authors' approach (± 20%)
	LSG cost	6963	5570.40	8355.60	
	IGB cost	4500	3600.00	5400.00	
	Semaglutide cost	1926	1540.80	2311.20	
7b. Increasing/decreasing intervention costs by 10%					
	ESG cost	4409	3527.20	5290.80	Authors' approach (± 10%)
	LSG cost	6963	6266.70	7659.30	
	IGB cost	4500	4050.00	4950.00	
	Semaglutide cost	1926	1733.40	2118.60	
8. Varying the disease severity in the baseline population					
	Baseline distribution in model 1	Obesity III = 0.3854; Obesity II = 0.6146	Obesity III = 1	achObesity II = 1	Authors' approach
	Baseline distribution in model 2	Obesity I = 0.7171; Obesity II = 0.2829	Obesity II = 1	Obesity I = 1	
	Baseline distribution in model 3	Obesity II = 0.2829; Obesity I = 0.7171	Obesity II = 1	Obesity I = 1	
9a. Increasing/decreasing health state utilities by 20%					
	Obesity III	0.61	0.49	0.73	Authors' approach (± 20%)
	Obesity II	0.7	0.56	0.84	
	Obesity I	0.78	0.62	0.94	
	No obesity	0.8267	0.66	0.99	

Scenario	Parameter	Base case	Variation		
			Lower value	Upper value	Value source
9b. Increasing/decreasing health state utilities by 10%					
	Obesity III	0.61	0.55	0.67	Authors' approach (± 10%)
	Obesity II	0.7	0.63	0.77	
	Obesity I	0.78	0.70	0.86	
	No obesity	0.8267	0.74	0.91	
10a. Increasing/decreasing comorbidity costs by 20%					
			All comorbidity costs were reduced by 20%	All comorbidity costs were increased by 20%	Authors' approach (± 20%)
10b. Increasing/decreasing comorbidity costs by 10%					
			All comorbidity costs were reduced by 10%	All comorbidity costs were increased by 10%	Authors' approach (± 10%)
11. Varying long-term transition probabilities based on optimistic (upper value) and pessimistic (lower value) scenarios informed by clinical advice					
	ESG transition probabilities (vs. LSG)		Pessimistic scenario	Optimistic scenario	Clinical advice
	LSG transition probabilities (vs. ESG)				
	ESG transition probabilities (vs. semaglutide)				
	Semaglutide transition probabilities (vs. ESG)				
	Semaglutide transition probabilities (vs. IGB)				
	IGB transition probabilities (vs. Semaglutide)				

DOI: 10.3310/PWKQ2310

Health Technology Assessment 2025 Vol. 29 No. 68

TABLE 15 Summary of base-case results

Analysis	Cost (£)	QALY	ICER (£/QALY)
Model 1 (ESG vs. LSG)			
ESG	6425.10	3.2735	
LSG	8863.44	3.5037	
Difference	−2438	−0.2302	(LSG) 10,593
Model 2 (ESG vs. semaglutide)			
ESG	6223.58	3.5420	
Semaglutide	5829.35	3.4878	
Difference	394.23	0.0543	(ESG) 7267
Model 3 (IGB vs. semaglutide)			
IGB	6432.16	3.4385	
Semaglutide	5829.09	3.4878	
Difference	603.07	−0.0492	Semaglutide is dominant

Model 3: Intragastric balloon versus semaglutide

According to model 3, semaglutide was cheaper and more effective than IGB; hence, it is considered the dominant treatment option. The mean difference in costs between the two interventions was £603, and there were 0.0492 more QALYs generated by semaglutide at 5 years. This means that there is a cost-saving effect from administering the semaglutide therapy compared with IGB; however, the effect differences are very small.

The cost-effectiveness results are predominantly driven by the long-term weight trajectories of the population in each model, shown in *Table 16*. In model 1, a higher proportion of patients ended the model in the 'No obesity' state at 5 years when treated with LSG compared to ESG, whereas more patients in the ESG arm remained in the 'Severe obesity' state. This result is because ESG is associated with a higher rate of weight regain (and therefore higher BMI) than LSG. In model 2, at end of year 5, the semaglutide arm has more patients in the higher BMI health states (obesity III and obesity II) than ESG. While Model 3 reflects a more complex pattern with more patients in the no obesity state when treated with IGB after 5 years, but also more in the severe obesity state, this is reflective of the uncertainty within the estimates of treatment effect for IGB.

Scenario analysis models 2 and 3

When semaglutide was administered for 5 years instead of 2 years, this led to it being less cost-effective in both models (*Table 17*). For model 3, by altering the administration period from 2 to 5 years, semaglutide changed from being the dominant option in comparison to IGB, to not being cost-effective. This reduction in cost-effectiveness is driven by the increased costs over years 3–5 (£2285 per year), and while patients do experience a QALY improvement from sustaining the WL up to 5 years, this is offset by a considerable 0.037 disutility related to the ongoing treatment and weekly injections.

Deterministic (one-way) sensitivity analysis results

This section reports the results of a range of one-way DSAs. In most of the DSAs, the findings aligned with the base-case results. Detailed values of the ICERs for each DSA are presented in *Appendix 4*, *Table 107*.

The parameters that had the most impact on the base-case ICERs are presented below (*Table 18*) together with the tornado diagrams in *Figures 5* and *6* for models 1 and 2 which had non-dominance in the base-case results.

TABLE 16 Long-term weight trajectories in the models

	Model 1			Model 2			Model 3		
	Baseline	5th year (ESG)	5th year (LSG)	Baseline	5th year (ESG)	5th year (Sema)	Baseline	5th year (IGB)	5th year (Sema)
Obesity III	0.3854	0.2760	0.0622	0.000	0.0517	0.0769	0.0000	0.0963	0.0769
Obesity II	0.6146	0.2411	0.1060	0.283	0.1336	0.2586	0.2829	0.1925	0.2586
Obesity I	0.0000	0.2762	0.3767	0.717	0.2919	0.4445	0.7171	0.3387	0.4445
No obesity	0.0000	0.1962	0.4457	0.000	0.5142	0.2114	0.0000	0.3623	0.2114
Dead	0.0000	0.0104	0.0094	0.000	0.0086	0.0086	0.0000	0.0102	0.0086

TABLE 17 Scenario analysis for patients taking semaglutide for 5 years

Analysis	Cost (£)	QALY	ICER (£/QALY)
Model 2 (ESG vs. 5-year semaglutide)[a]			
ESG	6223.58	3.5420	
Semaglutide (5-year)	11,930.44	3.4934	
Diff	5706.89	0.0486	ESG dominant
Model 3 (IGB vs. 5-year semaglutide)[b]			
IGB	6432.32	3.4385	
Semaglutide (5-ear)	11,930.44	3.4934	
Difference			Semaglutide £100,147/QALY

a Model 2 base-case ESG £7267/QALY (+ 0.23/£2438).
b Model 3 base-case semaglutide dominant (−0.049/£603).

Model 1: None of the analyses within the DSA changed the treatment recommendation from model 1, indicating relative robustness in the model results to the uncertainty in the evidence base. It should be noted though that the pessimistic scenario for LSG long-term efficacy did lead to an ICER that was approaching an upper threshold limit of £30,000/QALY.

Model 2: For model 2, two model parameters explored within the DSA had the greatest impact on the treatment recommendation. The first one related to the cost of ESG. While the base case reported more QALYs at a higher cost for ESG versus semaglutide, the DSA showed that a 20% reduction in ESG intervention cost would lead to ESG being both cheaper and more effective than semaglutide, establishing its dominance. A similar result was found for a 10% reduction in ESG intervention costs. However, when the ESG costs increased by 20% (from baseline value) the ICER for ESG versus semaglutide increased to over the threshold £20,000/QALY. These results indicate the sensitivity of the model results to the assumed ESG cost. The other model parameter within the DSA that impacted the model results was for the most optimistic long-term scenario (50% lower rate of weight regain than in the base-case scenario) for semaglutide, as when this was explored, the ICER for ESG shifted to over £25,000/QALY.

Model 3: For model 3, only a 20% reduction in IGB intervention costs shifted the cost-effectiveness recommendation, with semaglutide losing its dominance and becoming more expensive than IGB with an ICER of £6030 per QALY gained.

Other parameters explored within the DSA related to restricting the treatment to patients within certain BMI groups. When this was done for model 1, and LSG and ESG were restricted to patients with higher levels of BMI (obesity III only), LSG became even more cost effective (lower ICER). For model 2, if ESG and semaglutide were restricted to treating patients with obesity class II only, then ESG remained cost-effective (but the ICER was increased). For model 3, semaglutide was still the dominant treatment option when both IGB and semaglutide were restricted to obesity class II patients only.

While the evidence for SAEs for all treatments was highly uncertain, with different definitions and effect sizes, the DSAs show that these parameters do not impact the results significantly (as the events are relatively rare).

Probabilistic sensitivity analysis results

For model 1, the PSA showed that at a WTP threshold of £20,000, LSG had a 99% probability of being cost-effective when compared to ESG (*Figure 7*). As shown by the cost-effectiveness plane in *Figure 8*, the majority of points resided in the northeast (NE) quadrant with sizeable QALY gains at a modest extra cost, indicating that LSG is cost-effective when compared to ESG. There was a low degree of uncertainty regarding the incremental QALY gain for LSG, reflective of the large size and number of studies from which efficacy data were drawn. Costs were more uncertain and demonstrated a larger degree of variability, although LSG was nearly always more expensive, reflective of the fact the treatment is more expensive than ESG.

DOI: 10.3310/PWKQ2310

TABLE 18 Deterministic sensitivity analysis leading to change in base-case cost-effectiveness

Scenario	ICER (cost per QALY)		Incremental differences	
	Base case	Sensitivity analysis	Base case	Sensitivity analysis
Model 3 (IGB vs. semaglutide)				
Decreasing IGB cost by 20% in model 3	Semaglutide dominant (negative ICER)	£6030.39	N/A	IC: −297 IE: −0.049
Model 2 (ESG vs. semaglutide)				
Decreasing ESG cost by 20% in model 2	£7267	ESG is dominant	IC: 394.24 IE: 0.054	N/A
Decreasing ESG cost by 10% in model 2	£7267	ESG is dominant	IC: 394.24 IE: 0.054	N/A
Increasing ESG cost by 20% in model 2	£7267	£23,521	IC: 394.24 IE: 0.054	IC: 1276 IE: 0.0543
Varying the long-term semaglutide transition probabilities based on the optimistic scenario in model 2	£7267	£26,299.03	IC: 394.24 IE: 0.054	IC: 457.2 IE: 0.0174
Obesity II as baseline population (model 2)	£7267	£11,972.20	IC: 394.24 IE: 0.054	IC: 413 IE: 0.0345
Model 1 (ESG vs. LSG)				
Varying the long-term LSG transition probabilities based on the pessimistic scenario in model 1	£10,593.27	£28,762.2	IC: 2424.41 IE:−0.230	IC: −2599.8 IE: −0.0904
Obesity III as baseline population (model 1)	£10,593.27	£8045.20	IC: 2424.41 IE:−0.230	IC: −2415 IE: −0.3001

Model 1: ESG vs. LSG;
Model 2: ESG vs. semaglutide
Model 3: IGB vs. semaglutide

IC, incremental costs; IE, incremental effectiveness (QALYs).

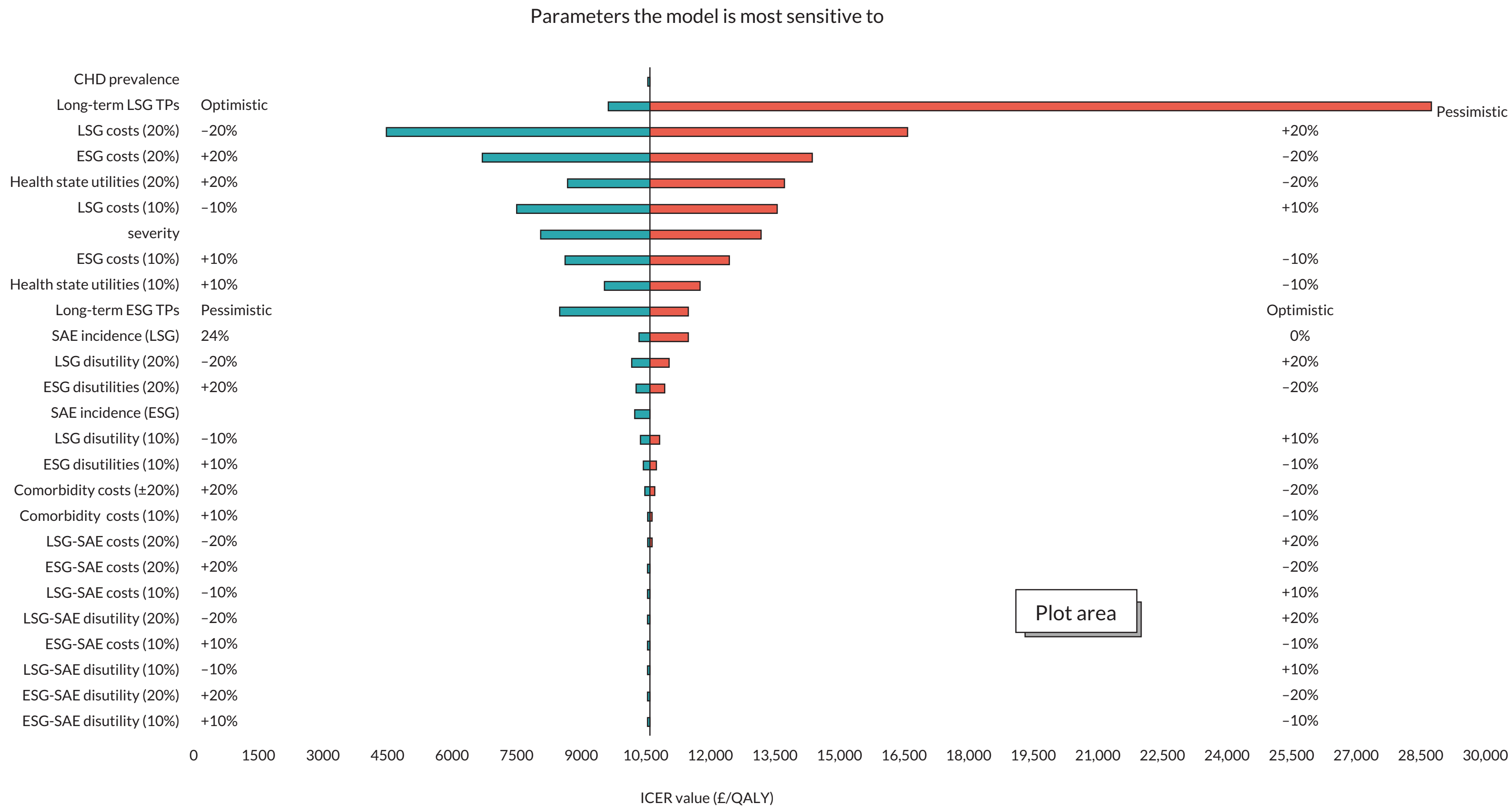

FIGURE 5 Tornado diagram (model 1).

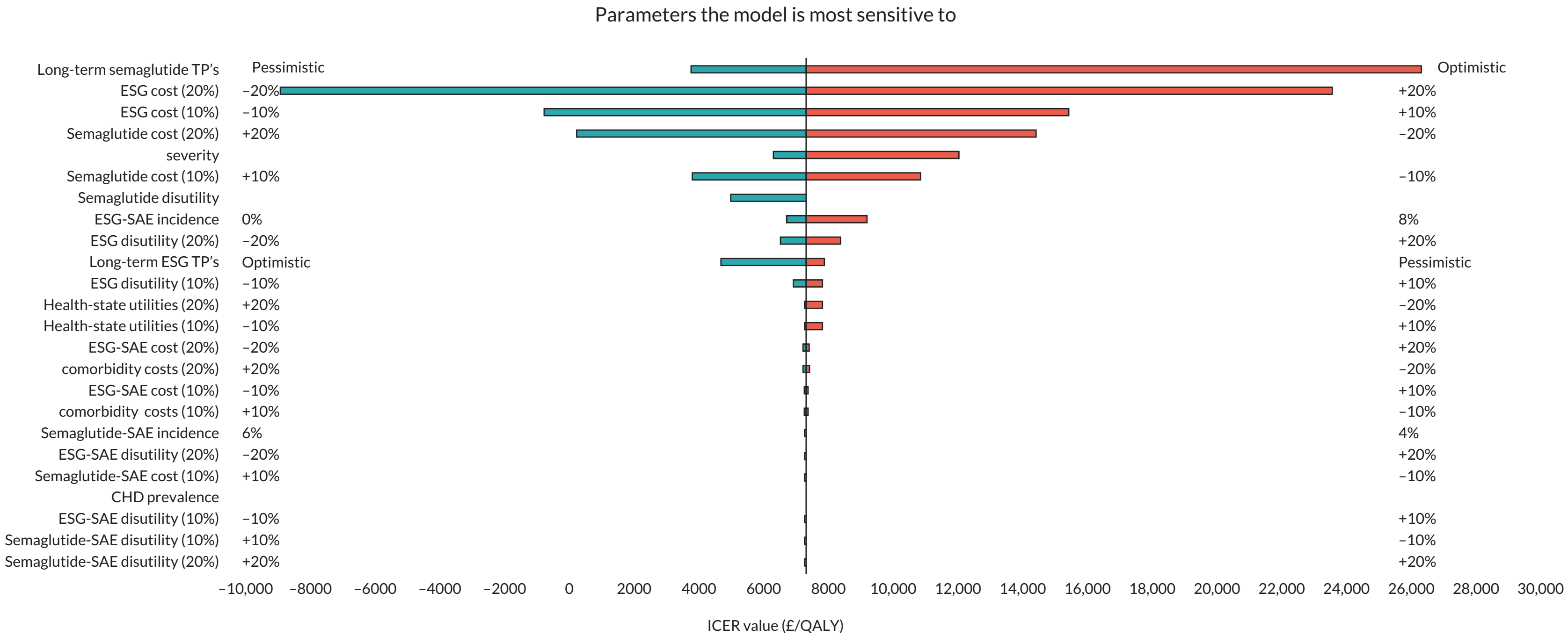

FIGURE 6 Tornado diagram (model 2).

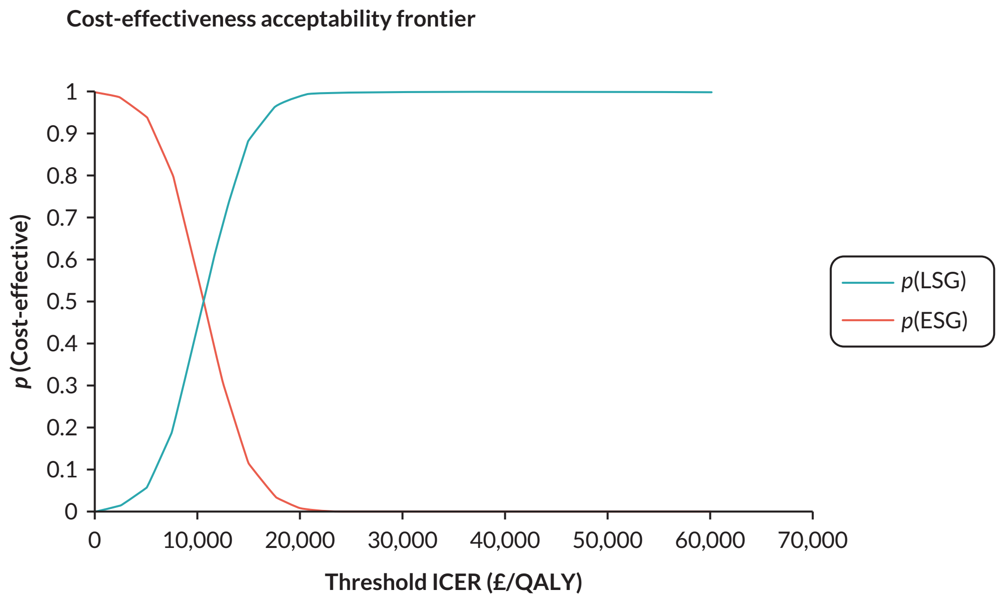

FIGURE 7 Cost-effectiveness acceptability curve (model 1).

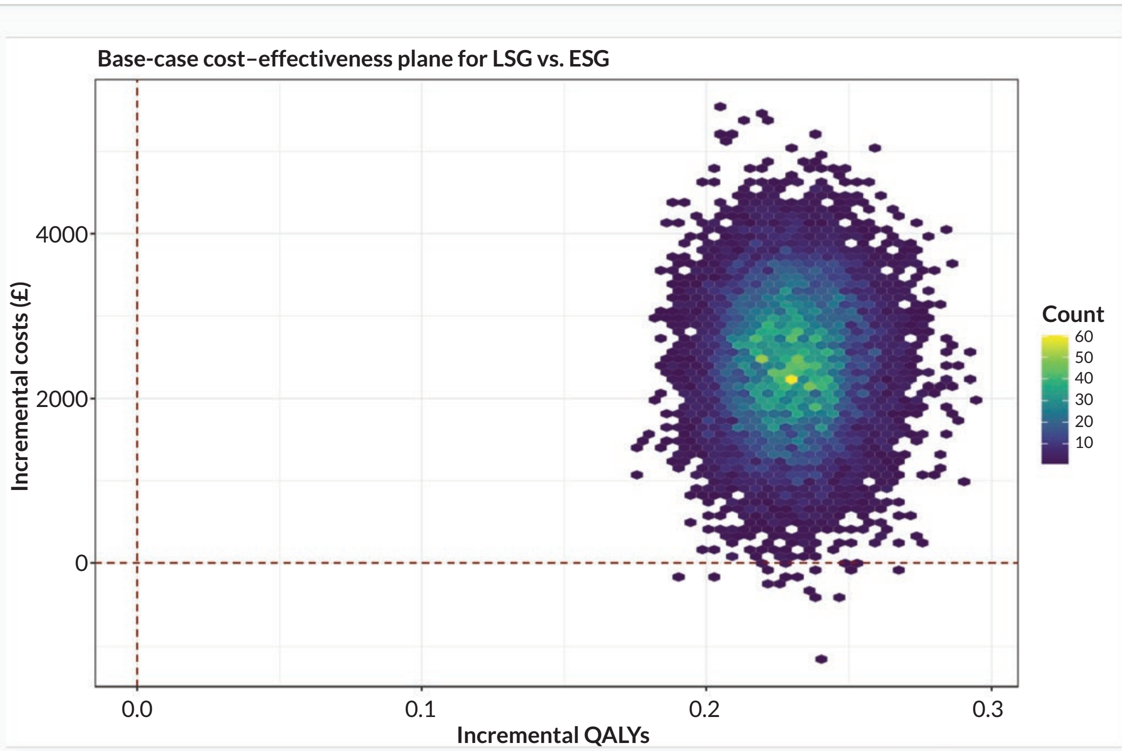

FIGURE 8 Cost-effectiveness plane (model 1).

For model 2, the CEAC demonstrated that ESG had an 85% probability of being cost-effective when compared to semaglutide at a £20,000 WTP threshold, increasing to 94% at £30,000 WTP threshold (*Figure 9*). The cost-effectiveness plane shown in *Figure 10* demonstrated that ESG is cost-effective since the majority of points are concentrated in the east quadrants showing increased effectiveness, with either a cost saving or a small additional cost.

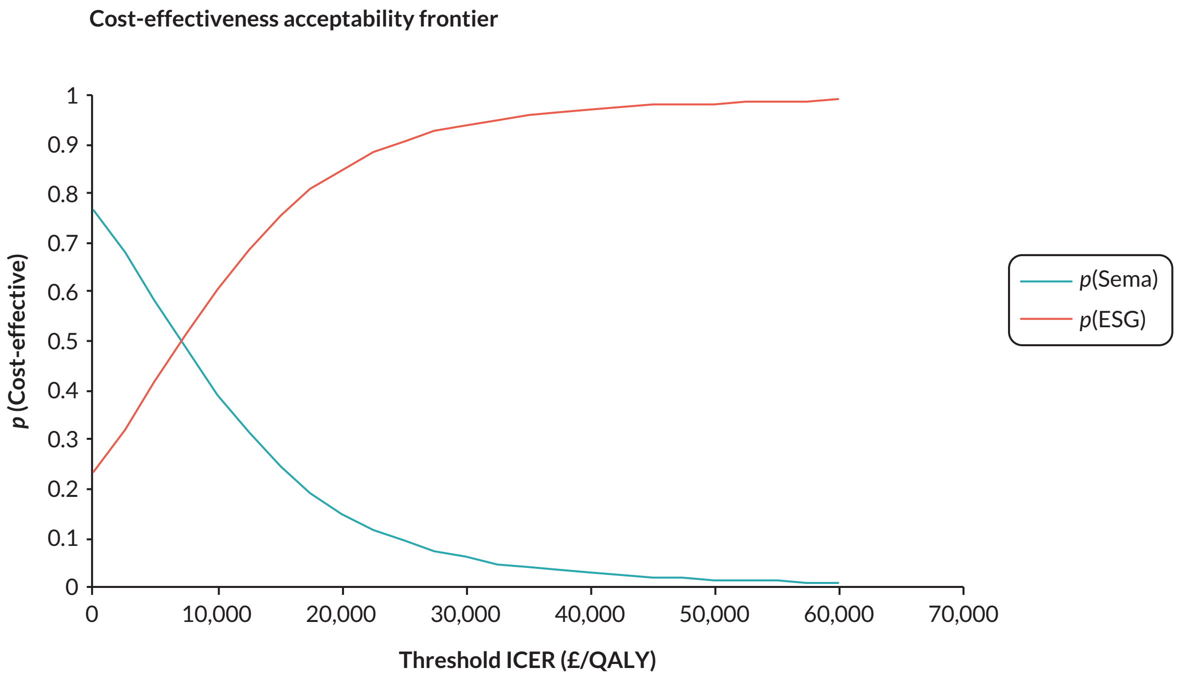

FIGURE 9 Cost-effectiveness acceptability curve (model 2).

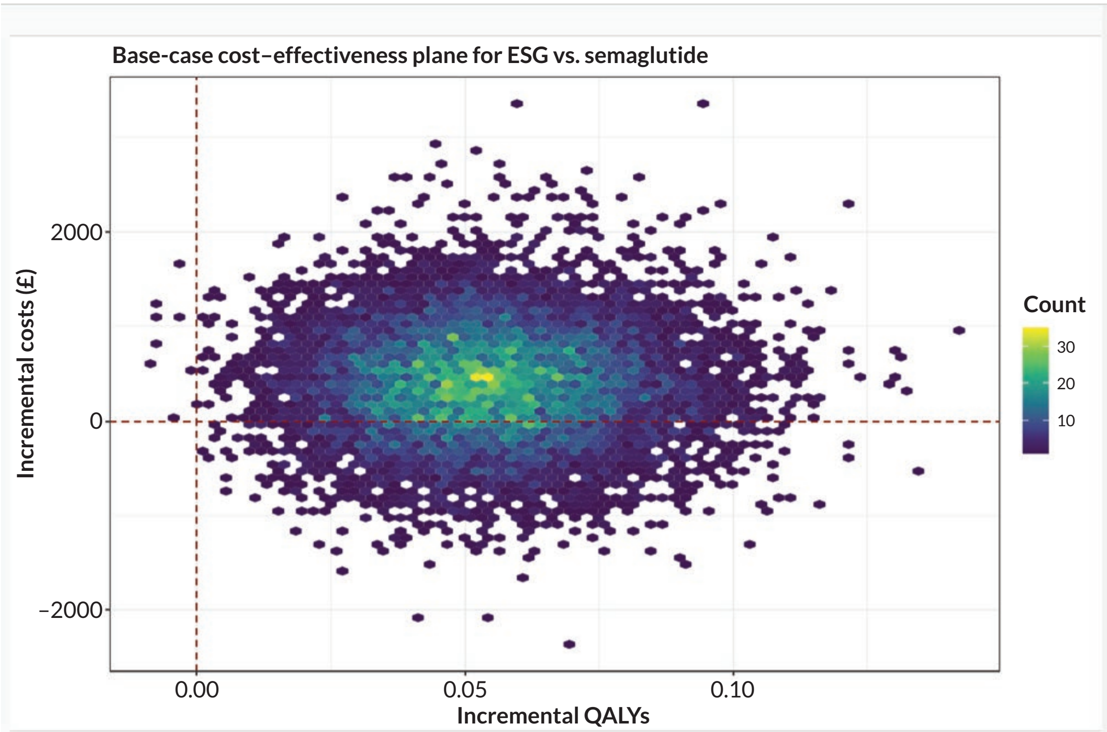

FIGURE 10 Cost-effectiveness plane (model 2).

In model 3, the PSA results show that semaglutide is highly likely to be cost-effective when compared to IGB at all WTP thresholds (*Figure 11*). The scatterplot in *Figure 12* reflects this result with most iterations lying in the more effective and cost-saving south-west quadrant.

An alternate PSA was performed to estimate the probability of cost-effectiveness of interventions with lower certainty around estimates, and WL simulations performed using normal distributions (*Table 19*).

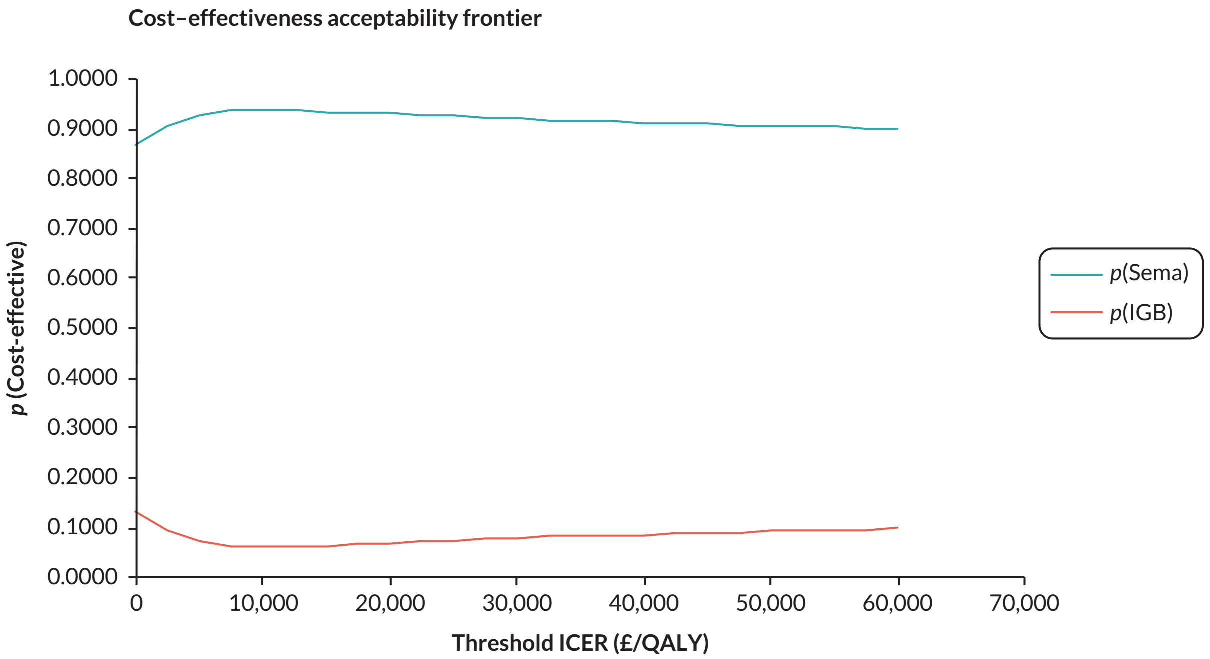

FIGURE 11 Cost-effectiveness acceptability curve (model 3).

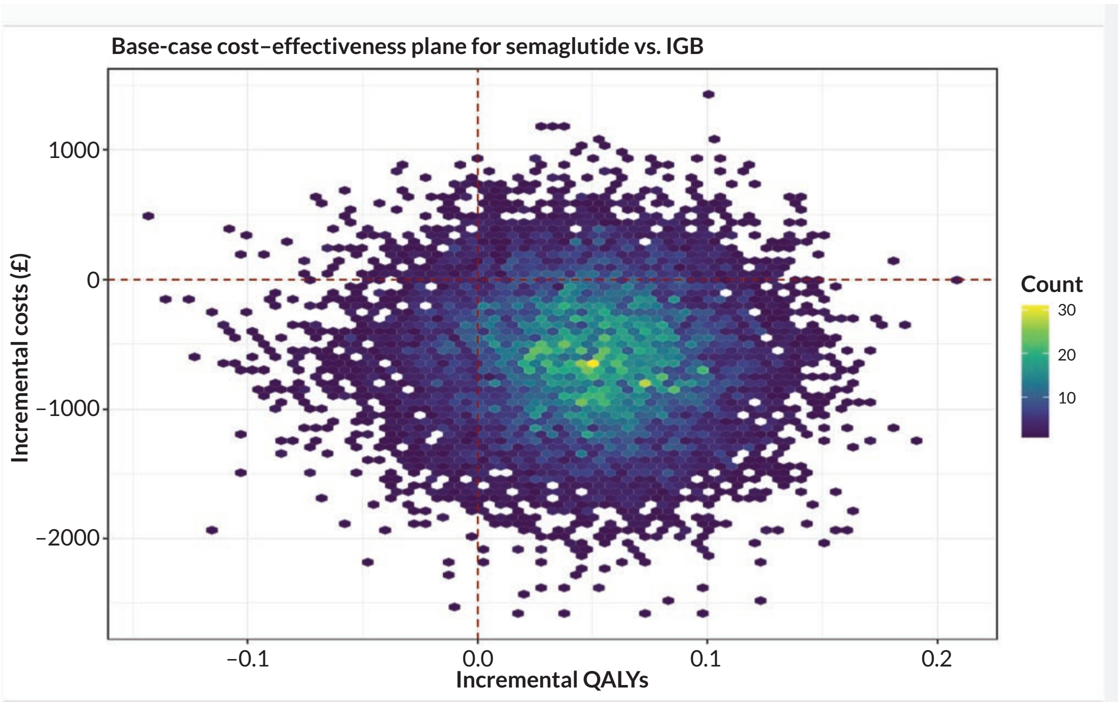

FIGURE 12 Cost-effectiveness plane (model 3).

TABLE 19 Alternate PSA using wider uncertainty around WL

Analysis	Cost (£)	QALY	ICER (£/QALY), % cost-effective
Model 1 (ESG vs. LSG)[a]			
ESG	6431.21	3.2302	
LSG	8891.05	3.4993	
Diff	−2459.84	−0.2691	(LSG) 9198, 99%
Model 2 (ESG vs. semaglutide)[a]			
ESG	6342.08	3.4378	
Semaglutide	5889.13	3.3947	
Diff	452.87	0.0431	(ESG) 10,507, 88%
Model 3 (IGB vs. semaglutide)[a]			
IGB	6463.55	3.3732	
Semaglutide	5889.13	3.3947	
Diff	574.42	−0.021	Semaglutide is dominant, 93%

a All confidence intervals for WL were doubled vs. base-case analysis, and beta distribution parameters were halved. Normal distribution was used to simulate WL.

Model 1 saw limited impact with similar ICER and cost-effectiveness probabilities. The overall ICER rose for ESG in model 2, although cost-effectiveness probability was similar and still high (88%). Model 3 saw semaglutide still dominant, but with a smaller incremental QALY and 7% of iterations returning cost-effective for IGB.

Discussion

Statement of principal findings

The three models presented in this chapter provide early estimates of the cost-effectiveness of endoscopic therapies for patients with obesity. The models conduct separate comparisons of endoscopic therapies (ESG and/or IGB) and two alternative interventions, bariatric surgery (LSG) or pharmacotherapy (semaglutide). The three Markov models were developed with a 5-year time horizon and informed by evidence sourced from the evidence map, additional targeted searches for relevant evidence and clinical expert opinion. The models represent the best available evidence that exists to date.

Model 1 found that when compared with ESG, LSG was highly likely to be cost-effective at WTP thresholds over £20,000, for treatment of patients with obesity class II and III. Within model 2, the use of ESG was found to be a cost-effective option for treatment of patients with obesity class I and obesity II, when compared with semaglutide. Finally, for model 3, semaglutide was dominant for treating patients with obesity class I and II, when compared with IGB.

The finding that LSG is more cost-effective than ESG for treatment of patients with obesity II and III (model 1) was robust to the deterministic and PSAs. This result was driven primarily by a single study[111] demonstrating that LSG was superior at sustaining WL over the longer term, as well as achieving higher initial rates of WL. In summary, evidence from this clinical review showed LSG held a 10% higher WL at 12 months over ESG, which impacted the model results.

The cost-effectiveness of ESG over semaglutide in model 2 was likely due to the assumption of a high rate of weight regain following the removal of semaglutide at 2 years. The model 2 base-case results were found to be more sensitive to the DSA than in model 1, in particular from the assumptions surrounding the ESG intervention costs. However, when considering the joint distribution of parameter uncertainty in the PSA, the likelihood of cost-effectiveness of ESG when compared to semaglutide remained at 85% at the standard WTP threshold (£20,000/QALY).

For model 3, the base-case results of semaglutide being the dominant treatment option for patients with obesity class I and obesity class II was largely unaffected by both PSA and the DSA. The DSA showed a small variation in result due to altering the IGB intervention cost; however, semaglutide remained cost-effective (at £20,000/QALY), and the PSA demonstrated cost-effectiveness of semaglutide at all levels of WTP threshold. These results are reflective of the relative cheaper intervention (semaglutide when compared to IGB) and the level of evidence on the size of WL achieved when continuing to take semaglutide for 2 years. Of particular note is what happened to the model results under the scenario when semaglutide was extended to 5 years. This altered the treatment recommendation to IGB, due to semaglutide incurring an ongoing treatment cost (from years 3 to 5) combined with the disutility associated with administering weekly injections up to end of year 5.

Across all three models, the degree of confidence in the base-case model results implied by the PSA reflect first the large evidence base for which the utility values for the obesity health states have been drawn (hence limited sampling variation), and second, the size of studies used to parameterise the WL estimates. For example, the meta-analysis by Beran *et al.*[100] contained over 3000 patients receiving ESG for 2 years, supplemented by study data on over 3000 patients receiving ESG to 3 years.[110] Even the 5-year data on LSG had over 200 patients followed up over 5 years,[111] a smaller number but still sufficient to produce small sampling ranges, and the estimates on IGB were drawn from over 400 patients receiving balloons and followed up over 5 years.[113] While there is considerable uncertainty regarding the treatment effects of semaglutide within models 2 and 3, the sample sizes of comparator studies for IGB and ESG determine that uncertainty over the effectiveness of semaglutide do not impact the uncertainty in the probabilistic analyses significantly.

While the sample sizes of studies used to estimate long-term weight trajectories were relatively large (and therefore sampling distributions relatively narrow), it is important to acknowledge that we cannot be certain of the comparability of the included studies. For example, none of the long-term model parameters were drawn from direct comparisons, and only model 1 used a direct comparison on WL to year 3. It is therefore the case that the PSA results most likely overestimate the certainty of the cost-effectiveness results A potential solution could be to manually adjust the distribution parameters around the long-term efficacy to reflect this type of qualitative uncertainty as shown in *Table 19*. However, this did not have any significant impact upon likely cost-effectiveness. Widening confidence intervals around WL on each intervention does increase the range of sampled transition probabilities for movement between WL states within the PSA. However, this increased sampling range does not especially impact the proportion of times each intervention is favoured. There could be two predominant reasons for this, as even extreme sampling uncertainty averages out over a large model with over 130 parameters; also as above, the mean effect differences are fairly large. It is unclear if artificially further altering the distributions (beyond doubling the confidence intervals for WL and halving the beta distributions) is warranted. Best- and worst-case deterministic analyses may represent the best method for understanding the extent of qualitative uncertainty at present.

Strengths and limitations of modelling and the evidence base

The three models presented have synthesised information from multiple sources and assessed the health system costs, the (assumed) longer-term impact of treatment upon patient weight, as well as incorporated the QoL effects from receiving these treatments. This synthesis will help ascertain whether the clinical benefits identified by the clinical review are worth the costs within a healthcare system that has finite resources.

In terms of strengths of the models, there are two methodological issues to note. First, the methodology for deriving the transition probabilities was developed by the study team and could be utilised in future modelling studies with access to data upon baseline population weights, heights and/or BMI. Second, we tried, where possible, to identify relevant broader literature aside from reliance upon RCTs for the longer-term patient transitions within the model to prevent the over reliance upon clinical assumption.

The models had some weaknesses. First, the utility values were based upon values associated with the obesity health states, and not values associated with the treatments after WL. This could have led to bias in the utility scores, which is particularly relevant to models 2 and 3 where there are only small differences in effect between the two comparators. The same is true of costs, which included the costs associated with the comorbidities associated with each obesity state; as such, it is assumed that when a patient rapidly loses weight their risk of comorbidity was determined by their new BMI health state, and not the BMI they had transitioned from. This imbedded assumption may have overstated the short-term effects. A second weakness relates to the model time horizon. Treatments such as LSG and ESG which have a longer-term influence over sustained WL would likely have benefits which span beyond the 5-year time horizon; however, a longer model time horizon was not possible due to the lack of evidence on long-term weight trajectory following treatment. Third, the short-term effectiveness data were limited in quality and were either from non-randomised controlled studies or from indirect comparisons. And fourth, the trajectories beyond 12 months for semaglutide are based solely upon clinical assumption, and therefore the base-case estimates should be considered only alongside the sensitivity analyses for models 2 and 3. Also, for the longer-term data for ESG, LSG and IGB, these have been taken from a small number of studies that are limited in quality. To account for this, the PSAs were artificially altered by using higher variation in distributions to reflect the high degree of uncertainty in the evidence. A fourth potential weakness in the modelling was that, although the PSA showed a high degree of certainty in the model results, this was largely due to the large sample sizes within the evidence base for the long-term data; however, none of the data used to parameterise either the short- or long-term effects were from direct randomised controlled trials, which means the PSA could have overestimated the certainty in the results.

Other modelling studies have adopted alternative model structures including individual simulation models to ensure that individual characteristics reflect weight trajectories. However, the choice of model type within this study reflected an assessment of the level and quality of evidence available from the clinical (and economics) systematic review. For example, if cohort-level estimates are not available for semaglutide beyond 68 weeks, then individual simulation of parameters based upon assumptions are likely to lead to an exacerbation of uncertainty, not minimisation of it. Although we accept a Markov cohort model design has its limitations, we feel it presented a more appropriate model structure considering the uncertainty within the available evidence, and we did not want to give illusion of spurious accuracy.

Comparison with other studies

The systematic review presented in *Chapter 4* found three studies that included model-based CEA of endoscopic therapy. These published models were for different treatments options to the treatments compared in this chapter; however, it is interesting to draw comparisons. One of these studies, Kelly *et al.*,[79] found ESG to be more cost-effective than lifestyle management for treatment of patients with class II obesity (ICER £2453 per QALY) and the authors noted similar limitations to the models reported in this chapter with lack of long-term data on WL, the reliance on separate studies for intervention comparison, and the use of non-RCT data for WL effects. Similarly, within the other two models identified from the systematic review, there were similar limitations noted for the long-term WL, combined with having to use non-RCT data to estimate WL effects.

Implications for clinicians and policy-makers

The cost-effectiveness analyses reported in this chapter show that from a healthcare perspective, LSG is the cost-effective treatment choice when compared to ESG for patients with class II and class III obesity. This finding was unaltered by both PSA and DSA.

For patients with obesity class I and class II, the CEA has shown with some degree of certainty that ESG is the cost-effective choice when compared to semaglutide; and with a high degree of certainty that semaglutide is the dominant treatment option when compared to IGB. However, when the model was adjusted to semaglutide being administered for 5 years, it was no longer a cost-effective option because of the ongoing incremental costs of treatment (compared to IGB), and ongoing treatment-associated disutility from years 3 to 5.

Overall, all three models are only as robust as the data available to parameterise them and as noted in several places throughout this chapter, and within the economics systematic review, there remains a noticeable lack of direct comparisons of the relevant treatments within RCTs and of long-term weight trajectory data for patients who receive these treatments, and particularly for semaglutide. It is only as these data emerge from the published evidence, can these models be extrapolated beyond 5 years, and we can gain an improved understanding of cost-effectiveness over a lifetime.

Summary

This chapter presented the findings of an economic evaluation of endoscopic therapy for treatment of patients with obesity. The models presented indicate, based on current evidence, that LSG is more cost-effective when compared to ESG for treatment of class II and class III obesity; ESG is more cost-effective than semaglutide, and semaglutide is more cost-effective than IGB, for treatment of patients with class I and class II obesity. These model-based economics evaluations were developed based on the best available evidence combined with clinical expert opinion. It is important to interpret the results alongside the limitations noted, particularly with respect to the long-term WL data and thus further research is needed to follow patients up for longer to obtain more accurate information.

Chapter 6 Overarching discussion

The aim was to undertake a systematic review of the clinical and cost-effectiveness of endoscopic treatments for obesity and to undertake a model-based CEA.

Systematic searches were undertaken for both clinical and cost-effectiveness evidence. Due to the large number of included records on clinical effectiveness of endoscopic therapies (*n* = 1574), formal systematic reviews of effectiveness were not feasible; instead, and in agreement with the steering group, the evidence was summarised in an evidence map with a descriptive overview. A systematic review was undertaken on cost-effectiveness studies of endoscopic therapies.

Three state transition cohort Markov models were designed to estimate the cost-effectiveness of endoscopic therapies compared to alternative weight management interventions for adult patients with obesity (BMI of > 30 kg/m^2). CUA was conducted based on the outcome of cost per QALY. The base-case analysis was from the perspective of the NHS and PSS over a 5-year time horizon. The following treatments were compared in three distinct models: (1) ESG versus LSG, (2) ESG versus semaglutide and (3) IGB versus semaglutide.

Evidence to inform the design of the models and model parameters came from the evidence map; an indirect comparison analysis; the cost-effectiveness review; targeted searches for models that included treatments for obesity beyond endoscopic therapies; targeted searches to inform specific model parameters; and guidance from the steering committee. A base-case analysis was conducted for each model and DSA and PSA were performed to explore the uncertainty around model parameters.

Evidence map: summary of findings and strengths and weaknesses

The map provides a searchable repository of all evidence on endoscopic therapies. The value of the evidence map was demonstrated through informing model parameters, such as the effectiveness estimates for ESG versus LSG (based on non-randomised controlled studies since there were no RCTs of ESG vs. LSG). The map highlighted the lack of evidence for direct comparisons of ESG versus semaglutide or IGB versus semaglutide, which prompted the need for indirect comparisons, and on long-term data on each endoscopic intervention. The majority of studies of any design did not follow patients up beyond 6–12 months. Only 11 studies with longer follow-up (24 months or beyond) were identified, and of these, only 4 were used to inform model parameter estimates. Problems with longer-term effectiveness data where it existed included substantial loss to follow-up and confounding with successive obesity treatments.

While outcome measures for WL could not be assessed systematically across all studies in the evidence map, WL appeared to be mainly reported as %TBWL, %EWL, change in mean BMI or number of patients reaching a 5% or 10% WL threshold. Far fewer studies reported WL as the proportion of patients moving between different obesity groups/BMI categories which had implications for transition probability estimates for the modelling.

There was a large amount of inconsistency in how SAEs were defined and reported. The estimates of SAE rates to inform model parameters were based mainly on existing systematic reviews, but even where primary studies were reviewed, there was often a lack of clarity. Problems included a lack of definition for SAEs, variation in AEs designated as 'severe' and a lack of clarity between the overlap of SAEs, hospitalisations and reoperations.

Review of cost-effectiveness: summary of findings and strengths and weaknesses

The systematic review of cost-effectiveness studies identified only three full economic evaluations conducted as cost–utility analyses and reporting costs per QALYs. While ICERs could not be compared directly due to heterogeneity in the interventions, settings and methods used, there was some consistency, in that ESG, swallowable IGB and aspiration therapy were all cost-effective when compared to LSI but were dominated when compared to bariatric surgery. Common limitations across the three studies were a lack of long-term data on the effectiveness of endoscopic therapies and a lack of direct comparison data, which is consistent with our own findings. One of the studies was set in the UK (Kelly *et al.* 2023)[79] and was deemed the most useful for informing the new models due to the relevance of the setting and the population.

Economic evaluation: summary of findings and strengths and weaknesses

Three Markov models were developed, respectively comparing ESG with LSG, ESG with semaglutide and IGB with semaglutide, over a 5-year time horizon.

LSG is likely to be cost-effective compared with ESG, for the treatment of patients with obesity class II and III (£10,593 per additional QALY with LSG when compared with ESG in base case). This finding was robust to DSA and PSA and was primarily driven by the finding from a systematic review of seven non-randomised controlled studies which found greater WL with LSG. Only the most pessimistic scenario regarding long-term efficacy with LSG led to an ICER approaching an upper threshold limit of £30,000/QALY. ESG is likely to be cost-effective compared with semaglutide for the treatment of patients with obesity class I and II (£7267 per additional QALY with ESG when compared with semaglutide in base case). This finding was more sensitive to DSAs, particularly cost, with a reduction in ESG costs by 10–20% resulting in ESG becoming dominant. The results were also sensitive to a reduction in assumed weight regain with semaglutide, resulting in an increased ICER for ESG. For model 3, semaglutide was the dominant (cheaper and more effective) treatment option when compared with IGB in patients with obesity class I and II, but the effect differences were very small. Under the scenario analysis when IGB costs were reduced by 20%, semaglutide lost this dominance but remained cost-effective.

The PSA found a degree of confidence in the base-case estimates due to the large evidence base from which utility values for the obesity health states were drawn, and due to the relatively large sample sizes of the studies used for estimating WL. Nonetheless, there was uncertainty relating to the comparability of the included studies evaluating the different therapies. None of the effectiveness data were based on direct comparisons from RCTs and the PSA may therefore have overestimated the certainty of the results. Other limitations included basing the utility values and comorbidity costs on obesity health states rather than being directly associated with WL, and a 5-year time horizon which may not have captured longer-term benefits from ESG or LSG. WL beyond 12 months was based solely on clinical assumption for semaglutide and as such base-case estimates for models 2 and 3 should only be considered in the context of the sensitivity analyses.

It should be acknowledged, however, that the treatment comparisons within the models are not necessarily reflective of treatment pathways in reality, which tend to be more complex, with patients likely to undergo successive interventions over time, or receive a combination of treatments (e.g. adding pharmacotherapy to an endoscopic intervention). If WL is not sustained, or there is weight regain, patients could, for example, have a revision of ESG, have a repeat IGB, or move on to laparoscopic bariatric surgery. There was no single defined pathway, however, that could be modelled, as this will differ by patient characteristics (e.g. starting BMI), resource availability, patient preference and treatment history. Furthermore, there is no clear position for endoscopic treatments in current NICE recommended pathways and no routine use of endoscopic treatments in UK. And, even if a feasible pathway could be defined, there was no evidence available to populate such a model, as studies mostly considered two individual comparators with a short follow-up. So, the inherent uncertainty in such a model would render any findings unusable.

Within the models presented, alternative therapies were considered that had different durations of treatment, due to their licensing requirements in the UK. IGB, for example, was assumed to be placed for 6 months, and semaglutide given for 2 years. The models accounted for this with varying the assumed WL/gain following therapy; however, the sensitivity analyses highlighted the sensitivity of the semaglutide model when that was administered for 5 years instead of 2 years.

The models also did not consider the role of IGB as a bridge to bariatric surgery, which is how it is commonly used to ensure patients achieve sufficient WL for bariatric surgery to be performed more safely. IGB is less commonly used as stand-alone treatment, though it is more popular in private practice. Further, it was not possible to consider variations in the type of IGB and therefore the model considered a more 'generic' endoscopic balloon only and there may be differences in cost-effectiveness between different types of balloons.

Although we found that ESG is likely more cost-effective than semaglutide, and semaglutide is likely more cost-effective than IGB, it is not possible to draw any conclusions on the relative cost-effectiveness of ESG compared to IGB. It was decided not to model this comparison as patients undergoing ESG are likely to differ from those having an IGB.

Implications for stakeholders (clinicians, policy-makers, patient and public involvement)

The evidence provided in this report provide very useful information to stakeholders to aid decision-making regarding choices of obesity treatments that can be cost-effective to offer to people living with obesity. This report, however, also highlights some important limitations to the available evidence, particularly the lack of RCTs of direct comparison of treatments, the lack of longer-term data and the lack of studies reporting the impact of treatment on a wide range of obesity-related complications. It is crucial to address these limitations in order to aid informed decision-making by patients, clinicians, payers and policy-makers. These limitations need to be seen in a wider context.

Until recently, the main available treatments for obesity have been LSI and bariatric surgery. The former can be applied widely but has modest efficacy and does not result in sustained WL in the majority of patients. While the latter is highly effective clinically and economically, there are major access limitations with only a minority of eligible and willing patients receiving the treatment. Hence, there was a clear unmet need for treatment options that result in significant sustained WL and improve health to a greater extent than LSI and can be applied on a larger scale than bariatric surgery. As a result, endoscopic treatments for obesity and pharmacotherapy agents have been developed. The number of these treatment options is expanding rapidly, and over the coming decade there is likely to be an increasing number of treatment options (both endoscopic and pharmacotherapy) with greater WL efficacy and potentially better safety profiles. With the availability of a variety of treatment options with a wide range of efficacy (both in terms of WL and impact on health) and safety, there is greater need to provide stakeholders with the appropriate evidence to aid decision-making. Such evidence will need to include RCTs directly comparing the variety of options available as has happened with other chronic diseases such as T2D and CVD.

Considering the chronic nature of the disease of obesity, there is a need to have longer-term data about the efficacy and safety of obesity treatments, in addition to RCTs comparing treatment effects. This is going to be challenging considering the expansion of all treatment options. However, such data are crucial for considering the potential differences in long-term efficacy between the different interventions and the variance in weight regain trajectories.

Furthermore, there is a need to understand the longer-term impact of these interventions on health and its relationship to weight changes. This is important as some health benefits might 'outlast' the WL and persist for a certain time despite weight regain, while other health gains might be lost with weight regain. In addition, there may be intervention-specific impacts on health which are at least in part independent from any impacts directly linked to WL. All these factors support the need for direct comparisons between interventions over a prolonged time horizon.

It is also important to consider that the RCTs comparing interventions may not take into account the chronic nature of obesity and the need for lifelong approaches. For example, patients with obesity might require different treatments during different stages of their lives based on their needs (e.g. pre- and perinatal planning might limit the use of pharmacotherapy). In addition, many patients with obesity require combination therapy either sequentially or simultaneously. In order for policy-makers, clinicians and patients to make informed choices, the evidence generated needs to consider the realities of obesity management beyond simply comparing one treatment with another.

Increasing treatment options will also increase the need for better phenotyping of people living with obesity, with and without obesity-related complications, in order to understand more about the disease pathogenesis, identify the groups with the highest risk of progression and identify the groups with the best responses to the different treatments. Such information is essential to personalise treatment approaches, and guide policy-makers towards prioritising treatment access considering the limited available NHS resources and the high prevalence of obesity in the UK.

Despite the above-mentioned unmet needs and limitations, the current data clearly suggest that LSG is likely to be cost-effective compared with ESG for patients with obesity class II and III, ESG is likely to be cost-effective compared with semaglutide for patients with obesity class I and II, and semaglutide is dominant over IGB in patients with obesity class I and II. However, direct comparative data, including longer-term follow-up, on these treatments, the expanding treatment options with potentially greater efficacy and/or safety and the potential for impact of these on treatment cost will likely challenge these findings over time and will require further economic analyses.

Unanswered questions and future research

Neither the evidence map nor existing systematic reviews identified many studies with a pharmacotherapy comparator (such as liraglutide), and there were no studies comparing semaglutide to an endoscopic therapy. Given the recent NICE recommendations, it will be important to assess the effectiveness of semaglutide and any emerging clinically effective or cost-effective pharmacotherapy against endoscopic interventions in future direct comparisons, ideally in RCTs. Future studies should also consider following patients up for longer (beyond 12 months) to evaluate whether the effects of endoscopic treatments are maintained in the longer term and to assess their impact on comorbidities.

Studies may also want to consider evaluating more complex treatment pathways where patients undergo successive treatments for WL, including endoscopic therapies. This would more accurately reflect a real-life situation where patients are unlikely to undergo a single WL intervention in isolation. The design of such studies may be hampered by the fact that there is no single treatment pathway and the place of endoscopic treatments within the treatment pathway is not well defined.

The economic evaluations were chosen to represent the decision problems felt to be most relevant to the current clinical context. Each model therefore considered a typical patient population within each of the obesity classes covered (as indicated above). As such, there is scope for more refined analyses in key defined subgroups, particularly those more at risk of adverse outcomes from obesity and should reasonably robust evidence emerge then the models can be refined further.

Future primary studies should also consider more comprehensive reporting of AEs and SAEs, for example defining which AEs are considered as a SAE and ensuring the overlap between SAEs, hospital admissions and reoperation is clear. It would also be useful to report WL as the proportion of patients moving between obesity states/BMI groups, in addition to common measures like %TBWL, so that data can be used more easily by future economic models.

It is common to perform value of information analysis to assess the potential value of future research. However, we have opted not to include this analysis due to the high level of certainty provided by the PSA. A value of information analysis, including expected value of perfect information, expected value of partial perfect information and expected value of sample information, is most useful when there is significant uncertainty in the economic results. As this is not the case, instead we have adjusted parameter estimates to increase the uncertainty and highlighted, within our discussion, the importance of direct treatment comparisons and the need for longer-term effectiveness studies.

The evidence map is current to January 2023. As research into endoscopic treatments is a fast-moving field, it will need updating in the near future. In particular, we anticipate further research on semaglutide, other emerging WL drugs (such as tirzepatide), and on swallowable IGB – while the latter is not an endoscopic treatment as such, the mechanism of action is very similar to endoscopic IGB and is associated with fewer risks as endoscopy is not usually needed for placement or removal. As such, it may also be preferred by patients.

Qualitative research to gain an insight into patient perspectives on endoscopic and pharmaceutical therapies is needed. Patient preferences should be considered, especially where there is a lack of strong evidence for differences in effectiveness or where a treatment is associated with challenging side effects.

Conclusion

A vast amount of research has been undertaken on endoscopic therapies, as shown in the evidence map with 1574 records of RCTs, non-randomised controlled studies and single-arm studies. This map provides a useful repository of evidence which is searchable by population, intervention, comparator, sample size and length of follow-up and can be used for planning and informing future research. It was used in this report to inform some of the model parameters included in the three models, but there were no RCTs directly comparing any endoscopic treatment to bariatric surgery or to semaglutide. The systematic review of cost-effectiveness evaluations identified few such studies and only one that was undertaken from a UK perspective. The models developed for this report will therefore add to the evidence base on cost-effectiveness of endoscopic therapies.

The three Markov models found that over a 5-year time horizon LSG was likely to be cost-effective compared with ESG, ESG was likely to be cost-effective compared with semaglutide, and IGB was dominated by semaglutide. Model 1 (ESG vs. LSG) was robust in sensitivity analyses, while the other models were somewhat sensitive to intervention costs. None of the effectiveness data used to inform the model were from RCTs and there was substantial uncertainty around long-term WL for both semaglutide and IGB. Future research should focus on direct comparisons of endoscopic interventions and WL drugs such as semaglutide, long-term studies, and studies which better reflect the complex treatment pathway of obesity where patients are likely to receive successive obesity treatments over time.

Reporting patient and public involvement

What form did the patient and public involvement take and at what stages did it occur during the study?

There were multiple forms of patient and public involvement (PPI) in the study including having a PPI co-applicant on grant application, three people living with obesity as members of the oversight committee and regular PPI meetings. The PPI meetings took place before the oversight committee meetings in order for the outcomes of the PPI meetings to feed to the discussions with the oversight committee (which also included people living with obesity). The PPI meetings included people living with obesity that received variety of obesity treatments (including combination therapy) and some also had endoscopic obesity treatments.

What impact did patient and public involvement have during the study? How was it useful?

The PPI co-applicant contributed to all aspects of the grant proposal like all the co-applicants. During the conduct of the project, and via the PPI group meetings and the oversight committee, the PPI contributed to shaping the evidence map, the choice of which interventions to focus on and what comparators should be examined. In addition, the PPI contributed to what outcomes and AEs that need to be examined.

How will patient and public involvement support dissemination of the results?

The PPI reviewed the lay language summary and will support the dissemination of the findings in variety of patients groups (bariatric surgery groups) and the charities and societies that represent people living with obesity including Obesity UK and European Coalition for People Living with Obesity. In addition, the PPI will disseminate the findings during the obesity professional conferences such as the UK and European Congresses for Obesity.

Equality, diversity, and inclusion

Participant representation: This study utilises publicly available research and therefore reflects the diversity of this evidence.

Research team and wider involvement: The research team were compiled for their relevant clinical and methodological expertise. They were employed by equal opportunities employers with active inclusive staff development programmes.

Patient and public involvement members were approached for participation based on having received the intervention under consideration and on potential clinical similarity to those for whom the intervention is being considered in this report.

Additional information

CRediT contribution statement

Esther Albon (https://orcid.org/0009-0004-4183-3591): Data curation (Map), Formal analysis (Map), Investigation, Methodology, Project administration, Supervision, Visualisation, Writing – original draft (Map), Writing – editing and reviewing.

Nafsika Afentou (https://orcid.org/0000-0003-1337-7029): Data curation (Model), Formal analysis (Model), Investigation (Model), Methodology, Visualisation, Writing – original draft (Model), Writing – editing and reviewing (Model).

Janine Dretzke (https://orcid.org/0000-0002-2591-6918): Conceptualisation, Data curation (Map), Formal analysis (Map), Funding acquisition (Supporting), Investigation, Methodology, Project administration, Supervision, Validation, Visualisation, Writing – original draft, Writing – editing and reviewing.

James Hall (https://orcid.org/0000-0001-8024-5427): Data curation (Model), Formal analysis (Model), Investigation (Model), Methodology, Supervision, Visualisation, Writing – original draft (Model), Writing – editing and reviewing (Model).

Chidubem Okeke Ogwulu (https://orcid.org/0000-0002-8133-7021): Data curation (Model), Investigation (Model), Methodology, Visualisation, Writing – original draft (Model).

Malcolm J Price (https://orcid.org/0000-0002-7352-3027): Formal analysis (Model), Funding acquisition (Supporting), Investigation, Methodology, Visualisation, Writing – original draft (Model), Writing – editing and reviewing (Model).

Ken Clare (https://orcid.org/0000-0001-7054-444X): Funding acquisition (Supporting), Methodology, Supervision (PPI), PPI chair.

Rishi Singhal (https://orcid.org/0000-0002-2797-2569): Funding acquisition (Supporting), Methodology, Clinical advice.

Abd Tahrani (https://orcid.org/0000-0001-9037-1937): Conceptualisation (Equal lead), Funding acquisition (Equal lead), Methodology, Project administration, Supervision, Validation, Visualisation, Writing – original draft, Writing – editing and reviewing.

Emma Frew (https://orcid.org/0000-0002-5462-1158): Conceptualisation, Data curation (Model), Supported funding acquisition, Methodology, Project administration, Supervision, Validation, Visualisation, Writing – original draft, Writing – editing and reviewing.

David J Moore (https://orcid.org/0000-0002-4163-4080): Conceptualisation (Equal lead), Funding acquisition (Equal lead), Methodology, Project administration, Supervision, Validation, Visualisation, Writing – original draft, Writing – editing and reviewing.

Acknowledgements

We would like to thank Katie Scandrett (Research Associate, University of Birmingham) and Sophie Beese (Senior Research Fellow, University of Birmingham) for their contribution to screening at the inclusion and exclusion stage and for help with recording information from the articles for the map of evidence. We also want to thank Isobel Harris (Research fellow, University of Birmingham) and Ridhi Agarwal (Research Fellow, University of Birmingham) for their contribution to screening of articles for the evidence map. We are grateful to Francesa Crowe for her advice and support for the use of the CPRD database. We also extend our thanks and appreciation to the members of our patient and public involvement group for offering their invaluable insight into living with obesity and their experiences of bariatric treatments. We thank those members for attending and offering input during both PPI and steering group meetings. Finally, we also thank our steering group members for their vital experience and input on many aspects of the project. In particular, we are grateful for the advice given by Professor Barham Abu Dayyeh, consultant in gastroenterology and advanced therapeutic endoscopy, Mayo Clinic, Rochester, Minnesota, USA, Professor Kamal Mahwar, consultant bariatric surgeon, Sunderland Royal Hospital, and visiting Professor, University of Sunderland, UK and Dr Abdullah Mawas, consultant gastroenterologist, West Suffolk Hospitals NHS Trust, UK.

Data-sharing statement

This is a systematic review study and therefore the data generated are not suitable for sharing beyond that contained within the manuscript. Further information can be obtained from the corresponding author. The map of evidence will be available subject to NIHR terms and conditions.

Ethics statement

Ethical approval was not required for this study because it involves systematic reviews and an economic analysis using publicly available evidence.

Information governance statement

The University of Birmingham is committed to handling all personal information in line with the UK Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679. National Institute for Health and Care Research is committed to handling all personal information in line with the UK Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679. Under Data Protection legislation NIHR is the Data Processor; the Department for Health and Social Care (DHSC) is the Data Controller, and we process personal data in accordance with their instructions. You can find out more about how we handle personal data, including how to exercise your individual rights and the contact details for DHSC's Data Protection Officer here: https://www.gov.uk/government/organisations/department-of-health-and-social-care/about/personal-information-charter. This study did not utilise any personal information or data.

Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/PWKQ2310

Primary conflicts of interest: Ken Clare has received funding from industry. Ken Clare is a member of the Patient Advisory Board Novo Nordisk, Patient Advisory Board Boehringer Ingelheim and has received consulting fees from Eli Lilly. Ken Clare has membership of IHCOM board, was a Trustee ASO (resigned September 2023) and is Director of Operations Obesity UK, Chair of European Coalition of People Living with Obesity and Chair of WLSinfo Charity. Abd Tahrani has received funding from industry. Abd Tahrani is currently an employee and shareholder of Novo Nordisk. This work was funded before Abd Tahrani became a Novo Nordisk employee and Novo Nordisk has no role in this project. The views expressed in this report are those of the authors and not those of Novo Nordisk. Emma Frew has received funding from industry and has received consulting fees from Novo Nordisk. Emma Frew has Membership of NIHR-funded trial steering committees Elected Board member, is an International Health Economics Association Trustee, is a member of Association for Study of Obesity Member of strategic council, APPG-obesity. No conflicts of interest were declared by other authors.

Disclaimer

Every effort has been made to obtain the necessary permissions for reproduction, to credit original sources appropriately and to respect copyright requirements. However, despite our diligence, we acknowledge the possibility of unintentional omissions or errors and we welcome notifications of any concerns regarding copyright or permissions.

References

1. Tahrani AA, Morton J. Benefits of weight loss of 10% or more in patients with overweight or obesity: a review. *Obesity (Silver Spring)* 2022;**30**:802–40. https://doi.org/10.1002/oby.23371
2. Wilson R, Aminian A, Tahrani AA. Metabolic surgery: a clinical update. *Diabetes Obes Metab* 2021;**23**:63–83. https://doi.org/10.1111/dom.14235
3. Telese A, Sehgal V, Magee CG, Naik S, Alqahtani SA, Lovat LB, Haidry RJ. Bariatric and metabolic endoscopy: a new paradigm. *Clin Transl Gastroenterol* 2021;**12**:e00364. https://doi.org/10.14309/ctg.0000000000000364
4. Simons M, Sharaiha RZ. Updates in metabolic bariatric endoscopy. *Dig Endosc* 2024;**36**:107–15. https://doi.org/10.1111/den.14633
5. World Health Organization. *Obesity*. 2024. URL: www.who.int/health-topics/obesity/#tab=tab_1 (accessed 29 February 2024).
6. National Institute for Health and Care Excellence. *Obesity: What Is It?* 2023. URL: https://cks.nice.org.uk/topics/obesity/background-information/definition/#:~:text=Different%20weight%20classes%20are%20defined,%E2%80%9339.9%20kg%2Fm2 (accessed 29 February 2024).
7. World Health Organisation Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;**363**:157–63. https://doi.org/10.1016/S0140-6736(03)15268-3
8. National Institute for Health and Care Excellence. *Obesity: Identification, Assessment and Management*. 2023. URL: www.nice.org.uk/guidance/cg189/ (accessed 29 February 2024).
9. Khan I, Chong M, Le A, Mohammadi-Shemirani P, Morton R, Brinza C, *et al*. Surrogate adiposity markers and mortality. *JAMA Netw Open* 2023;**6**:e2334836. https://doi.org/10.1001/jamanetworkopen.2023.34836
10. Khanna D, Khanna S, Khanna P, Kahar P, Patel BM. Obesity: a chronic low-grade inflammation and its markers. *Cureus* 2022;**14**:e22711. https://doi.org/10.7759/cureus.22711
11. World Obesity Federation. *World Obesity Atlas*. 2023. URL: https://data.worldobesity.org/publications/WOF-Obesity-Atlas-V5.pdf (accessed 29 February 2024).
12. NHS England. *Statistics on Obesity, Physical Activity and Diet, England, 2020*. 2020. URL: https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/england-2020#:~:text=The%20majority%20of%20adults%20were,of%20women%20who%20were%20obese.&text=Prevalence%20was%20over%20twice%20as,than%20the%20least%20deprived%20areas (accessed 29 February 2024).
13. Office for Health Improvement and Disparities. *Ethnicity Facts and Figures: Overweight Adults*. 2023. URL: www.ethnicity-facts-figures.service.gov.uk/health/diet-and-exercise/overweight-adults/latest/ (accessed 29 February 2024).
14. Abdelaal M, le Roux CW, Docherty NG. Morbidity and mortality associated with obesity. *Ann Transl Med* 2017;**5**:161. https://doi.org/10.21037/atm.2017.03.107
15. Bhaskaran K, Dos-Santos-Silva I, Leon DA, Douglas IJ, Smeeth L. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3.6 million adults in the UK. *Lancet Diabetes Endocrinol* 2018;**6**:944–53. https://doi.org/10.1016/S2213-8587(18)30288-2
16. NHS England. *Overview Obesity*. 2023. URL: www.nhs.uk/conditions/obesity/ (accessed 29 February 2024).
17. Taylor VH, Forhan M, Vigod SN, McIntyre RS, Morrison KM. The impact of obesity on quality of life. *Best Pract Res Clin Endocrinol Metab* 2013;**27**:139–46. https://doi.org/10.1016/j.beem.2013.04.004

18. Public Health England. *Adult Obesity and Type 2 Diabetes*. 2014. URL: https://assets.publishing.service.gov.uk/media/5a7f069140f0b6230268d059/Adult_obesity_and_type_2_diabetes_.pdf (accessed 4 March 2024).
19. Kitahara CM, Flint AJ, Berrington de Gonzalez A, Bernstein L, Brotzman M, MacInnis RJ, *et al*. Association between class III obesity (BMI of 40–59 kg/m^2) and mortality: a pooled analysis of 20 prospective studies. *PLOS Med* 2014;**11**:e1001673. https://doi.org/10.1371/journal.pmed.1001673
20. Le Brocq S, Clare K, Bryant M, Roberts K, Tahrani AA, writing group form Obesity UK, *et al*. Obesity and COVID-19: a call for action from people living with obesity. *Lancet Diabetes Endocrinol* 2020;**8**:652–4. https://doi.org/10.1016/S2213-8587(20)30236-9
21. Mahase E. Global cost of overweight and obesity will hit $4.32tn a year by 2035, report warns. *BMJ* 2023;**380**:523. https://doi.org/10.1136/bmj.p523
22. Public Health England. *Health Matters: Obesity and the Food Environment*. 2017. URL: www.gov.uk/government/publications/health-matters-obesity-and-the-food-environment/health-matters-obesity-and-the-food-environment--2 (accessed 4 March 2024).
23. Tremmel M, Gerdtham UG, Nilsson PM, Saha S. Economic burden of obesity: a systematic literature review. *Int J Environ Res Public Health* 2017;**14**:435. https://doi.org/10.3390/ijerph14040435
24. Wharton S, Lau DCW, Vallis M, Sharma AM, Biertho L, Campbell-Scherer D, *et al*. Obesity in adults: a clinical practice guideline. *CMAJ* 2020;**192**:E875–91. https://doi.org/10.1503/cmaj.191707
25. Hazlehurst JM, Logue J, Parretti HM, Abbott S, Brown A, Pournaras DJ, Tahrani AA. Developing integrated clinical pathways for the management of clinically severe adult obesity: a critique of NHS England policy. *Curr Obes Rep* 2020;**9**:530–43. https://doi.org/10.1007/s13679-020-00416-8
26. Ryan DH, Yockey SR. Weight loss and improvement in comorbidity: differences at 5%, 10%, 15%, and over. *Curr Obes Rep* 2017;**6**:187–94. https://doi.org/10.1007/s13679-017-0262-y
27. Fildes A, Charlton J, Rudisill C, Littlejohns P, Prevost AT, Gulliford MC. Probability of an obese person attaining normal body weight: cohort study using electronic health records. *Am J Public Health* 2015;**105**:e54–9. https://doi.org/10.2105/AJPH.2015.302773
28. Fothergill E, Guo J, Howard L, Kerns JC, Knuth ND, Brychta R, *et al*. Persistent metabolic adaptation 6 years after 'The Biggest Loser' competition. *Obesity (Silver Spring)* 2016;**24**:1612–9. https://doi.org/10.1002/oby.21538
29. Guo J, Brager DC, Hall KD. Simulating long-term human weight-loss dynamics in response to calorie restriction. *Am J Clin Nutr* 2018;**107**:558–65. https://doi.org/10.1093/ajcn/nqx080
30. Hall KD, Guo J. Obesity energetics: body weight regulation and the effects of diet composition. *Gastroenterology* 2017;**152**:1718–27.e3. https://doi.org/10.1053/j.gastro.2017.01.052
31. Hall KD, Kahan S. Maintenance of lost weight and long-term management of obesity. *Med Clin North Am* 2018;**102**:183–97. https://doi.org/10.1016/j.mcna.2017.08.012
32. Mann T, Tomiyama AJ, Westling E, Lew AM, Samuels B, Chatman J. Medicare's search for effective obesity treatments: diets are not the answer. *Am Psychol* 2007;**62**:220–33. https://doi.org/10.1037/0003-066X.62.3.220
33. Sumithran P, Prendergast LA, Delbridge E, Purcell K, Shulkes A, Kriketos A, Proietto J. Long-term persistence of hormonal adaptations to weight loss. *N Engl J Med* 2011;**365**:1597–604. https://doi.org/10.1056/NEJMoa1105816
34. Carlsson LMS, Sjoholm K, Jacobson P, Andersson-Assarsson JC, Svensson PA, Taube M, *et al*. Life expectancy after bariatric surgery in the Swedish obese subjects study. *N Engl J Med* 2020;**383**:1535–43. https://doi.org/10.1056/NEJMoa2002449

35. Pi-Sunyer X, Astrup A, Fujioka K, Greenway F, Halpern A, Krempf M, *et al*. SCALE obesity and prediabetes NN8022-1839 study group a randomized, controlled trial of 3.0 mg of liraglutide in weight management. *N Engl J Med* 2015;**373**:11–22. https://doi.org/10.1056/NEJMoa1411892
36. National Institute for Health and Care Excellence. *Semaglutide for Managing Overweight and Obesity*. 2023. URL: www.nice.org.uk/guidance/ta875/ (accessed 4 March 2024).
37. National Institute for Health and Care Excellence. *Liraglutide for Managing Overweight and Obesity*. 2020. URL: www.nice.org.uk/guidance/ta664/ (accessed 4 March 2024).
38. National Institute for Health and Care Excellence. *Pharmacological Interventions*. URL: www.nice.org.uk/guidance/cg189/chapter/Recommendations#pharmacological-interventions (accessed 29 February 2024).
39. The United Kingdom National Bariatric Surgery Registry. *Third Registry Report*. 2020. URL: https://e-dendrite.com/Publishing/Reports/Bariatric/NBSR2020.pdf (accessed 4 March 2024).
40. Colquitt JL, Pickett K, Loveman E, Frampton GK. Surgery for weight loss in adults. *Cochrane Database Syst Rev* 2014;**2014**:CD003641. https://doi.org/10.1002/14651858.CD003641.pub4
41. Yin J, Hou X. Complications of laparoscopic versus open bariatric surgical interventions in obesity management. *Cell Biochem Biophys* 2014;**70**:721–8. https://doi.org/10.1007/s12013-014-0041-2
42. Gudur AR, Geng CX, Kshatri S, Martin D, Haug R, Radlinski M, *et al*. Comparison of endoscopic sleeve gastroplasty versus surgical sleeve gastrectomy: a Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program database analysis. *Gastrointest Endosc* 2023;**97**:11–21.e4. https://doi.org/10.1016/j.gie.2022.07.017
43. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, *et al*. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. *Health Technol Assess* 2018;**22**:1–246. https://doi.org/10.3310/hta22680
44. O'Brien PE, Hindle A, Brennan L, Skinner S, Burton P, Smith A, *et al*. Long-term outcomes after bariatric surgery: a systematic review and meta-analysis of weight loss at 10 or more years for all bariatric procedures and a single-centre review of 20-year outcomes after adjustable gastric banding. *Obes Surg* 2019;**29**:3–14. https://doi.org/10.1007/s11695-018-3525-0
45. National Bariatric Surgery Registry. *Surgeon Specific Outcome Reports for NHS Bariatric Surgery*. 2022. URL: https://nbsr.e-dendrite.com/ (accessed 1 February 2024).
46. Borisenko O, Colpan Z, Dillemans B, Funch-Jensen P, Hedenbro J, Ahmed AR. Clinical indications, utilization, and funding of bariatric surgery in Europe. *Obes Surg* 2015;**25**:1408–16. https://doi.org/10.1007/s11695-014-1537-y
47. Public Health England. *Weight Management Services: National Mapping*. 2015. URL: www.gov.uk/government/publications/weight-management-services-national-mapping (accessed 4 March 2024).
48. Rubin JK, Hinrichs-Krapels S, Hesketh R, Martin A, Herman WH, Rubino F. Identifying barriers to appropriate use of metabolic/bariatric surgery for type 2 diabetes treatment: policy lab results. *Diabetes Care* 2016;**39**:954–63. https://doi.org/10.2337/dc15-2781
49. Bazerbachi F, Vargas Valls EJ, Abu Dayyeh BK. Recent clinical results of endoscopic bariatric therapies as an obesity intervention. *Clin Endosc* 2017;**50**:42–50. https://doi.org/10.5946/ce.2017.013
50. Choi HS, Chun HJ. Recent trends in endoscopic bariatric therapies. *Clin Endosc* 2017;**50**:11–6. https://doi.org/10.5946/ce.2017.007
51. Stimac D, Majanovic SK. Endoscopic approaches to obesity. *Dig Dis* 2012;**30**:187–95. https://doi.org/10.1159/000336683.
52. Jung Y. Role of endoscopic gastroplasty techniques in the management of obesity. *Clin Endosc* 2017;**50**:21–5. https://doi.org/10.5946/ce.2016.147

53. Kral J, Machytka E, Horka V, Selucka J, Dolecek F, Spicak J, *et al*. Endoscopic treatment of obesity and nutritional aspects of bariatric endoscopy. *Nutrients* 2021;**13**:4268. https://doi.org/10.3390/nu13124268

54. Pruijssers S, van Heurn E, Bouvy N. Endoluminal Techniques to Treat Obesity. In Francisco M, Sánchez Margallo JASM, editors. *Recent Advances in Laparoscopic Surgery*. London: IntechOpen; 2019.

55. Qureshi H, Saeed N, Jovani M. Updates in endoscopic bariatric and metabolic therapies. *J Clin Med* 2023;**12**:1126. https://doi.org/10.3390/jcm12031126

56. Stimac D, Klobucar Majanovic S, Belancic A. Endoscopic treatment of obesity: from past to future [published online ahead of print January 20 2020]. *Dig Dis* 2020. https://doi.org/10.1159/000505394

57. Abu Dayyeh BK, Acosta A, Camilleri M, Mundi MS, Rajan E, Topazian MD, Gostout CJ. Endoscopic sleeve gastroplasty alters gastric physiology and induces loss of body weight in obese individuals. *Clin Gastroenterol Hepatol* 2017;**15**:37–43.e1. https://doi.org/10.1016/j.cgh.2015.12.030

58. Dolan RD, Schulman AR. Endoscopic approaches to obesity management. *Annu Rev Med* 2022;**73**:423–38. https://doi.org/10.1146/annurev-med-042320-125832

59. Reja D, Zhang C, Sarkar A. Endoscopic bariatrics: current therapies and future directions. *Transl Gastroenterol Hepatol* 2022;**7**:21. https://doi.org/10.21037/tgh.2020.03.09

60. Shenoy A, Schulman AR. Advances in endobariatrics: past, present, and future. *Gastroenterol Rep (Oxf)* 2023;**11**:goad043. https://doi.org/10.1093/gastro/goad043

61. De Siena M, Polidori G, Vincenzo B, Pontecorvi V, Matto MV, Carlino G, *et al*. Overstitch versus Endomina for endoscopic sleeve gastroplasty. *Endoscopy* 2023;**55**:S165.

62. Sullivan S, Swain JM, Woodman G, Antonetti M, De La Cruz-Munoz N, Jonnalagadda SS, *et al*. Randomized sham-controlled trial evaluating efficacy and safety of endoscopic gastric plication for primary obesity: the ESSENTIAL trial. *Obesity (Silver Spring)* 2017;**25**:294–301. https://doi.org/10.1002/oby.21702

63. Crossan K, Sheer AJ. *Intragastric Balloon*. 2024. URL: www.ncbi.nlm.nih.gov/books/NBK578184/ (accessed 4 March 2024).

64. Machytka E, Buzga M, Zonca P, Lautz DB, Ryou M, Simonson DC, Thompson CC. Partial jejunal diversion using an incisionless magnetic anastomosis system: 1-year interim results in patients with obesity and diabetes. *Gastrointest Endosc* 2017;**86**:904–12. https://doi.org/10.1016/j.gie.2017.07.009

65. Goyal H, Kopel J, Perisetti A, Mann R, Ali A, Tharian B, *et al*. Endobariatric procedures for obesity: clinical indications and available options. *Ther Adv Gastrointest Endosc* 2021;**14**:984627. https://doi.org/10.1177/2631774520984627

66. National Institute for Health and Care Excellence. *Endoscopic Sleeve Gastroplasty for Obesity*. 2024. URL: www.nice.org.uk/guidance/ipg783 (accessed 4 March 2024).

67. National Institute for Health and Care Excellence. *Implantation of a Duodenal–Jejunal Bypass Liner for Managing Type 2 Diabetes*. 2015. URL: www.nice.org.uk/guidance/ipg518 (accessed 4 March 2024).

68. National Institute for Health and Care Excellence. *Swallowable Gastric Balloon Capsule for Weight Loss*. 2020. URL: www.nice.org.uk/guidance/IPG684/chapter/1-Recommendations (accessed 4 March 2024).

69. Lexchin J, Mintzes B. Semaglutide: a new drug for the treatment of obesity. *Drug Ther Bull* 2023;**61**:182–8. https://doi.org/10.1136/dtb.2023.000007

70. Dretzke J, Tahrani A, Singhal R, Moore D, Frew E, Price M, *et al*. *Systematic Review of Clinical and Cost-Effectiveness of Endoscopic Treatments for Obesity to Inform a Model-based Cost-effectiveness Analysis*. National Institute for Health and Care Research; 2022. URL: www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022302942 (accessed 4 Narch 2024).

71. Mourad Ouzzani HH, Zbys F, Ahmed E. Rayyan: a web and mobile app for systematic reviews. *Syst Rev* 2016;**5**:210. https://doi.org/10.1186/s13643-016-0384-4

72. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;**372**:n71. https://doi.org/10.1136/bmj.n71
73. Di Angelantonio E, Bhupathiraju ShN, Wormser D, Gao P, Kaptoge S, Berrington de Gonzalez A, *et al*. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet* 2016;**388**:776–86. https://doi.org/10.1016/S0140-6736(16)30175-1
74. Grover SA, Kaouache M, Rempel P, Joseph L, Dawes M, Lau DC, Lowensteyn I. Years of life lost and healthy life-years lost from diabetes and cardiovascular disease in overweight and obese people: a modelling study. *Lancet Diabetes Endocrinol* 2015;**3**:114–22. https://doi.org/10.1016/S2213-8587(14)70229-3
75. Gulliford MC, Charlton J, Prevost T, Booth H, Fildes A, Ashworth M, *et al*. Costs and outcomes of increasing access to bariatric surgery: cohort study and cost-effectiveness analysis using electronic health records. *Value Health* 2017;**20**:85–92. https://doi.org/10.1016/j.jval.2016.08.734
76. *NICE Says Non-Invasive Weight Loss Procedure Can Be an Option to Treat Obesity*. Press release. URL: Non-invasive weight loss procedure can be an option to treat obesity | NICE (accessed 1 January 2024).
77. Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, *et al*. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess* 2004;**8**:iii–v, ix. https://doi.org/10.3310/hta8360
78. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: consensus on health economic criteria. *Int J Technol Assess Health Care* 2005;**21**:240–5.
79. Kelly J, Menon V, O'Neill F, Elliot L, Combe E, Drinkwater W, *et al*. UK cost-effectiveness analysis of endoscopic sleeve gastroplasty versus lifestyle modification alone for adults with class II obesity. *Int J Obes (Lond)* 2023;**47**:1161–70. https://doi.org/10.1038/s41366-023-01374-6
80. Mital S, Nguyen HV. Cost-effectiveness of procedure-less intragastric balloon therapy as substitute or complement to bariatric surgery. *PLOS ONE* 2021;**16**:e0254063. https://doi.org/10.1371/journal.pone.0254063
81. Mital S, Nguyen HV. Incremental cost-effectiveness of aspiration therapy vs bariatric surgery and no treatment for morbid obesity. *Am J Gastroenterol* 2019;**114**:1470–7. https://doi.org/10.14309/ajg.0000000000000359
82. Stephenson J, Smith CM, Kearns B, Haywood A, Bissell P. The association between obesity and quality of life: a retrospective analysis of a large-scale population-based cohort study. *BMC Public Health* 2021;**21**:1990. https://doi.org/10.1186/s12889-021-12009-8
83. Ienca R, Al Jarallah M, Caballero A, Giardiello C, Rosa M, Kolmer S, *et al*. The procedureless elipse gastric balloon program: multicenter experience in 1770 consecutive patients. *Obes Surg* 2020;**30**:3354–62. https://doi.org/10.1007/s11695-020-04539-8
84. Rowen D, Brazier J, Roberts J. Mapping SF-36 onto the EQ-5D index: how reliable is the relationship? *Health Qual Life Outcomes* 2009;**7**:27. https://doi.org/10.1186/1477-7525-7-27
85. Abu Dayyeh BK, Bazerbachi F, Vargas EJ, Sharaiha RZ, Thompson CC, Thaemert BC, *et al*.; MERIT Study Group. Endoscopic sleeve gastroplasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial. *Lancet* 2022;**400**:441–51. https://doi.org/10.1016/S0140-6736(22)01280-6
86. Alsumali A, Eguale T, Bairdain S, Samnaliev M. Cost-effectiveness analysis of bariatric surgery for morbid obesity. *Obes Surg* 2018;**28**:2203–14. https://doi.org/10.1007/s11695-017-3100-0
87. Campbell J, McGarry LA, Shikora SA, Hale BC, Lee JT, Weinstein MC. Cost-effectiveness of laparoscopic gastric banding and bypass for morbid obesity. *Am J Manag Care* 2010;**16**:e174–87.
88. Athanasiadis DI, Martin A, Kapsampelis P, Monfared S, Stefanidis D. Factors associated with weight regain post-bariatric surgery: a systematic review. *Surg Endosc* 2021;**35**:4069–84. https://doi.org/10.1007/s00464-021-08329-w
89. Nystrom M, Machytka E, Noren E, Testoni PA, Janssen I, Turro Homedes J, *et al*. Aspiration therapy as a tool to treat obesity: 1- to 4-year results in a 201-patient multi-center post-market European Registry Study. *Obes Surg* 2018;**28**:1860–8. https://doi.org/10.1007/s11695-017-3096-5

90. Chang SH, Stoll CR, Song J, Varela JE, Eagon CJ, Colditz GA. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003–2012. *JAMA Surg* 2014;**149**:275–87. https://doi.org/10.1001/jamasurg.2013.3654

91. Office for National Statistics. *Mortality Rates (qx), Males and Females, Ages 0 to 100, UK, England, Wales, Scotland and Northern Ireland, 1980–1982 to 2018–2020, 2021, 2022*. 2023. URL: www.beta.ons.gov.uk/file?uri=/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/datasets/mortalityratesqxbysingleyearofage/current/3yearqxtimeseries.xlsx (accessed 1 January 2024).

92. Borrell LN, Samuel L. Body mass index categories and mortality risk in US adults: the effect of overweight and obesity on advancing death. *Am J Public Health* 2014;**104**:512–9. https://doi.org/10.2105/AJPH.2013.301597

93. National Institute for Health and Care Excellence. *Tirzepatide for Treating Type 2 Diabetes*. 2023. URL: www.nice.org.uk/guidance/ta924 (accessed 19 March 2024).

94. Picot J, Jones J, Colquitt JL, Gospodarevskaya E, Loveman E, Baxter L, Clegg AJ. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. *Health Technol Assess* 2009;**13**:1–190, 215–357, iii–iv. https://doi.org/10.3310/hta13410

95. National Institute for Health and Care Excellence. *Guide to the Methods of Technology Appraisal*. 2013. URL: www.nice.org.uk/process/pmg9/chapter/foreword (accessed 1 January 2024).

96. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, *et al*.; ISPOR Health Economic Evaluation Publication Guidelines-CHEERS Good Reporting Practices Task Force. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) – explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. *Value Health* 2013;**16**:231–50. https://doi.org/10.1016/j.jval.2013.02.002

97. Jerome E, Giet L, Wiggins T, Graham Y, Pouwels S, Rajeev Y, *et al*. Global trends in BMS research using publication as a surrogate marker: a 30 year review. *Obes Res Clin Pract* 2023;**17**:271–4. https://doi.org/10.1016/j.orcp.2023.05.003

98. Mauro A, Lusetti F, Scalvini D, Bardone M, De Grazia F, Mazza S, *et al*. A comprehensive review on bariatric endoscopy: where we are now and where we are going. *Medicina (Kaunas)* 2023;**59**:636. https://doi.org/10.3390/medicina59030636

99. Carr P, Keighley T, Petocz P, Blumfield M, Rich GG, Cohen F, *et al*. Efficacy and safety of endoscopic sleeve gastroplasty and laparoscopic sleeve gastrectomy with 12+ months of adjuvant multidisciplinary support. *BMC Prim Care* 2022;**23**:26. https://doi.org/10.1186/s12875-022-01629-7

100. Beran A, Matar R, Jaruvongvanich V, Rapaka BB, Alalwan A, Portela R, *et al*. Comparative effectiveness and safety between endoscopic sleeve gastroplasty and laparoscopic sleeve gastrectomy: a meta-analysis of 6775 individuals with obesity. *Obes Surg* 2022;**32**:3504–12. https://doi.org/10.1007/s11695-022-06254-y

101. Haase CL, Eriksen KT, Lopes S, Satylganova A, Schnecke V, McEwan P. Body mass index and risk of obesity-related conditions in a cohort of 2.9 million people: evidence from a UK primary care database. *Obes Sci Pract* 2021;**7**:137–47. https://doi.org/10.1002/osp4.474

102. Sandhu H, Xu W, Olivieri AV, Lubker C, Smith I, Antavalis V. Once-weekly subcutaneous semaglutide 2.4 mg injection is cost-effective for weight management in the United Kingdom. *Adv Ther* 2023;**40**:1282–91. https://doi.org/10.1007/s12325-022-02423-8

103. Abramson A, Halperin F, Kim J, Traverso G. Quantifying the value of orally delivered biologic therapies: a cost-effectiveness analysis of oral semaglutide. *J Pharm Sci* 2019;**108**:3138–45. https://doi.org/10.1016/j.xphs.2019.04.022

104. Docimo S Jr, Aylward L, Albaugh VL, Afaneh C, El Djouzi S, Ali M, *et al*.; American Society for Metabolic and Bariatric Surgery Clinical Issues Committee. Endoscopic sleeve gastroplasty and its role in the treatment of obesity: a systematic review. *Surg Obes Relat Dis* 2023;**19**:1205–18. https://doi.org/10.1016/j.soard.2023.08.020

105. Singh S, de Moura DTH, Khan A, Bilal M, Chowdhry M, Ryan MB, *et al*. Intragastric balloon versus endoscopic sleeve gastroplasty for the treatment of obesity: a systematic review and meta-analysis. *Obes Surg* 2020;**30**:3010–29. https://doi.org/10.1007/s11695-020-04644-8

106. Wang HI, Han L, Jacobs R, Doran T, Holt RIG, Prady SL, *et al*. Healthcare resource use and costs for people with type 2 diabetes mellitus with and without severe mental illness in England: longitudinal matched-cohort study using the Clinical Practice Research Datalink. *Br J Psychiatry* 2022;**221**:402–9. https://doi.org/10.1192/bjp.2021.131

107. Galvain T, Patel S, Kabiri M, Tien S, Casali G, Pournaras DJ. Cost-effectiveness of bariatric and metabolic surgery, and implications of COVID-19 in the United Kingdom. *Surg Obes Relat Dis* 2021;**17**:1897–904. https://doi.org/10.1016/j.soard.2021.07.009

108. CPRD. *Primary Care Data for Public Health Research*. 2023. URL: https://cprd.com/primary-care-data-public-health-research (accessed 4 March 2024).

109. Shiekh SI, Harley M, Ghosh RE, Ashworth M, Myles P, Booth HP, Axson EL. Completeness, agreement, and representativeness of ethnicity recording in the United Kingdom's Clinical Practice Research Datalink (CPRD) and linked Hospital Episode Statistics (HES). *Popul Health Metr* 2023;**21**:3. https://doi.org/10.1186/s12963-023-00302-0

110. Alqahtani AR, Elahmedi M, Aldarwish A, Abdurabu HY, Alqahtani S. Endoscopic gastroplasty versus laparoscopic sleeve gastrectomy: a noninferiority propensity score-matched comparative study. *Gastrointest Endosc* 2022;**96**:44–50. https://doi.org/10.1016/j.gie.2022.02.050

111. Wölnerhanssen BK, Peterli R, Hurme S, Bueter M, Helmiö M, Juuti A, *et al*. Laparoscopic Roux-en-Y gastric bypass versus laparoscopic sleeve gastrectomy: 5-year outcomes of merged data from two randomized clinical trials (SLEEVEPASS and SM-BOSS). *Br J Surg* 2020;**108**:49–57. https://doi.org/10.1093/bjs/znaa011

112. Wilding JPH, Batterham RL, Davies M, Van Gaal LF, Kandler K, Konakli K, *et al*.; STEP 1 Study Group. Weight regain and cardiometabolic effects after withdrawal of semaglutide: the STEP 1 trial extension. *Diabetes Obes Metab* 2022;**24**:1553–64. https://doi.org/10.1111/dom.14725

113. Kotzampassi K, Grosomanidis V, Papakostas P, Penna S, Eleftheriadis E. 500 intragastric balloons: what happens 5 years thereafter? *Obes Surg* 2012;**22**:896–903. https://doi.org/10.1007/s11695-012-0607-2

114. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, *et al*.; SELECT Trial Investigators. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med* 2023;**389**:2221–32. https://doi.org/10.1056/NEJMoa2307563

115. World Health Organisation. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* 2000;**894**:i–xii, 1–253.

116. Wiggins T, Sharma O, Sarfaraz Y, Fry H, Baker J, Singhal R. Safety and efficacy of 12-month intra-gastric balloon-series of over 1100 patients. *Obes Surg* 2024;**34**:176–82. https://doi.org/10.1007/s11695-023-06953-0.

117. Ulger TG, Tayfur M, Cakiroglu FP, Ozcan C. A systematic review on intragastric balloons and TransPyloric shuttle in obesity treatment. *İzmir Kâtip Çelebi Üniv Sağlık Bilim Fakül Dergisi* 2022;**7**:321–9.

118. Saber AA, Shoar S, Almadani MW, Zundel N, Alkuwari MJ, Bashah MM, Rosenthal RJ. Efficacy of first-time intragastric balloon in weight loss: a systematic review and meta-analysis of randomized controlled trials. *Obes Surg* 2017;**27**:277–87. https://doi.org/10.1007/s11695-016-2296-8

119. Yorke E, Switzer NJ, Reso A, Shi X, de Gara C, Birch D, *et al*. Intragastric balloon for management of severe obesity: a systematic review. *Obes Surg* 2016;**26**:2248–54. https://doi.org/10.1007/s11695-016-2307-9

120. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the Economic Evaluation of Health Care Programmes*. Oxford: Oxford University Press; 2005.

121. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, *et al*. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017;**358**:j4008. https://doi.org/10.1136/bmj.j4008

122. Ding L, Fan Y, Li H, Zhang Y, Qi D, Tang S, *et al*. Comparative effectiveness of bariatric surgeries in patients with obesity and type 2 diabetes mellitus: a network meta-analysis of randomized controlled trials. *Obes Rev* 2020;**21**:e13030. https://doi.org/10.1111/obr.13030

123. Jung SH, Yoon JH, Choi HS, Nam SJ, Kim KO, Kim DH, *et al*.; Korean Research Group for Endoscopic Management of Metabolic Disorder and Obesity. Comparative efficacy of bariatric endoscopic procedures in the treatment of morbid obesity: a systematic review and network meta-analysis. *Endoscopy* 2020;**52**:940–54. https://doi.org/10.1055/a-1149-1862

124. Huberty V, Boskoski I, Bove V, Van Ouytsel P, Costamagna G, Barthet MA, Devière J. Endoscopic sutured gastroplasty in addition to lifestyle modification: short-term efficacy in a controlled randomised trial. *Gut* 2021;**70**:1479–85. https://doi.org/10.1136/gutjnl-2020-322026

125. Abu Dayyeh BK, Maselli DB, Rapaka B, Lavin T, Noar M, Hussan H, *et al*. Adjustable intragastric balloon for treatment of obesity: a multicentre, open-label, randomised clinical trial. *Lancet* 2021;**398**:1965–73. https://doi.org/10.1016/S0140-6736(21)02394-1

126. Courcoulas A, Abu Dayyeh BK, Eaton L, Robinson J, Woodman G, Fusco M, *et al*. Intragastric balloon as an adjunct to lifestyle intervention: a randomized controlled trial. *Int J Obes (Lond)* 2017;**41**:427–33. https://doi.org/10.1038/ijo.2016.229

127. Fuller NR, Pearson S, Lau NS, Wlodarczyk J, Halstead MB, Tee HP, *et al*. An intragastric balloon in the treatment of obese individuals with metabolic syndrome: a randomized controlled study. *Obesity (Silver Spring)* 2013;**21**:1561–70. https://doi.org/10.1002/oby.20414

128. Garvey WT, Batterham RL, Bhatta M, Buscemi S, Christensen LN, Frias JP, *et al*.; STEP 5 Study Group. Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. *Nat Med* 2022;**28**:2083–91. https://doi.org/10.1038/s41591-022-02026-4

129. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, *et al*.; STEP 1 Study Group. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med* 2021;**384**:989–1002. https://doi.org/10.1056/NEJMoa2032183

130. Higgins JPT, Li T, Deeks JJ. Chapter 6: Choosing Effect Measures and Computing Estimates of Effect. In Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 6.4 (Updated August 2023)*. London: Cochrane; 2023. URL: www.training.cochrane.org/handbook (accessed 2 July 2025).

131. Raudenbush SW. Analyzing Effect Sizes: Random-Effects Models. In Cooper H, Hedges LV, Valentine JC, editors. *The Handbook of Research Synthesis and Meta-Analysis*. 2nd edn. New York, NY: Russell Sage Foundation; 2009. pp. 295–316.

132. Hartung J, Knapp G. A refined method for the meta-analysis of controlled clinical trials with binary outcome. *Stat Med* 2001;**20**:3875–89. https://doi.org/10.1002/sim.1009

133. Bucher HC, Guyatt GH, Griffith LE, Walter SD. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol* 1997;**50**:683–91. https://doi.org/10.1016/s0895-4356(97)00049-8

134. Bhandari M, Kosta S, Reddy M, Mathur W, Neto MG, Bhandari M. Four-year outcomes for endoscopic sleeve gastroplasty from a single centre in India. *J Minim Access Surg* 2022;**19**:101–6. https://doi.org/10.4103/jmas.jmas_3_22

135. Queiroz Sander B, de Moura DTH, Alberti LR. Evaluation of the efficacy and safety of endoscopic sleeve gastroplasty (ESG) in the management of patients with obesity in a follow-up from 12 to 48 months. *United European Gastroenterol J* 2022;**10**:589

136. Lopez-Nava G, Asokkumar R, Bautista-Castano I, Laster J, Negi A, Fook-Chong S, *et al*. Endoscopic sleeve gastroplasty, laparoscopic sleeve gastrectomy, and laparoscopic greater curve plication: do they differ at 2 years? *Endoscopy* 2021;**53**:235–43. https://doi.org/10.1055/a-1224-7231

137. Lind R, Hage K, Ghanem M, Shah M, Vierkant RA, Jawad M, *et al*. Long-term outcomes of sleeve gastrectomy: weight recurrence and surgical non-responders. *Obes Surg* 2023;**33**:3028–34. https://doi.org/10.1007/s11695-023-06730-z

138. Genco A, Lopez-Nava G, Wahlen C, Maselli R, Cipriano M, Sanchez MM, *et al*. Multi-centre European experience with intragastric balloon in overweight populations: 13 years of experience. *Obes Surg* 2013;**23**:515–21. https://doi.org/10.1007/s11695-012-0829-3

139. de Miranda Neto AA, de Moura DTH, Ribeiro IB, Khan A, Singh S, da Ponte Neto AM, *et al*. Efficacy and safety of endoscopic sleeve gastroplasty at mid term in the management of overweight and obese patients: a systematic review and meta-analysis. *Obes Surg* 2020;**30**:1971–87. https://doi.org/10.1007/s11695-020-04449-9

140. Marincola G, Gallo C, Hassan C, Raffaelli M, Costamagna G, Bove V, *et al*. Laparoscopic sleeve gastrectomy versus endoscopic sleeve gastroplasty: a systematic review and meta-analysis. *Endosc Int Open* 2021;**9**:E87–95. https://doi.org/10.1055/a-1300-1085

141. Sharaiha RZ, Hajifathalian K, Kumar R, Saunders K, Mehta A, Ang B, *et al*. Five-year outcomes of endoscopic sleeve gastroplasty for the treatment of obesity. *Clin Gastroenterol Hepatol* 2021;**19**:1051–7.e2. https://doi.org/10.1016/j.cgh.2020.09.055

142. Zhao K, Liu J, Wang M, Yang H, Wu A. Safety and efficacy of laparoscopic sleeve gastrectomy versus laparoscopic Roux-en-Y gastric bypass: a systematic review and meta-analysis. *J Eval Clin Pract* 2020;**26**:290–8. https://doi.org/10.1111/jep.13170

143. Kumar SB, Hamilton BC, Wood SG, Rogers SJ, Carter JT, Lin MY. Is laparoscopic sleeve gastrectomy safer than laparoscopic gastric bypass? a comparison of 30-day complications using the MBSAQIP data registry. *Surg Obes Relat Dis* 2018;**14**:264–9. https://doi.org/10.1016/j.soard.2017.12.011

144. Kapur A, Thodiyil P. Primary laparoscopic sleeve gastrectomy versus gastric bypass: a propensity-matched comparison of 30-day outcomes. *Surg Obes Relat Dis* 2021;**17**:1369–82. https://doi.org/10.1016/j.soard.2021.01.022

145. Qin W, Yang J, Deng C, Ruan Q, Duan K. Efficacy and safety of semaglutide 2.4 mg for weight loss in overweight or obese adults without diabetes: an updated systematic review and meta-analysis including the 2-year STEP 5 trial. *Diabetes Obes Metab* 2023;**26**:911–23. https://doi.org/10.1111/dom.15386

146. Borisenko O, Adam D, Funch-Jensen P, Ahmed AR, Zhang R, Colpan Z, Hedenbro J. Bariatric surgery can lead to net cost savings to health care systems: results from a comprehensive European decision analytic model. *Obes Surg* 2015;**25**:1559–68. https://doi.org/10.1007/s11695-014-1567-5

147. Borisenko O, Lukyanov V, Ahmed AR. Cost-utility analysis of bariatric surgery. *Br J Surg* 2018;**105**:1328–37. https://doi.org/10.1002/bjs.10857

148. Borisenko O, Lukyanov V, Debergh I, Dillemans B. Cost-effectiveness analysis of bariatric surgery for morbid obesity in Belgium. *J Med Econ* 2018;**21**:365–73. https://doi.org/10.1080/13696998.2017.1419958

149. Borisenko O, Lukyanov V, Johnsen SP, Funch-Jensen P. Cost analysis of bariatric surgery in Denmark made with a decision-analytic model. *Dan Med J* 2017;**64**:A5401.

150. Borisenko O, Mann O, Dupree A. Cost-utility analysis of bariatric surgery compared with conventional medical management in Germany: a decision analytic modeling. *BMC Surg* 2017;**17**:87. https://doi.org/10.1186/s12893-017-0284-0

151. Elliot L, Frew E, Mollan SP, Mitchell JL, Yiangou A, Alimajstorovic Z, *et al*. Cost-effectiveness of bariatric surgery versus community weight management to treat obesity-related idiopathic intracranial hypertension: evidence from a single-payer healthcare system. *Surg Obes Relat Dis* 2021;**17**:1310–6. https://doi.org/10.1016/j.soard.2021.03.020

152. Klebanoff MJ, Chhatwal J, Nudel JD, Corey KE, Kaplan LM, Hur C. Cost-effectiveness of bariatric surgery in adolescents with obesity. *JAMA Surg* 2017;**152**:136–41. https://doi.org/10.1001/jamasurg.2016.3640

153. Lauren BN, Lim F, Krikhely A, Taveras EM, Woo Baidal JA, Bellows BK, Hur C. Estimated cost-effectiveness of medical therapy, sleeve gastrectomy, and gastric bypass in patients with severe obesity and type 2 diabetes. *JAMA Netw Open* 2022;**5**:e2148317. https://doi.org/10.1001/jamanetworkopen.2021.48317

154. Lucchese M, Borisenko O, Mantovani LG, Cortesi PA, Cesana G, Adam D, *et al*. Cost-utility analysis of bariatric surgery in Italy: results of decision-analytic modelling. *Obes Facts* 2017;**10**:261–72. https://doi.org/10.1159/000475842

155. Maklin S, Malmivaara A, Linna M, Victorzon M, Koivukangas V, Sintonen H. Cost-utility of bariatric surgery for morbid obesity in Finland. *Br J Surg* 2011;**98**:1422–9. https://doi.org/10.1002/bjs.7640

156. Meads DM, Hulme CT, Hall P, Hill AJ. The cost-effectiveness of primary care referral to a UK commercial weight loss programme. *Clin Obes* 2014;**4**:324–32. https://doi.org/10.1111/cob.12077

157. Picot J, Jones J, Colquitt JL, Loveman E, Clegg AJ. Weight loss surgery for mild to moderate obesity: a systematic review and economic evaluation. *Obes Surg* 2012;**22**:1496–506. https://doi.org/10.1007/s11695-012-0679-z

158. Wentworth JM, Dalziel KM, O'Brien PE, Burton P, Shaba F, Clarke PM, *et al*. Cost-effectiveness of gastric band surgery for overweight but not obese adults with type 2 diabetes in the U.S. *J Diabetes Complications* 2017;**31**:1139–44. https://doi.org/10.1016/j.jdiacomp.2017.04.009

159. Kim N, Wang J, Burudpakdee C, Song Y, Ramasamy A, Xie Y, *et al*. Cost-effectiveness analysis of semaglutide 2.4 mg for the treatment of adult patients with overweight and obesity in the United States. *J Manag Care Spec Pharm* 2022;**28**:740–52. https://doi.org/10.18553/jmcp.2022.28.7.740

160. Lee M, Lauren BN, Zhan T, Choi J, Klebanoff M, Abu Dayyeh B, *et al*. The cost-effectiveness of pharmacotherapy and lifestyle intervention in the treatment of obesity. *Obes Sci Pract* 2020;**6**:162–70. https://doi.org/10.1002/osp4.390

161. Veerman JL, Barendregt JJ, Forster M, Vos T. Cost-effectiveness of pharmacotherapy to reduce obesity. *PLOS ONE* 2011;**6**:e26051. https://doi.org/10.1371/journal.pone.0026051

162. Boyers D, Retat L, Jacobsen E, Avenell A, Aveyard P, Corbould E, *et al*.; and the REBALANCE Team. Cost-effectiveness of bariatric surgery and non-surgical weight management programmes for adults with severe obesity: a decision analysis model. *Int J Obes (Lond)* 2021;**45**:2179–90. https://doi.org/10.1038/s41366-021-00849-8

Appendix 1 Additional information for the map for evidence

Search strategies for map of evidence

Cochrane CENTRAL

#1 MeSH descriptor: [Obesity] explode all trees
#2 (obes*):ti,ab,kw
#3 MeSH descriptor: [Bariatrics] explode all trees
#4 (bariatric*):ti,ab,kw
#5 MeSH descriptor: [Bariatric Surgery] explode all trees
#6 (weight loss surgery):ti,ab,kw
#7 (gastric balloon):ti,ab,kw
#8 (intragastric balloon* or gastric balloon*):ti,ab,kw
#9 (adjustable balloon system or swallowable balloon or fluid-filled balloon or gas-filled balloon):ti,ab,kw
#10 (transpyloric shuttle):ti,ab,kw
#11 (POSE):ti,ab,kw
#12 (primary obesity surgery endolum*nal):ti,ab,kw
#13 ((gastric* or greater curv*) NEAR plicat*):ti,ab,kw
#14 ((endoscopic or endolum*nal) NEAR (sutur* or stitch*)):ti,ab,kw
#15 ((endoscopic or gastric or endolum*nal or curv*) NEAR plication):ti,ab,kw
#16 (gastroplication):ti,ab,kw
#17 (aspiration device*):ti,ab,kw
#18 (aspiration therap*):ti,ab,kw
#19 (bypass NEAR (sleeve* or liner*)):ti,ab,kw
#20 (bypass NEAR magnet*):ti,ab,kw
#21 ((endoscop* or endolum*nal) NEAR (gastrectomy or gastroplasty or liner or sleeve)):ti,ab,kw
#22 (ESG):ti,ab,kw
#23 (endoscopic gastric sleeve*):ti,ab,kw
#24 ((duodenaljejunal or duodenojejunal or duodenal-jejunal or gastroduodenaljejunal or gastroduodenojejunal or gastroduodenal-jejunal) NEAR (liner or bypass or sleeve)):ti,ab,kw
#25 (duodenal mucosal resurfac*):ti,ab,kw
#26 ((endoscopic or gastric or intragastric) NEAR (botox or botulinum)):ti,ab,kw
#27 (gastric electrical stimulation or gastric pacing or implantable gastric stimulation or vagal nerve blockade or vbloc):ti,ab,kw
#28 (transoral or trans-oral):ti,ab,kw
#29 (gastric volume reduction):ti,ab,kw
#30 (TOGA or TRIM or TERIS):ti,ab,kw
#31 (endomina or endobarrier):ti,ab,kw
#32 (aspireassist):ti,ab,kw
#33 (full sense):ti,ab,kw
#34 (endocinch or overstitch or stomaphyx or endozip or restore sutur*):ti,ab,kw
#35 (heliosphere bag or ellipse balloon or elipse balloon or allurion or orbera or obalon):ti,ab,kw
#36 (silimed balloon or reshape balloon or endball or spatz or medsil or ullorex or satisphere or endosphere):ti,ab,kw
#37 (gelesis or plenity):ti,ab,kw
#38 (magnetic anastomos*):ti,ab,kw
#39 (gastric NEAR balloon):ti,ab,kw
#40 #1 OR #2 OR #3 OR #4 OR #5 OR #6

#41 #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39
#42 #40 AND #41

EMBASE (Ovid)

1 exp obesity/or obes*.ti,ab.
2 exp bariatrics/or bariatric*.ti,ab.
3 exp bariatric surgery/or weight loss surgery.ti,ab.
4 exp gastric balloon/
5 (intragastric balloon* or gastric balloon*).ti,ab.
6 (adjustable balloon system or swallowable balloon or fluid-filled balloon or gas-filled balloon).ti,ab.
7 transpyloric shuttle.ti,ab.
8 POSE.ti,ab.
9 primary obesity surgery endolum*nal.ti,ab.
10 ((gastric* or greater curv*) adj3 plicat*).ti,ab.
11 ((endoscopic or endolum*nal) adj3 (sutur* or stitch*)).ti,ab.
12 ((endoscopic or gastric or endolum*nal or curv*) adj3 plication).ti,ab.
13 gastroplication.ti,ab.
14 aspiration device*.ti,ab.
15 aspiration therap*.ti,ab.
16 (bypass adj2 (sleeve* or liner*)).ti,ab.
17 (bypass adj4 magnet*).ti,ab.
18 ((endoscop* or endolum*nal) adj3 (gastrectomy or gastroplasty or liner or sleeve)).ti,ab.
19 ESG.ti,ab.
20 endoscopic gastric sleeve*.ti,ab.
21 ((duodenaljejunal or duodenojejunal or duodenal-jejunal or gastroduodenaljejunal or gastroduodenojejunal or gastroduodenal-jejunal) adj3 (liner or bypass or sleeve)).ti,ab.
22 duodenal mucosal resurfac*.ti,ab.
23 ((endoscopic or gastric or intragastric) adj3 (botox or botulinum)).ti,ab.
24 (gastric electrical stimulation or gastric pacing or implantable gastric stimulation or vagal nerve blockade or vbloc).ti,ab.
25 (transoral or trans-oral).ti,ab.
26 gastric volume reduction.ti,ab.
27 (TOGA or TRIM or TERIS).ti,ab.
28 (endomina or endobarrier).ti,ab.
29 aspireassist.ti,ab.
30 full sense.ti,ab.
31 (endocinch or overstitch or stomaphyx or endozip or restore sutur*).ti,ab.
32 (heliosphere bag or ellipse balloon or elipse balloon or allurion or orbera or obalon).ti,ab.
33 (silimed balloon or reshape balloon or endball or spatz or medsil or ullorex or satisphere or endosphere).ti,ab.
34 (gelesis or plenity).ti,ab.
35 magnetic anastomos*.ti,ab.
36 (gastric adj3 balloon).ti,ab.
37 1 or 2 or 3
38 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
39 37 and 38

Ovid MEDLINE(R) and In-Process, In-Data-Review and Other Non-Indexed Citations

1 exp obesity/or obes*.ti,ab.

2 exp bariatrics/or bariatric*.ti,ab.
3 exp bariatric surgery/or weight loss surgery.ti,ab.
4 gastric balloon/
5 (intragastric balloon* or gastric balloon*).ti,ab.
6 (adjustable balloon system or swallowable balloon or fluid-filled balloon or gas-filled balloon).ti,ab.
7 transpyloric shuttle.ti,ab.
8 POSE.ti,ab.
9 primary obesity surgery endolum*nal.ti,ab.
10 ((gastric* or greater curv*) adj3 plicat*).ti,ab.
11 ((endoscopic or endolum*nal) adj3 (sutur* or stitch*)).ti,ab.
12 ((endoscopic or gastric or endolum*nal or curv*) adj3 plication).ti,ab.
13 gastroplication.ti,ab.
14 aspiration device*.ti,ab.
15 aspiration therap*.ti,ab.
16 (bypass adj2 (sleeve* or liner*)).ti,ab.
17 (bypass adj4 magnet*).ti,ab.
18 ((endoscop* or endolum*nal) adj3 (gastrectomy or gastroplasty or liner or sleeve)).ti,ab.
19 ESG.ti,ab.
20 endoscopic gastric sleeve*.ti,ab.
21 ((duodenaljejunal or duodenojejunal or duodenal-jejunal or gastroduodenaljejunal or gastroduodenojejunal or gastroduodenal-jejunal) adj3 (liner or bypass or sleeve)).ti,ab.
22 duodenal mucosal resurfac*.ti,ab.
23 ((endoscopic or gastric or intragastric) adj3 (botox or botulinum)).ti,ab.
24 (gastric electrical stimulation or gastric pacing or implantable gastric stimulation or vagal nerve blockade or vbloc).ti,ab.
25 (transoral or trans-oral).ti,ab.
26 gastric volume reduction.ti,ab.
27 (TOGA or TRIM or TERIS).ti,ab.
28 (endomina or endobarrier).ti,ab.
29 aspireassist.ti,ab.
30 full sense.ti,ab.
31 (endocinch or overstitch or stomaphyx or endozip or restore sutur*).ti,ab.
32 (heliosphere bag or ellipse balloon or elipse balloon or allurion or orbera or obalon).ti,ab.
33 (silimed balloon or reshape balloon or endball or spatz or medsil or ullorex or satisphere or endosphere).ti,ab.
34 (gelesis or plenity).ti,ab.
35 magnetic anastomos*.ti,ab.
36 (gastric adj3 balloon).ti,ab.
37 1 or 2 or 3
38 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
39 37 and 38

Inclusion and exclusion criteria for the map of evidence

TABLE 20 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Population	
People of any age with obesity (as defined by study authors) with or without obesity-related comorbidities	Animal studies
Intervention	
Any endoscopic treatments for obesity Studies reporting *swallowable* balloons Studies reporting endoscopic procedures as a bridge to WL in preparation for bariatric surgery Studies reporting endoscopic procedures to address weight regain, WL plateau or other obesity-related outcomes after bariatric surgery Studies reporting intragastric balloon removal	Swallowable pseudobezoars Vagal nerve stimulation or blockade Revisional or 'redo' procedure carried out endoscopically immediately or soon after bariatric surgery, for example to correct an AE such as repairing leaks Studies using balloons solely as a means of measuring stomach capacity or satiety when the outcomes such as weight change, complications or safety are not included Endoscopy as an exploratory assessment in preparation for bariatric surgery
Comparator	
Any comparator (alternative endoscopic obesity treatment, sham treatment, bariatric surgery, lifestyle intervention, medical management or no treatment) No comparator	N/A
Outcomes	
Any one or more of:	
Clinical effectiveness: any weight-related outcome (including BMI); changes in diabetes status or treatment and/or CVD risk; AEs; reintervention/revisional surgery; any obesity-related morbidity; mortality (all cause, CVD-related and cancer-related); QoL assessed by any tool; micronutrient status. Composite outcomes that may include any of the above	Any other outcome not listed
Cost-effectiveness: costs; QALYs; DALYs; life years gained; measures of cost-effectiveness (e.g. incremental cost effectiveness ratios, net monetary benefit); utilities	Solely qualitative outcomes
Study design	
Any study design Ongoing studies, study protocols Cost, cost-effectiveness and health economic studies	Qualitative studies Single case reports Commentaries, comments, letters, etc., with no primary study data Narrative (non-systematic) reviews Systematic reviews
Publication type	
Any (including fully published or conference abstracts, and unpublished studies)	N/A

Excluded articles from the map of evidence

TABLE 21 Excluded articles from the map of evidence with reasons

Study ID	Reason for exclusion
Abu Dayyeh BK, Maselli DB, Rapaka B, Lavin T, Noar M, Hussan H, *et al*. Adjustable intragastric balloon for treatment of obesity: a multicentre, open-label, randomised clinical trial. *Lancet* 2021;**398**:1965–73	Duplicate
Anon. AspireAssist: a new device for weight loss. *Med Lett Drugs Ther* 2016;**58**:109–10	Letter
Anon. A gastric balloon for treatment of obesity. *Med Lett Drug Therap* 1986;**28**: 77–8	Letter
Asokkumar R, Babu MP, Bautista I, Lopez-Nava G. The use of the over stitch for bariatric weight loss in Europe. *Gastrointest Endosc Clin N Am* 2020;**30**:129–45	Review (Publication type)
Carvalho GL, Carvalho G, Ferreira M, Moraes C, Rocha RG, Lima D, *et al*. Intragastric balloons are effective for the weight control in non obese patients. *Obes Surg* 2009;**19**:1039	Population overweight, not obese (BMI < 30)
Carvalho GL, Novaes ML, Okazaki MO, Fernandes Junior FAM, Rocha RG, Silva JSN, *et al*. Intragastric balloons are effective for the weight control in non obese patients. *Surg Endosc* 2011;**25**:S129	Population overweight, not obese (BMI < 30)
Carvalho GL, Barros CB, Moraes CE, Okazaki M, de Novaes Lima Ferreira M, Silva JSN, *et al*. The use of an improved intragastric balloon technique to reduce weight in pre-obese patients: preliminary results. *Obes Surg* 2011;**21**:924	Population overweight, not obese (BMI < 30)
Carvalho GL, Junior FA, Moraes CE, Silva JS, Lima DL, Chaves EC, *et al*. Intragastric silicone water filled balloon is safe and effective to reduce weight in pre-obese patients. *Surg Endosc* 2011;**25**:S256	Population overweight, not obese (BMI < 30)
de Castro ML, Pineda JR, Cid L, Estevez P, Rodriguez-Prada JI, Morales MJ, *et al*. Safety and effectiveness of gastric balloons associated with a hypocaloric diet for the treatment of obesity. *Rev Esp Enferm Dig* 2013;**105**:529	Duplicate
Donadio F, Sburlati LF, Masserini B, Lunati EM, Lattuada E, Zappa MA, *et al*. Metabolic parameters after BioEnterics Intragastric Balloon placement in obese patients. *J Endocrinol Invest* 2009;**32**:165–8	Duplicate
Ferhatoglu MF, Kartal A, Filiz AI, Kebudi A. Correction to: the positive effects of a calorie-restricting high-protein diet combined with intragastric botulinum toxin type A application among morbidly obese patients: a prospective, obariatric surgeryervational analysis of eighty-seven grade 2 obese patients. *Obes Surg* 2021;**31**:1901	Correction
Fuller N, Pearson S, Lau N, Markovic T, Steinbeck K, Chettiar R, *et al*. prospective, randomised, controlled trial of the BioEnterics® Intragastric Balloon (BIB) in the treatment of obese individuals with metabolic syndrome. *Obes Rev* 2010;**11**:436	Duplicate
Genco A, Maselli R, Cipriano M, Lorenzo M, Basso N, Redler A. Long-term multiple intragastric balloon treatment – a new strategy to treat morbid obese patients refusing surgery: prospective 6-year follow-up study. *Surg Obes Relat Dis* 2014;**10**:307–11	Duplicate
Giuricin M, Nagliati C, Palmisano S, Simeth C, Urban F, Buri L, *et al*. Short- and long-term efficacy of intragastric air-filled balloon (Heliosphere R BAG) among obese patients. *Obes Surg* 2012;**22**:1686–9	Duplicate
Herzog P, Wollbrink W, Holtermuller KH. Endoscopic implantation of a gastric balloon: a method of weight reduction with few complications? *Dtsch Med Wochenschr* 1988;**113**:1064–6	Duplicate
Kim D, De Moura EGH, Escalona A, Malomo K, Cormier J, Liao A, *et al*. Endoscopic, duodenal-jejunal bypass liner exerts robust improvement in glycemia and body weight in obese patients with type 2 diabetes. *Diabetes* 2014;**63**:A287	Pooled analysis of five studies in a conference abstract
Krakamp B, Leidig P, Gehmlich D, Paul A. Gastric balloon: a good method for weight losing? *Zentralbl Chir* 1997;**122**:349–57	Duplicate
Lopez-Nava G, Sharaiha RZ, Vargas EJ, Bazerbachi F, Manoel GN, Bautista-Castano I, *et al*. Endoscopic sleeve gastroplasty for obesity: a multicenter study of 248 patients with 24 months follow-up. *Obes Surg* 2017;**27**:2649–55	Duplicate

TABLE 21 Excluded articles from the map of evidence with reasons (*continued*)

Study ID	Reason for exclusion
Maekawa S, Niizawa M, Harada M. Erratum: a comparison of the weight loss effect between a low-carbohydrate diet and a calorie-restricted diet in combination with intragastric balloon therapy. *Intern Med* 2020;**59**:1579	Erratum/correction
NCT (ongoing). *Metabolic Effects of Gastrointestinal Surgery in T2DM*. 2013. URL: https://clinicaltrials.gov/show/NCT01771185	Not endoscopic
Nikolic M, Mirosevic G, Ljubicic N, Boban M, Supanc V, Zjacic-Rotkvic V, *et al*. Obesity treatment using a bioenterics intragastric balloon (BIB) – preliminary croatian results. *Obes Surg* 2011;**21**:1305–10	Duplicate
Nimeri A, Zaman MB, Maasher A, Ibrahim M, Salim E, Shaban TA. Endoscopic intra-gastric botulinum toxin injection for obesity leading to total gastrectomy and Roux en y Esophago-Jejunostomy. *Surg Obes Relat Dis* 2016;**12**:S116	Single case report
Nobili V, Della Corte C, Liccardo D, Mosca A, Caccamo R, Morino GS, *et al*. Obalon intragastric balloon in the treatment of paediatric obesity: a pilot study: obalon intragastric balloons in obese children. *Pediatr Obes* 2018;**13**:273	Erratum to author name
Nobili V, Della Corte C, Liccardo D, Mosca A, Caccamo R, Morino GS, *et al*. Obalon intragastric balloon in the treatment of paediatric obesity: a pilot study. *Pediatr Obes* 2018;**13**:273	Duplicate
Ribeiro IB, de Moura DTH, de Moura EGH. Response: EUS-guided intragastric injection of botulinum toxin A in the preoperative treatment of super-obese patients: a randomized clinical trial. *Obes Surg* 2019;**29**:1016–7	Response to letter
Sandler BJ, Rumbaut R, Swain CP, Torres G, Morales L, Gonzales L, *et al*. Human experience with an endoluminal, endoscopic, gastrojejunal bypass sleeve. *Surg Endosc* 2011;**25**:3028–33	Described as endoscopic and laparoscopic techniques
Villa E, Chapman CG. Endoscopic sleeve gastroplasty: a meta-analysis of weight loss outcomes. *Gastrointest Endosc* 2019;**89**:AB263	Meta-analysis only

Tables of articles of comparative studies from the map of evidence

This appendix includes the tables of articles reporting RCTs and non-randomised controlled studies compared to bariatric surgery, sham procedures, LSIs, other endoscopic procedures, pharmacotherapy and in other combinations. Studies with multiple comparator arms are listed in more than one table.

Evidence for restrictive procedures

Evidence for endoscopic sleeve gastroplasty

Endoscopic sleeve gastroplasty versus bariatric surgery

TABLE 22 Endoscopic sleeve gastroplasty vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 22/17					
930783505	Marshall, 2022	ESG	LSG	2 weeks	50
930783341	Hadi, 2022	ESG	LSG	1 month	180
930783331	Gudur, 2023	ESG	LSG	1 month	603,517
264633638	Alghafees, 2020	ESG	LSG	3 months	37
264637780	Lopez-Nava, 2020	ESG	LSG	6 months	24
264637781	Lopez-Nava, 2020	ESG	LSG	6 months	24
264638002	Marshall, 2019	ESG	LSG	6 months	24
264635681	Fiorillo, 2019	ESG	LSG	6 months	46
264635682	Fiorillo, 2020	ESG	LSG	6 months	46
264639983	Schweitzer, 2018	ESG	LSG	6 months	86
264635611	Fayad, 2019	ESG	LSG	6 months	137
264639748	Sadek and Wassef, 2017	ESG	LSG	6 months	300
930783188	Carr, 2022	ESG	LSG	12 months	61
264638001	Marshall, 2021	ESG	LSG	12 months	61
264634169	Benias, 2020	ESG	LSG	24 months	25
930783077	Alqahtani, 2022	ESG	LSG	36 months	6036
264633324	Abu Dayyeh, 2017	ESG	LGP; LSI	6 months	29
264633325	El Mohsen, 2017	ESG	LGP; LSI	6 months	29
264637741	Lopez-Nava, 2021	ESG	LSG; LGP	24 months	296
264638858	Novikov, 2018	ESG	LSG; LAGB	12 months	278
264638859	Novikov, 2017	ESG	LSG; LAGB	12 months	278
264634096	Bazarbashi, 2020	Revision-ESG	Surgical re-sleeve	12 months	18

Endoscopic sleeve gastroplasty versus sham procedures

TABLE 23 Endoscopic sleeve gastroplasty vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 1/1					
264633434	Abu Dayyeh, 2016	Botox; Endoscopic IGB; DJBS; ESG	LSI; sham	6 months	118

Endoscopic sleeve gastroplasty versus lifestyle interventions

TABLE 24 Endoscopic sleeve gastroplasty vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 4/3					
930783790	Vargas, 2022	ESG	LSI	18 months	36
930783049	Abu Dayyeh, 2022	ESG + LSI	LSI	24 months	208
930783047	Abu Dayyeh, 2022	ESG + LSI	LSI	24 months	209
930783780	di Prampero, 2022	ESG; distal-POSE; EVG	LSI	6 months	120
Non-randomised controlled articles/studies: 6/4					
2646333E24	Abu Dayyeh, 2017	ESG	LGP; LSI	6 months	29
264633325	El Mohsen, 2017	ESG	LGP; LSI	6 months	29
264634754	Cheskin, 2020	ESG + LSI (low intensity diet)	LSI (high-intensity diet)	12 months	386
930783648	Rapaka, 2022	Endoscopic IGB; ESG; POSE 2.0	LSI	12 months	521 (ESG is in a mixed group with POSE 2.0)
930783650	Rapaka, 2022	Endoscopic IGB; ESG; POSE 2.0	LSI	12 months	521 (ESG is in a mixed group with POSE 2.0)
264633434	Abu Dayyeh, 2016	Botox; Endoscopic IGB; DJBS; ESG	LSI; sham	6 months	118

Endoscopic sleeve gastroplasty versus other endoscopic interventions (including endoscopic sleeve gastroplasty, various suturing patterns, locations, generations, additions)

TABLE 25 Endoscopic sleeve gastroplasty vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 10/3					
264639852	Sander, 2019	ESG full-thickness U-shaped sutures + reinforcement	ESG full-thickness U-shaped sutures	18 months	126
930783247	di Prampero, 2022	ESG; distal-POSE	EVG	NR	54
930783782	di Prampero, 2022	ESG; distal-POSE	EVG	6 months	54
930783783	di Prampero, 2022	ESG; distal-POSE	EVG	6 months	54
930783784	di Prampero, 2022	ESG; distal-POSE	EVG	6 months	54
930783781	di Prampero, 2022	ESG; distal-POSE	EVG	6 months	90
930783780	di Prampero, 2022	ESG; distal-POSE; EVG	LSI	6 months	120
930783315	Gkolfakis, 2022	ESG + LSI (3 arms with different suture patterns and locations in combination with LSI)	ESG + LSI (3 arms with different suture patterns and locations in combination with LSI)	12 months	48
930783316	Gkolfakis, 2022	ESG + LSI (3 arms with different suture patterns and locations in combination with LSI)	ESG + LSI (3 arms with different suture patterns and locations in combination with LSI)	12 months	48
264636575	Huberty, 2021	ESG + LSI (3 arms with different suture patterns and locations in combination with LSI)	ESG + LSI (3 arms with different suture patterns and locations in combination with LSI)	12 months	48
Non-randomised controlled articles/studies: 35/20					
930783340	Hadi, 2022	ESG	Endoscopic IGB	1 month	168
930783607	Ouni, 2022	ESG	Endoscopic IGB	1 month	5209
930783608	Ouni, 2022	ESG	Endoscopic IGB	1 month	5209
264636004	Gew, 2019	ESG	Endoscopic IGB	3 months	13
264640916	Vargas, 2019	ESG	Endoscopic IGB	3 months	88
930783647	Rapaka, 2022	ESG	Endoscopic IGB (Orbera)	6 months	41
930783649	Rapaka, 2022	ESG	Endoscopic IGB (Orbera)	6 months	41
264637743	Lopez-Nava, 2020	ESG	Endoscopic IGB	NR (9 months post procedure)	160
264635610	Fayad, 2018	ESG	Endoscopic IGB	12 months (6 months IGB)	88
264637759	Lopez-Nava, 2017	ESG	Endoscopic IGB	12 months	107
264637750	Lopez-Nava, 2018	ESG	Endoscopic IGB	12 months	107

TABLE 25 Endoscopic sleeve gastroplasty vs. other endoscopic interventions (*continued*)

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
264635612	Fayad, 2019	ESG	Endoscopic IGB	12 months (6 months IGB)	137
264633976	Badurdeen, 2020	ESG	Endoscopic IGB (Orbera, ReShape Duo)	12 months	NR
264634217	Bhakta, 2019	ESG	Endoscopic IGB	24 months (6 months IGB)	15 (NAFLD)
264637768	Lopez-Nava, 2019	ESG (U-, V-, Z-shaped suture patterns)	TORe	NR	175
264637769	Lopez-Nava, 2019	ESG (U-, V-, Z-shaped suture patterns)	TORe	NR	175
264637757	Lopez-Nava, 2020	ESG (U-, V-, Z-shaped suture patterns)	TORe	12 months	800
264636053	Glaysher, 2019	ESG standard suturing (no compression)	ESG longitudinal compression suturing	6 months	32
264636052	Glaysher, 2019	ESG standard suturing (no compression)	ESG longitudinal compression suturing	6 months	32
264635591	Farha, 2021	ESG with fundal suturing	ESG without fundal suturing	12 months	247
264635590	Farha, 2020	ESG with fundal suturing	ESG without fundal suturing	12 months	247
930783454	Kozlowska-Petriczko, 2022	ESG + LSI	Endoscopic IGB 6 months + LSI; Endoscopic IGB Orbera 365 12 months + LSI	12 months	227?
264637760	Lopez-Nava, 2017	ESG	Endoscopic IGB (Orbera, ReShape Duo); POSE	12 months	717
264637747	Lopez-Nava, 2019	ESG	Endoscopic IGB (Orbera, ReShape Duo); POSE	12 months	962
264637753	Lopez-Nava, 2019	ESG	Endoscopic IGB (Orbera, ReShape Duo); POSE	12 months	962
264637751	Lopez-Nava, 2019	ESG	Endoscopic IGB (Orbera, ReShape Duo); POSE	12 months	962
264637776	Lopez-Nava, 2018	ESG	Endoscopic IGB (Orbera, ReShape Duo); POSE	12 months	1020
264640924	Vargas, 2020	ESG	Endoscopic IGB; TORe	6 months	206
264640923	Vargas, 2021	ESG	Endoscopic IGB; TORe	NR	NR
264637298	Kozan, 2021	ESG	TORe; endoscopic revision of surgical sleeve gastrectomy	NR	95 (71 TORe; 13 re-sleeve; 11 ESG)
264641384	Young, 2021	ESG	Three interventions were compared: single endoscopic therapy with IGB or ESG vs obesity pharmacotherapy vs. combination therapy consisting of serial EBTs ± OPT. All plus LSI	24 months	38

TABLE 25 Endoscopic sleeve gastroplasty vs. other endoscopic interventions (*continued*)

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
930783847	Young, 2022	ESG	Three interventions were compared: single endoscopic therapy with IGB or ESG vs. obesity pharmacotherapy vs. combination therapy consisting of serial EBTs ± OPT. All plus LSI	24 months	128
264637299	Kozan, 2021	ESG	TORe; endoscopic revision of surgical sleeve gastrectomy; TORe-G	1 month	84 (33 TORe; 31 TORe-G; 12 revision: 8 ESG)
264633686	Almuhaidb, 2019	ESG (Apollo OverStitch)	Endoscopic IGB (Orbera, ReShape); swallowable IGB (Obalon); aspiration (AspireAssist)	6 months	98
264635512	Espinet Coll, 2017	ESG	Endoscopic IGB; POSE; DJBL	NR	NR (6771 procedures)

Endoscopic sleeve gastroplasty versus pharmacotherapy

TABLE 26 Endoscopic sleeve gastroplasty vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 2/1					
264641384	Young, 2021	ESG	Three interventions were compared: single endoscopic therapy with IGB or ESG vs. obesity pharmacotherapy vs. combination therapy consisting of serial EBTs ± OPT. All plus LSI	24 months	38
930783847	Young, 2022	ESG	Three interventions were compared: single endoscopic therapy with IGB or ESG vs. obesity pharmacotherapy vs. combination therapy consisting of serial EBTs ± OPT. All plus LSI	24 months	128

Endoscopic sleeve gastroplasty in other combinations

TABLE 27 Endoscopic sleeve gastroplasty in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 3/3					
264638768	Nevmark, 2017	ESG: traditional mode of ventilation	ESG: modified mode of ventilation	NR	37
264636464	Hoff, 2020	ESG + LSI	ESG + LSI + liraglutide	12 months	30
264634581	Hoff, 2021	ESG + LSI + semaglutide	ESG + LSI + sham semaglutide	NR	55
Non-randomised controlled articles/studies: 8/4					
264633978	Badurdeen, 2021	ESG	ESG + liraglutide	12 months	52
264633979	Badurdeen, 2020	ESG	ESG + liraglutide	12 months	66
264634369	Boskoski, 2019	ESG with multidisciplinary evaluation	ESG without multidisciplinary evaluation	6 months	31
264634370	Boskoski, 2019	ESG with multidisciplinary evaluation	ESG without multidisciplinary evaluation	6 months	31
264634368	Boskoski, 2019	ESG with multidisciplinary evaluation	ESG without multidisciplinary evaluation	12 months	89
264634372	Boskoski, 2019	ESG with multidisciplinary evaluation	ESG without multidisciplinary evaluation	12 months	89
930783330	Gudur, 2022	ESG (bariatric surgeons)	ESG (gastroenterologists)	1 month	Over 6000
930783403	Jirapinyo, 2022	ESG with three types of general anaesthetic	ESG with three types of general anaesthetic	1 month	128

Evidence for Primary Obesity Surgery Endoluminal

Primary Obesity Surgery Endoluminal versus bariatric surgery

TABLE 28 Primary Obesity Surgery Endoluminal vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 1/1					
264633553	Al Rasheid, 2014	POSE	RYGB	2 months	16

Primary Obesity Surgery Endoluminal versus sham procedures

TABLE 29 Primary Obesity Surgery Endoluminal vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 7/1 (all the ESSENTIAL trial)					
264635109	De La Cruz-Munoz, 2016	POSE + LSI	Sham + LSI	12 months	32
264634396	Boyer, 2016	POSE + LSI	Sham + LSI	12 months	61
264637472	Lavin, 2015	POSE + LSI	Sham + LSI	12 months	332
264637474	Lavin, 2016	POSE + LSI	Sham + LSI	12 months	332
264640449	Sullivan, 2017	POSE + LSI	Sham + LSI	12 months	332
264640450	Sullivan, 2016	POSE + LSI	Sham + LSI	12 months	332
264637473	Lavin, 2016	POSE + LSI	Sham + LSI	24 months	332
Non-randomised controlled articles/studies: 0 articles					

Primary Obesity Surgery Endoluminal versus lifestyle interventions

TABLE 30 Primary Obesity Surgery Endoluminal vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 13/2 (12 are the MILEPOST study)					
264638208	Miller, 2014	POSE + LSI	LSI	2 months	14
264634337	Borda, 2016	POSE + LSI	LSI	6 months	44
264636162	Greve, 2015	POSE + LSI	LSI	12 months	44
264636163	Greve, 2017	POSE + LSI	LSI	12 months	44
264638204	Miller, 2016	POSE + LSI	LSI	12 months	44
264638206	Miller, 2016	POSE + LSI	LSI	12 months	44
264638210	Miller, 2016	POSE + LSI	LSI	12 months	44
264638211	Miller, 2017	POSE + LSI	LSI	12 months	44
264640810	Turro, 2016	POSE + LSI	LSI	12 months	44
264640814	Turro, 2015	POSE + LSI	LSI	12 months	44
264638213	Miller, 2019	POSE + LSI	LSI	24 months	44
264638205	Miller, 2018	POSE + LSI	LSI	24 months	44
930783780	di Prampero, 2022	Distal-POSE; ESG; EVG	LSI	6 months	120
Non-randomised controlled articles/studies: 3/2					
930783072	Alkhatry, 2022	POSE 2.0 + LSI	LSI	12 months	42
930783648	Rapaka, 2022	POSE 2.0; ESG; Endoscopic IGB	LSI	12 months	521 (ESG is in a mixed group with POSE 2.0)
930783650	Rapaka, 2022	POSE 2.0; ESG; Endoscopic IGB	LSI	12 months	521 (ESG is in a mixed group with POSE 2.0)

Primary Obesity Surgery Endoluminal versus other endoscopic interventions (including various suturing patterns, locations, generations, additions)

TABLE 31 Primary Obesity Surgery Endoluminal vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 5/1 (all also under ESG)					
930783247	di Prampero, 2022	Distal-POSE	ESG; EVG	NR	54
930783782	di Prampero, 2022	Distal-POSE	ESG; EVG	6 months	54
930783783	di Prampero, 2022	Distal-POSE	ESG; EVG	6 months	54
930783784	di Prampero, 2022	Distal-POSE	ESG; EVG	6 months	54
930783781	di Prampero, 2022	Distal-POSE	ESG; EVG	6 months	90
Non-randomised controlled articles/studies: 11/6					
264638247	Miranda-Penarroya, 2022	POSE	Endoscopic IGB	12 months	463
264637760	Lopez-Nava, 2017	POSE	Endoscopic IGB (Orbera, ReShape Duo); ESG	12 months	717
264637747	Lopez-Nava, 2019	POSE	Endoscopic IGB (Orbera, ReShape Duo); ESG	12 months	962
264637753	Lopez-Nava, 2019	POSE	Endoscopic IGB (Orbera, ReShape Duo); ESG	12 months	962
264637776	Lopez-Nava, 2018	POSE	Endoscopic IGB (Orbera, ReShape Duo); ESG	12 months	1020
264635512	Espinet Coll, 2017	POSE	Endoscopic IGB; ESG; DJBL	NR	NR (6771 procedures)
264635893	Garcia, 2019	POSE reinforced in BMI = 47	POSE standard without reinforcement in BMI = 40	3 months	NR
264635897	Garcia, 2019	POSE reinforced in BMI = 47	POSE standard without reinforcement in BMI = 40	3 months	NR
264638042	Maselli, 2020	POSE 1.0	POSE 2.0	6 months	33
930783409	Jirapinyo, 2022	POSE single helix	POSE double helix	12 months	107
930783405	Jirapinyo, 2022	POSE single helix	POSE double helix	12 months	110

Primary Obesity Surgery Endoluminal versus pharmacotherapy

TABLE 32 Primary Obesity Surgery Endoluminal vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 0 articles					

Primary Obesity Surgery Endoluminal in other combinations

TABLE 33 Primary Obesity Surgery Endoluminal in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 0 articles					

Evidence for transoral outlet reduction by endoscopy

Transoral outlet reduction by endoscopy versus bariatric surgery

TABLE 34 Transoral outlet reduction by endoscopy vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 1/1					
930783408	Jirapinyo, 2022	TORe	Pharmacotherapy alone; TORe + pharmacotherapy; surgical revision of GJA	12 months	126

Transoral outlet reduction by endoscopy versus sham procedures

TABLE 35 Transoral outlet reduction by endoscopy vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 1/1					
264640660	Thompson, 2013	TORe + LSI	Sham + LSI	6 months	77
Non-randomised controlled articles/studies: 0 articles					

Transoral outlet reduction by endoscopy versus lifestyle interventions

TABLE 36 Transoral outlet reduction by endoscopy vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 0 articles					

Transoral outlet reduction by endoscopy versus other endoscopic interventions (including various suturing patterns, locations, generations, additions)

TABLE 37 Transoral outlet reduction by endoscopy vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 17/13					
264637768	Lopez-Nava, 2019	TORe	ESG (U-, V-, Z-shaped suture patterns)	NR	175
264637769	Lopez-Nava, 2019	TORe	ESG (U-, V-, Z-shaped suture patterns)	NR	175
264637757	Lopez-Nava, 2020	TORe	ESG (U-, V-, Z-shaped suture patterns)	12 months	800
264636485	Hollenbach, 2019	TORe + APC	TORe + ESD	12 months	41
264636816	Jirapinyo, 2020	TORe + APC	TORe + ESD	12 months	76
264636013	Ghazi, 2021	TORe	Tubular transoral pouchplasty (tTORe)	18 months	131
264637342	Kumar, 2013	TORe full-thickness sutures	TORe superficial sutures	6 months	118
264637348	Kumar, 2014	TORe full-thickness sutures	TORe superficial sutures	6 months	118
264639967	Schulman, 2016	TORe + serial APC	TORe 2nd gen	6 months	30
264639966	Schulman, 2016	TORe + serial APC	TORe with purse-string suture	6 months	175
930783530	Meyers, 2022	TORe with purse-string sutures	TORe without purse-string sutures	12 months	51
264639970	Schulman, 2018	TORe with purse-string suture	TORe with interrupted sutures	12 months	241
264640923 Also under ESG	Vargas, 2021	TORe	Endoscopic IGB; ESG	NR	NR
264640924	Vargas, 2020	TORe	Endoscopic IGB; ESG	6 months	206
264637298	Kozan, 2021	TORe	Endoscopic revision of surgical sleeve gastrectomy; ESG	NR	95 (71 TORe; 13 re-sleeve; 11 ESG)

continued

TABLE 37 Transoral outlet reduction by endoscopy vs. other endoscopic interventions (*continued*)

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
264640921	Vargas, 2017	TORe + botox	Botox	1	10
264637299	Kozan, 2021	TORe	Endoscopic revision of surgical sleeve gastrectomy; TORe-G; ESG	1 month	84 (33 TORe; 31 TORe-G; 12 revision: 8 ESG)

Transoral outlet reduction by endoscopy versus pharmacotherapy

TABLE 38 Transoral outlet reduction by endoscopy vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 1/1					
930783408	Jirapinyo, 2022	TORe	Pharmacotherapy alone; TORe + pharmacotherapy; surgical revision of GJA	12 months	126

Transoral outlet reduction by endoscopy in other combinations

TABLE 39 Transoral outlet reduction by endoscopy in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 0 articles					

Evidence for other forms of restrictive endoscopic therapy

Other restrictive endoscopic procedures versus bariatric surgery

TABLE 40 Other restrictive endoscopic procedures vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 8/6					
264639669	Ruiz, 2016	Endoscopic gastric plication	LSG; LGCP	12 months	173

TABLE 40 Other restrictive endoscopic procedures vs. bariatric surgery (*continued*)

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
264639670	Ruiz, 2017	Endoscopic gastric plication	LSG; LGCP	24 months	357
264634645	Cerri, 2021	Endoscopic gastric plication	LSG; RYGB (and LAGB removal)	24 months	92 (only 4 had endoscopic gastric plication)
264638499	Nanni, 2011	TOGA	RYGB; BPD	24 months	89
264638498	Nanni, 2012	TOGA	RYGB; BPD	24 months	89
264634309	Bolton, 2013	Endoscopic endoluminal pouch reduction (Stomaphyx)	RYGB	NR	37
264634515	Buzga, 2017	Endoscopic gastroplasty	Laparoscopic gastric plication	6 months	40
264635613	Fayad, 2020	Endoscopic therapies (not specified)	Laparoscopic therapies (not specified)	1 month	11,177

Other restrictive endoscopic procedures versus sham procedures

TABLE 41 Other restrictive endoscopic procedures vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 2/2					
264635398	Eid, 2014	Endoscopic gastric plication of gastric pouch and stoma	Sham	12 months	74
264636863	Jonnalagadda, 2012	TOGA	Sham	12 months	83
Non-randomised controlled articles/studies: 0 articles					

Other restrictive endoscopic procedures versus lifestyle interventions

TABLE 42 Other restrictive endoscopic procedures vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 2/2					
264636580	Huberty, 2021	Endoscopic sutured gastroplasty + LSI	LSI	12 months	71
930783780	di Prampero, 2022	Distal-POSE; ESG; EVG	LSI	6 months	120
Non-randomised controlled articles/studies: 0 articles					

Other restrictive endoscopic procedures (e.g. transoral gastroplasty) versus other endoscopic interventions

TABLE 43 Other restrictive endoscopic procedures (e.g. TOGA) vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 2/1					
264634463	Brunaldi, 2019	Endoscopic suturing (to reduce stoma and/pouch) + APC	APC	6 months	40
264634464	Brunaldi, 2020	Endoscopic suturing (to reduce stoma and/or pouch) + APC	APC	12 months	40
Non-randomised controlled articles/studies: 7/6					
264633424	Abu Dayyeh, 2012	Endoscopic suturing	Sclerotherapy	3 months	37 (only 4 suturing)
264635515	Espinet Coll, 2019	Endoscopic sutured gastroplasty	Endoscopic IGB	12 months	30 (NAFLD)
264635516	Espinet Coll, 2019	Endoscopic sutured gastroplasty	Endoscopic IGB	12 months	30 (NAFLD)
264639853	Sander, 2019	Endoscopic suturing + reinforcement	Endoscopic suturing	18 months	31
264640972	Verlaan, 2011	TERIS 1.0	TERIS 2.0	6 months	18
264636522	Hould, 2011	TERIS 1.0	TERIS 2.0	12 months	22
264636830	Jirapinyo, 2018	ROSE + APC	Endoscopic suturing	3 months	42

Other restrictive endoscopic procedures versus pharmacotherapy

TABLE 44 Other restrictive endoscopic procedures vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 0 articles					

Other restrictive endoscopic procedures in other combinations

TABLE 45 Other restrictive endoscopic procedures in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 0 articles					

Evidence for space-occupying devices

Evidence for endoscopic intragastric balloon

Endoscopic intragastric balloon versus bariatric surgery

TABLE 46 Endoscopic IGB vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0 articles					
Non-randomised controlled articles/studies: 21/20					
264638219	Milone, 2005	Endoscopic IGB	LSG	6 months	77
264635967	Genco, 2019	Endoscopic IGB	LSG	12 months	120
264639270	Plua Marcillo, 2019	Endoscopic IGB	LSG	12 months	60
264636786	Jearapongpakorn, 2019	Endoscopic IGB	LSG	24 months	16
264634166	Busetto, 2004	Endoscopic IGB	LAGB	6 months	86
264640601	Tayyem, 2011	Endoscopic IGB	LAGB	12 months	41
264640603	Tayyem, 2011	Endoscopic IGB	LAGB	Mean 14 months	47
264639166	Peker, 2011	Endoscopic IGB x2	LAGB	18 months	32
264640274	Solmaz, 2015	Endoscopic IGB	LGP	6 months	95
264638812	Nikolic, 2015	Endoscopic IGB	LSG; LAGB	12 months	88
264639725	Rzepa, 2019	Endoscopic IGB	LSG; RYGB	NR	933
264633630	Alfa Wali, 2014	Endoscopic IGB	LAGB; gastric bypass	12 months	983
264638777	Ng, 2009	Endoscopic IGB	LSG; LAGB; LGB	6 months	225
264637246	Kolesnikov, 2015	Endoscopic IGB	LSG; RYGB; revision- RYGB	6 months	238
264638462	Musella, 2014	Endoscopic IGB	LSG; LAGB; LMGB	6 months and longer	520
264638461	Musella, 2012	Endoscopic IGB	LAGB; LSG; gastric bypass	NR	110
264637175	Kirby, 1990	Endoscopic IGB	Bariatric surgery (not specified)	12 months	134
264635171	De Stefano, 2012	Endoscopic IGB	Bariatric surgery (not specified)	NR	12
264634022	Banks, 2021	Endoscopic IGB	Bariatric surgery (not specified)	NR	42
264635035	Dang, 2018	Endoscopic IGB	Bariatric surgery (not specified)	NR	1368
930783210	Chow, 2022	Endoscopic IGB	Bariatric surgery (not specified)	5 years	2910

Endoscopic intragastric balloon versus sham procedures

TABLE 47 Endoscopic IGB vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 17/12					
264639289	Ponce, 2015 (REDUCE trial)	Endoscopic IGB (ReShape Duo) + LSI	Sham + LSI	52 weeks (24 weeks IGB)	326
264638077	Mathus-Vliegen, 1990	Endoscopic IGB (Ballobes) + LSI	Sham + LSI	17 weeks	Unclear (super-morbid)
264638072	Mathus-Vliegen, 2013	Endoscopic IGB	Sham	6 months. Randomised to a 13-week period of sham or balloon treatment followed by a 13-week period of balloon therapy in everyone	42
264638073	Mathus-Vliegen, 2014	Endoscopic IGB	Sham	6 months. Randomised to a 13-week period of sham or balloon treatment followed by a 13-week period of balloon therapy in everyone	40
264638074	Mathus-Vliegen, 2002	Endoscopic IGB	Sham	52 weeks (13 weeks IGB + 9 months)	42
264638059	Mathus-Vliegen, 2021	Endoscopic IGB	Sham	6 months. Randomised to a 13-week period of sham or balloon treatment followed by a 13-week period of balloon therapy in everyone	18
264638076	Mathus-Vliegen, 2005	Endoscopic IGB	Sham	24 months (3 months initial IGB + 9 months if WL target met)	43
264638078	Mathus-Vliegen, 2003	Endoscopic IGB	Sham	8 months. Randomised to a 4-month period of sham or balloon treatment followed by a 4-month period of balloon therapy in everyone	32
264635964	Genco, 2006	Endoscopic IGB (Bioenterics)	Sham	6 months (3 months IGB and each crossover period)	32 (morbidly obese)
264636472	Hogan, 1989	Endoscopic IGB (Garren-Edwards) + LSI	Sham + LSI	12 months (3 months IGB)	59
930783369	Hollenbach, 2022 (the WET trial)	Endoscopic IGB; DJBL	Sham	12 months (6 months IGB; DJBL 12 months)	33
264637552	Lee, 2012	Endoscopic IGB (Bioenterics) + LSI	Sham + LSI	6 months (6 months IGB)	18 (NASH)
264637553	Lee, 2009	Endoscopic IGB (Bioenterics) + LSI	Sham + LSI	6 months (6 months IGB)	18 (NASH)
264637671	Lindor, 1987	Endoscopic IGB	Sham + 'conventional medical therapy'	3 months (2–3 months IGB)	22
264638021	Martinez-Brocca, 2007	Endoscopic IGB (Bioenterics)	Sham	Unclear 4 months?	22
264639437	Ramhamadany, 1989	Endoscopic IGB + LSI	Sham + LSI	6 months (3 months IGB)	24
264639555	Rigaud, 1995	Endoscopic IGB + LSI	Sham + LSI	12 weeks (12 weeks IGB?)	20 (severely obese)
Non-randomised controlled articles/studies: 3/3					
264633347	Hoff, 2020	Endoscopic IGB	Sham	12 months	87
264637567	Krakamp, 1997	Endoscopic IGB + LSI (intensive or limited advice)	Sham + LSI (intensive); no treatment + LSI (limited advice)	18 months (6 months IGB)	40
264633434	Abu Dayyeh, 2016	Endoscopic IGB; botox; DJBS; ESG	LSI; sham	6 months	118

Endoscopic intragastric balloon versus lifestyle interventions

TABLE 48 Endoscopic IGB vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 17/8					
930783425	Kashani, 2022	Endoscopic IGB	LSI	6 months	68
264638303	Mohammed, 2014	Endoscopic IGB (Bioenterics)	LSI	6 months (6 months IGB)	128
264640984	Vicente, 2020	Endoscopic IGB (Bioenterics)	LSI	6 months	66
264639397	Rabago, 2018	Endoscopic IGB (Bioenterics)	LSI	6 months	66
264640982	Vicente, 2017	Endoscopic IGB (Bioenterics)	LSI	6 months	66
264635003	Curran, 2011	Endoscopic IGB + LSI	LSI	6 months (6 months IGB)	12 adolescents
264636090	Gomez, 2016	Endoscopic IGB (Orbera) + LSI	LSI	12 months (6 months IGB)	29
264635817	Fuller, 2010 (6-month data)	Endoscopic IGB (Orbera) + LSI	LSI	12 months (6 months IGB)	66
264635819	Fuller, 2013	Endoscopic IGB + LSI	LSI	12 months (6 months IGB)	66
264639288	Ponce, 2013	Endoscopic IGB (Duo?) + LSI	LSI	48 weeks (24 weeks IGB)	30
264633428	Abu Dayyeh, 2019	Endoscopic IGB (Spatz3) + LSI	LSI	56 weeks (32 weeks/8 months IGB)	288
264633426	Abu Dayyeh, 2021	Endoscopic IGB (Spatz3) + LSI	LSI	56 weeks (32 weeks/8 months IGB)	288
264640927	Vargas, 2019	Endoscopic IGB (Spatz3) + LSI	LSI	56 weeks (32 weeks/8 months IGB)	17
930783380	Hussan, 2022	Endoscopic IGB (Spatz3) + LSI	LSI	56 weeks (32 weeks/8 months IGB)	12
264633421	Abu Dayyeh, 2015	Endoscopic IGB (Orbera) + LSI	LSI	12 months (6 months IGB)	255
264634955	Courcoulas, 2017	Endoscopic IGB (Orbera) + LSI	LSI	12 months (6 months IGB)	255
264635004	Curran, 2015	Endoscopic IGB + LSI	LSI	18 months (6 months IGB)	30 adolescents
Non-randomised controlled articles/studies: 24/21					
264635278	Doldi, 2002	Endoscopic IGB	LSI	4 months main study (18 months subtudy)	281
264640533	Takihata, 2014	Endoscopic IGB	LSI (intensive) + educational hospitalisation	6 months	16
264637560	Leeman, 2013	Endoscopic IGB	LSI	6 months	28 (WL pre-bariatric surgery)
264637973	Mariani, 2016	Endoscopic IGB	LSI	6 months	32

continued

TABLE 48 Endoscopic IGB vs. lifestyle interventions (*continued*)

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
264639845	Sanchez-Santos, 2011	Endoscopic IGB	LSI	6 months	200 (WL pre-bariatric surgery)
264636599	Hussan, 2019	Endoscopic IGB	LSI	8 months	12
264637259	Konopko-Zubrzycka, 2009	Endoscopic IGB	LSI	9 months (6 months IGB)	36
264637261	Konopko-Zubrzycka, 2009	Endoscopic IGB	LSI	9 months (6 months IGB)	36
264637260	Konopko-Zubrzycka, 2009	Endoscopic IGB	LSI	9 months (6 months IGB)	36
264635820	Fuller, 2013	Endoscopic IGB	LSI	12 months	66 (metabolic syndrome)
930783605	Oster, 2022	Endoscopic IGB	LSI	12 months (6 months IGB)	148
264638993	Oster, 2021	Endoscopic IGB	LSI	12 months (6 months IGB)	148
264633518	Ahmed, 2019	Endoscopic IGB	LSI (Atkins diet)	18 months	80
264640132	Shchukina, 2014	Endoscopic IGB	LSI	24 months	103
264633911	Ashem, 2013	Endoscopic IGB	LSI	6 months	10 Prader–Willi syndrome
264635961	Genco, 2008	Endoscopic IGB + LSI	LSI	24 months (6 months IGB)	260
264640736	Tosetti, 1996	Endoscopic IGB + LSI	LSI	4 months	40
264640983	Vicente, 2017	Endoscopic IGB + LSI	LSI	NR	58 (WL pre-bariatric surgery)
264634001	Balejko, 2018	Endoscopic IGB	Endoscopic IGB + LSI (American diet); endoscopic IGB + LSI (modified American diet)	8 months	90
264637567	Krakamp, 1997	Endoscopic IGB + LSI (intensive or limited advice)	Sham + LSI (intensive); no treatment + LSI (limited advice)	18 months (6 months IGB)	40
264635950	Geliebter, 1991	Endoscopic IGB; endoscopic IGB + LSI	LSI; no treatment	3 months	86
930783648	Rapaka, 2022	Endoscopic IGB; ESG; POSE 2.0	LSI	12 months	521
930783650	Rapaka, 2022	Endoscopic IGB; ESG; POSE 2.0	LSI	12 months	521
264633434	Abu Dayyeh, 2016	Endoscopic IGB; botox; DJBS; ESG	LSI; sham	6 months	118

Endoscopic intragastric balloon versus endoscopic intragastric balloon

TABLE 49 Endoscopic IGB vs. endoscopic IGB

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 4/4					
264635081	De Castro, 2010	Endoscopic IGB (Bioenterics saline-filled)	Endoscopic IGB (Heliosphere air-filled)	6 months (6 months IGB)	33
264636025	Giardiello, 2012	Endoscopic IGB (Bioenterics saline-filled)	Endoscopic IGB (Heliosphere air-filled)	NR	60
264635714	Fittipaldi-Fernandez, 2021	Endoscopic IGB (Spatz3) standard volume	Endoscopic IGB (Spatz3) greater volume	NR	180
264636465	Hoff, 2020	Endoscopic IGB (Spatz3) increased volume (air- into saline-filled)	Endoscopic IGB (Spatz3) sham increase in volume (remained as saline-filled)	Unclear	87
Non-randomised controlled articles/studies: 32/28					
264634250	Billing, 2018	Endoscopic IGB	(Compared liquid/gas)	6 months	59
264634317	Bonfante, 2011	Endoscopic IGB	(Compared liquid/gas)	6 months	123
264635082	de Castro, 2013	Endoscopic IGB	(Compared liquid/gas)	12 months	91
264639281	Poliwoda, 2011	Endoscopic IGB	(Compared liquid/gas)	18 months	55
264635490	Erdogan, 2013	Endoscopic IGB	(Compared liquid/gas)	NR	49
264640181	Siardi, 1990	Endoscopic IGB	(Compared two brands) (Ballobes; Garren Edwards)	3 months	60
264640182	Siardi, 1990	Endoscopic IGB	(Compared two brands) (Ballobes; Garren Edwards)	3 months? NR	60
264639497	Reed, 1988	Endoscopic IGB	(Compared two brands) (Ballobes; Garren Edwards)	4 months	12
264634533	Caglar, 2013	Endoscopic IGB	(Compared two brands) (BioEnterics; Heliosphere)	6 months	32
264634402	Bozkurt, 2011	Endoscopic IGB	(Compared two brands) (BioEnterics; Silimed)	6 months	50
264635007	Curry, 2017	Endoscopic IGB	(Compared two brands) (Orbera; ReShape)	6 months	100
264633337	Sartoretto, 2018	Endoscopic IGB	(Compared two brands) (Orbera; Spatz3)	6 months	103
264633376	Abeid, 2020	Endoscopic IGB	(Compared two brands) (Orbera; EndBall)	6 months	150
930783356	Hein, 2022	Endoscopic IGB	(Compared two brands) (Orbera; Medsil)	6 months	202
264640243	Sivero, 2017	Endoscopic IGB	(Compared two brands) (Bioenterics; Spatz adjustable)	9 months? Not clear	NR
264635968	Genco, 2013	Endoscopic IGB	(Compared two brands) (BioEnterics; Spatz)	12 months	120
264635195	Dellepiane, 2013	Endoscopic IGB	(Compared two brands) (BioEnterics; Spatz)	12 months	125

continued

TABLE 49 Endoscopic IGB vs. endoscopic IGB (*continued*)

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
264638471	Mylytsya, 2014	Endoscopic IGB	(Compared liquid/gas) BIB; Medsil; Heliosphere	36 months	12
264639695	Russo, 2017	Endoscopic IGB	(Compared two brands) (Bioenterics; Spatz adjustable)	NR	NR
264639223	Pezzo, 2019	Endoscopic IGB	(Compared two different volumes)	6 months	78
264641059	Wahlen, 2009	Endoscopic IGB	(Compared two different volumes; new valve) three versions of BioEnterics	7 months	1181
264637243	Kola, 2017	Endoscopic IGB	(Compared adjustable/ non-adjustable)	12 months	90
264639978	Schwaab, 2020	Endoscopic IGB	(Compared adjustable/ non-adjustable)	12 months	414
264634067	Barrichello, 2018	Endoscopic IGB	(Compared two different volumes)	NR	145
930783454	Kozlowska-Petriczko, 2022	Endoscopic IGB 6 months + LSI; Endoscopic IGB Orbera 365 12 months + LSI	ESG + LSI	12 months	227?
264633976	Badurdeen, 2020	Endoscopic IGB (Orbera, ReShape Duo)	ESG	12 months	NR
264637760	Lopez-Nava, 2017	Endoscopic IGB (Orbera, ReShape Duo)	ESG; POSE	12 months	717
264637747	Lopez-Nava, 2019	Endoscopic IGB (Orbera, ReShape Duo)	ESG; POSE	12 months	962
264637753	Lopez-Nava, 2019	Endoscopic IGB (Orbera, ReShape Duo)	ESG; POSE	12 months	962
264637751	Lopez-Nava, 2019	Endoscopic IGB (Orbera, ReShape Duo)	ESG; POSE	12 months	962
264637776	Lopez-Nava, 2018	Endoscopic IGB (Orbera, ReShape Duo)	ESG; POSE	12 months	1020
264633686	Almuhaidb, 2019	Endoscopic IGB (Orbera, ReShape)	ESG; Swallowable IGB (Obalon); Aspiration (AspireAssist)	6 months	98

Endoscopic intragastric balloon versus other endoscopic interventions

TABLE 50 Endoscopic IGB vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0					
Non-randomised controlled articles/studies: 32/24					
930783340	Hadi, 2022	Endoscopic IGB (NR)	ESG	1 month	168
930783607	Ouni, 2022	Endoscopic IGB	ESG	1 month	5209
930783608	Ouni, 2022	Endoscopic IGB	ESG	1 month	5209
264636004	Gew, 2019	Endoscopic IGB (NR)	ESG	3 months	13
264640916	Vargas, 2019	Endoscopic IGB	ESG	3 months	88
930783647	Rapaka, 2022	Endoscopic IGB (Orbera)	ESG	6 months	41
930783649	Rapaka, 2022	Endoscopic IGB (Orbera)	ESG	6 months	41
264637759	Lopez-Nava, 2017	Endoscopic IGB	ESG	12 months	107
264637743	Lopez-Nava, 2020	Endoscopic IGB	ESG	NR (9 months post procedure)	160
264637750	Lopez-Nava, 2018	Endoscopic IGB	ESG	12 months	107
264635610	Fayad, 2018	Endoscopic IGB	ESG	12 months (6 months IGB)	88
264635612	Fayad, 2019	Endoscopic IGB	ESG	12 months (6 months IGB)	137
264634217	Bhakta, 2019	Endoscopic IGB	ESG	24 months (6 months IGB)	15
264633976	Badurdeen, 2020	Endoscopic IGB (Orbera, ReShape Duo)	ESG	12 months	NR
930783454	Kozlowska-Petriczko, 2022	Endoscopic IGB 6 months + LSI; Endoscopic IGB Orbera 365 12 months + LSI	ESG + LSI	12 months	227?
264638247	Miranda-Penarroya, 2022	Endoscopic IGB	POSE	12 months	463
264637760	Lopez-Nava, 2017	Endoscopic IGB (Orbera, ReShape Duo)	ESG; POSE	12 months	717
264637747	Lopez-Nava, 2019	Endoscopic IGB (Orbera, ReShape Duo)	ESG; POSE	12 months	962
264637753	Lopez-Nava, 2019	Endoscopic IGB (Orbera, ReShape Duo)	ESG; POSE	12 months	962
264637751	Lopez-Nava, 2019	Endoscopic IGB (Orbera, ReShape Duo)	ESG; POSE	12 months	962
264637776	Lopez-Nava, 2018	Endoscopic IGB (Orbera, ReShape Duo)	ESG; POSE	12 months	1020
264640923	Vargas, 2021	Endoscopic IGB	ESG; TORe	NR	NR
264640924	Vargas, 2020	Endoscopic IGB	ESG; TORe	6 months	206

continued

TABLE 50 Endoscopic IGB vs. other endoscopic interventions (*continued*)

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
264635515	Espinet Coll, 2019	Endoscopic IGB	Endoscopic sutured gastroplasty	12 months	30 (NAFLD)
264635516	Espinet Coll, 2019	Endoscopic IGB	Endoscopic sutured gastroplasty	12 months	30 (NAFLD)
264635512	Espinet Coll, 2017	Endoscopic IGB	ESG; POSE; DJBL	NR	NR (6771 procedures)
264633686	Almuhaidb, 2019	Endoscopic IGB (Orbera, ReShape)	ESG; Swallowable IGB (Obalon); Aspiration (AspireAssist)	6 months	98
930783760	Theodoridou, 2022	Endoscopic IGB	DJBL	12 months	140
930783755	Tayyem, 2022	Endoscopic IGB	Botox	6 months	176
264635353	Durmus, 2019	Endoscopic IGB + LSI	Botox + LSI	3 months	52
264636939	Kanlioz, 2020	Endoscopic IGB	Endoscopic IGB + Botox; Botox	6 months	121
264633434	Abu Dayyeh, 2016	Endoscopic IGB	Botox; DJBS; ESG; sham; LSI	6 months	118

Endoscopic intragastric balloon versus pharmacotherapy

TABLE 51 Endoscopic IGB vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 5/4					
264638776	Ng, 2009	Endoscopic IGB	Sibutramine + LSI	6 months	99
264634977	Cruz, 2017	Endoscopic IGB	Sibutramine	10 years (6 months IGB)	99 (32 at 10-year review)
264634664	Chan, 2021	Endoscopic IGB	Sibutramine	10 years (6 months IGB)	99 (49 at 10-year review)
264635595	Farina, 2012	Endoscopic IGB (Bioenterics) + LSI	Sibutramine + LSI	6 months (6 months IGB)	50
264635051	Dargent, 2015	Endoscopic IGB	Endoscopic IGB + hyaluronic acid injections; hyaluronic acid injections alone	24 months (6 months IGB)	101
Non-randomised controlled articles/studies: 3/2					
264640366	Stier, 2015	Endoscopic IGB	1.8 mg GLP1 analogue plus amino acid infusion plus hypocaloric diet	NR	NR (20 in pharmacotherapy)
264640370	Stier, 2015	Endoscopic IGB	1.8 mg liraglutide plus amino acid infusion plus a low-calorie diet	6 months	46
264638165	Melnikova, 2016	Endoscopic IGB	GLP1 analogue	6 months	28

Endoscopic intragastric balloon in other combinations (including medical care, no treatment)

TABLE 52 Endoscopic IGB vs. non-endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 4/1					
264634868	Coffin, 2017	Endoscopic IGB	'Standard medical care'	6 months (6 months IGB)	115 super obese
264634869	Coffin, 2016	Endoscopic IGB	'Standard medical care'	6 months (6 months IGB)	115 super obese
264634870	Coffin, 2014	Endoscopic IGB	'Standard medical care'	6 months (6 months IGB)	115 super obese
264634871	Coffin, 2014	Endoscopic IGB	'Standard medical care'	6 months (6 months IGB)	115 super obese
Non-randomised controlled articles/studies: 2/2					
264637911	Majanovic, 2014	Endoscopic IGB	CBT	6 months	114
264640741	Tramontano, 2010	Endoscopic IGB	Endoscopic IGB + liposuction; liposuction only	4 months	NR (12 in IGB + liposuction)

TABLE 53 Endoscopic IGB vs. no treatment

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0					
Non-randomised controlled articles/studies: 13/10					
264634662	Chan, 2008	Endoscopic IGB	No treatment	6 months	18
264636114	Gostout, 2015	Endoscopic IGB	No treatment	39 weeks	29
264641449	Zerrweck, 2009	Endoscopic IGB	No treatment	12 months	36
264641448	Zerrweck, 2011	Endoscopic IGB	No treatment	12 months	60
264641447	Zerrweck, 2011	Endoscopic IGB	No treatment	12 months	60
264641451	Zerrweck, 2012	Endoscopic IGB	No treatment	12 months	60
930783633	Platt, 2022	Endoscopic IGB	No treatment	12 months	144
264640956	Veloso, 2013	Endoscopic IGB	No treatment	24 months	80
930783357	Hering, 2022	Endoscopic IGB	No treatment	24 months post bariatric surgery	78
264638291	Mocanu, 2017	Endoscopic IGB	No treatment	6 months + 36 months	133
930783675	Rzepa, 2022	Endoscopic IGB	No treatment	NR	30
264639396	Rabago, 2014	Endoscopic IGB	No treatment	NR	95
264635950	Geliebter, 1991	Endoscopic IGB;	Endoscopic IGB + LSI; LSI; No treatment	3 months	86

TABLE 54 Endoscopic IGB in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 3/2					
264635707	Fittipaldi-Fernandez, 2018	Endoscopic IGB (Orbera)	Endoscopic IGB (Orbera) + liraglutide	6 months (6 months IGB)	90
264635708	Fittipaldi-Fernandez, 2018	Endoscopic IGB (Orbera)	Endoscopic IGB (Orbera) + liraglutide	6 months (6 months IGB)	90
264635971	Genco, 2018	Endoscopic IGB (Orbera) + very-low-calorie ketogenic diet	Endoscopic IGB (Orbera) + low-calorie diet	6 months (6 months IGB, 4 months diet)	80
Non-randomised controlled articles/studies: 19/14					
264634166	Benetti, 2011	Endoscopic IGB or gastric band (mixed group)	LSI	6 months	30 hepatic steatosis (18 IGB or LAGB: 12 LSI)
264635738	Folini, 2011	Endoscopic IGB or gastric band (mixed group)	LSI	6 months	30 (18 IGB or LAGB: 12 LSI)
264635739	Folini, 2014	Endoscopic IGB or gastric band (mixed group)	LSI	NR	31 (18 IGB or LAGB: 13 LSI)
264635891	Garbossa, 2011	Endoscopic IGB or gastric band (mixed group)	LSI	6 months	30 (18 IGB or LAGB: 12 LSI)
264639295	Pontiroli, 2012	Endoscopic IGB or gastric band (mixed group)	LSI	6 months	24 (12 IGB or LAGB: 12 LSI)
264637870	Maekawa, 2020	Endoscopic IGB + LSI (low carbohydrate diet)	Endoscopic IGB + LSI (calorie-restricted diet)	12 months	31
264637871	Maekawa, 2020	Endoscopic IGB + LSI (low-carbohydrate diet)	Endoscopic IGB + LSI (calorie-restricted diet)	12 months	31
264637251	Kolli, 2020	Endoscopic IGB	Endoscopic IGB + pharmacotherapy	12 months	18
264638149	Mehta, 2021	Endoscopic IGB + LSI	Endoscopic IGB + pharmacotherapy	12 months	102
264634934	Coskun, 2010	Endoscopic IGB	Endoscopic IGB + Sibutramine	6 months	NR
264638391	Mosli, 2017	Endoscopic IGB	Endoscopic IGB + Liraglutide	NR (+6 months)	108
264639502	Reid, 2017	Endoscopic IGB	Endoscopic IGB + psycho-logical treatment	6 months	788
264638098	Mazure, 2009	Endoscopic IGB with multidisciplinary team	Endoscopic IGB without multidisciplinary team	6 months	116
264638220	Milone, 2011	Endoscopic IGB sedation	Endoscopic IGB general anaesthesia	12 months	203
264633769	Angrisani, 2006	Endoscopic IGB followed by bariatric surgery	Endoscopic IGB not followed by bariatric surgery	12 months	175
264638070	Mathus-Vliegen, 2018	Endoscopic IGB screening endoscopy	Endoscopic IGB fluoro-scopic guidance	NR	303
264637079	Khan, 2012	Endoscopic IGB with lymphoedema	Endoscopic IGB without lymphoedema	13 months	20
264634286	Blus, 2015	Endoscopic IGB	Healthy volunteer controls	6 months	36
264634498	Busetto 2005	Endoscopic IGB	Non obese controls	6 months	37

NR, not reported.

Evidence for swallowable intragastric balloon

Swallowable intragastric balloon versus bariatric surgery

TABLE 55 Swallowable IGB vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0					
Non-randomised controlled articles/studies: 2/2					
264637277	Kotelnikova, 2015	Swallowable IGB	Bariatric surgery (Scopinaro biliopancreatic diversion)	24 months	143?
264639407	Raftopoulos, 2019	Swallowable IGB (Elipse)	Bariatric surgery; 'non-surgical weight loss'	12 months	77

Swallowable intragastric balloon versus sham procedures

TABLE 56 Swallowable IGB vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 3/1					
264639351	Pryor, 2016	Swallowable IGB (Obalon) + LSI	Sham + LSI	12 months (6 months for RCT phase)	387
264640448	Sullivan, 2018	Swallowable IGB (Obalon) + LSI	Sham + LSI	12 months (6 months for RCT phase)	387
264640451	Sullivan, 2016	Swallowable IGB (Obalon) + LSI	Sham + LSI	12 months (6 months for RCT phase)	387
Non-randomised controlled articles/studies: 0					

Swallowable intragastric balloon versus lifestyle interventions

TABLE 57 Swallowable IGB vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0					
Non-randomised controlled articles/studies: 0					

Swallowable intragastric balloon versus other endoscopic interventions

TABLE 58 Swallowable IGB vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0					
Non-randomised controlled articles/studies: 6/5					
264633593	Alasfar, 2019	Swallowable IGB (Obalon) × 2 balloons	Swallowable IGB (Elipse)	Obalon 3 months treatment duration; Elipse 4 months treatment	75
264633556	Al Sharqawi, 2016	Swallowable IGB (Obalon)	Endoscopic IGB (Orbera)	3 months	143
264633685	Almuhaidb, 2020	Swallowable IGB (Obalon)	Endoscopic IGB (Orbera)	6 months	76
930783750	Swei, 2022	Swallowable IGB (Obalon)	Endoscopic IGB (Orbera)	12 months (20 weeks IGB)	87
264639430	Ramai, 2021	Swallowable IGB (Obalon)	Endoscopic IGB (Orbera; ReShape Duo)	NR (AEs only)	Unclear (773 cases)
264633686	Almuhaidb, 2019	Swallowable IGB (Obalon)	Endoscopic IGB (Orbera; ReShape); Aspiration; ESG	6 months (20 weeks therapy)	98

Swallowable intragastric balloon versus pharmacotherapy

TABLE 59 Swallowable IGB vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0					
Non-randomised controlled articles/studies: 0					

Swallowable intragastric balloon in other combinations

TABLE 60 Swallowable IGB in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 3/3					
264636637	Ienca, 2018	Swallowable IGB (Elipse) with Bluetooth	Swallowable IGB (Elipse) without Bluetooth	8 months (4 months IGB)	20
264636633	Ienca, 2018	Swallowable IGB (Elipse) + very-low-calorie ketogenic diet for 1 month	Swallowable IGB (Elipse) + very-low-calorie ketogenic diet for 4 months	4 months	24
264639940	Schiavo, 2021	Swallowable IGB (Elipse) + LSI (ketogenic diet)	Swallowable IGB (Elipse) + LSI (standard low-calorie diet)	4 months	48
Non-randomised controlled articles/studies: 0					

Evidence for other space-occupying devices

Other forms of space-occupying endoscopic device versus bariatric surgery

TABLE 61 Other forms of space-occupying endoscopic device vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0					
Non-randomised controlled articles/studies: 0					

Other forms of space-occupying endoscopic device versus sham procedures

TABLE 62 Other forms of space-occupying endoscopic device vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 2/2					
264639642	Rothstein, 2019 ENDObesity II study	TPS	Sham	12 months	270
264639368	Puri, 2021 Long-term follow-up sub tudy of ENDObesity II	TPS	Sham	48 months	44
Non-randomised controlled articles/studies: 0					

Other forms of space-occupying endoscopic device versus lifestyle interventions

TABLE 63 Other forms of space-occupying endoscopic device vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0					
Non-randomised controlled articles/studies: 0					

Other forms of space-occupying endoscopic device versus other endoscopic interventions

TABLE 64 Other forms of space-occupying endoscopic device vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0					
Non-randomised controlled articles/studies: 0					

Other forms of space-occupying endoscopic device versus pharmacotherapy

TABLE 65 Other forms of space-occupying endoscopic device vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 0					
Non-randomised controlled articles/studies: 0					

Other forms of space-occupying endoscopic device in other combinations

TABLE 66 Other forms of space-occupying endoscopic device in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs articles/studies: 1/1					
264639905	Sauer, 2013	SatiSphere	No device	3 months	31
Non-randomised controlled articles/studies: 1/1					
264637977	Marinos, 2014	TPS 3 months	TPS 6 months	6 months	20

Evidence for malabsorption devices and procedures

Evidence for duodenal–jejunal bypass liner

Duodenal–jejunal bypass liner versus bariatric surgery

TABLE 67 Duodenal–jejunal bypass liner vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 12/2					
264634841	Cinkajzlova, 2015	DJBL	Bariatric surgery? (gastric plication)	10 months	21
264634840	Cinkajzlova, 2015	DJBL	Bariatric surgery? (gastric plication)	10 months	22
264637199	Klouckova, 2015	DJBL	Bariatric surgery (gastric plication); healthy controls	10 months	30 (includes 14 healthy controls)
264638408	Mraz, 2018	DJBL	Bariatric surgery? (gastric plication)	10 months	31
264634838	Cinkajzlova, 2017	DJBL	Bariatric surgery (gastric plication); healthy controls	10 months	40 (includes 10 healthy controls)
264634839	Cinkajzlova, 2017	DJBL	Bariatric surgery? (gastric plication); healthy controls	10 months	40 (includes 10 healthy controls)

TABLE 67 Duodenal–jejunal bypass liner vs. bariatric surgery (*continued*)

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
264637309	Kratochvilova, 2019	DJBL	Bariatric surgery (gastric plication); healthy controls	10 months	59 (includes 12 healthy controls)
264636203	Guenthert, 2015	DJBL	Bariatric surgery (RYGB)	9 months	37
264636201	Guenthert, 2016	DJBL	Bariatric surgery (RYGB)	9 months	54
264636202	Guenthert, 2017	DJBL	Bariatric surgery (RYGB)	12 months	45
264640369	Stier, 2017	DJBL	Bariatric surgery (RYGB)	12 months	45
930783334	Guenthert, 2022	DJBL	Bariatric surgery (RYGB)	12 months	46

Duodenal–jejunal bypass liner versus sham procedures

TABLE 68 Duodenal–jejunal bypass liner vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 4/4					
264639585	Rodriguez, 2009	DJBL	Sham	12 months	18
930783761	Thompson, 2022	DJBL	Sham + LSI	12 months	325
264636000	Gersin, 2010	DJBL + LSI	Sham + LSI	3 months	47
930783369	Hollenbach, 2022 (the WET trial)	DJBL	Sham; endoscopic IGB	6 months IGB; Liner 12 months (+ 12 months after)	33
Non-randomised controlled studies (no. articles/no. studies): 1/1					
264633434	Abu Dayyeh, 2016	DJBS; botox; endoscopic IGB; ESG	LSI; sham	6 months	118

Duodenal–jejunal bypass liner versus lifestyle interventions

TABLE 69 Duodenal–jejunal bypass liner vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 4/3					
264640577	Tarnoff, 2009	DJBL + LSI	LSI	3 months (3 months DJBL)	39
264639658	Schouten, 2010	DJBL + LSI	LSI	3 months	41
264637222	Koehestanie, 2014	DJBL + LSI	LSI	12 months (6 months DJBL)	77
264637224	Koehestanie, 2012	DJBL + LSI	LSI	12 months (6 months DJBL)	77
Non-randomised controlled studies (no. articles/no. studies): 2/2					
264637462	Laubner, 2018	DJBL	LSI	NR	333
264633434	Abu Dayyeh, 2016	Botox; endoscopic IGB; DJBS; ESG	LSI; sham	6 months	118

Duodenal–jejunal bypass liner versus other endoscopic interventions

TABLE 70 Duodenal–jejunal bypass liner vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 3/3					
930783760	Theodoridou, 2022	DJBL	Endoscopic IGB	12 months	140
264635512	Espinet Coll, 2017	DJBL	Endoscopic IGB; POSE; ESG	NR	NR (6771 procedures)
264633434	Abu Dayyeh, 2016	DJBS	Botox; endoscopic IGB; ESG LSI; Sham	6 months	118

Duodenal–jejunal bypass liner versus pharmacotherapy

TABLE 71 Duodenal–jejunal bypass liner vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 9/1					
264640034	Sen Gupta, 2015	DJBL (EndoBarrier)	DJBL + 1.2 mg Liraglutide; Liraglutide 1.8 mg	3 months	38
264636366	Hayee, 2016	DJBL (EndoBarrier)	DJBL + 1.2 mg Liraglutide; Liraglutide 1.8 mg	3 months	55 (NAFLD)
264636844	Johal, 2016	DJBL (EndoBarrier)	DJBL + 1.2 mg Liraglutide; Liraglutide 1.8 mg	6 months	70
264640035	Sen Gupta, 2015	DJBL (EndoBarrier)	DJBL + 1.2 mg Liraglutide; Liraglutide 1.8 mg	12 months	40 (NAFLD)
264640036	Sen Gupta, 2016	DJBL (EndoBarrier)	DJBL + 1.2 mg Liraglutide; Liraglutide 1.8 mg	12 months	42
264639705	Ryder, 2016	DJBL	DJBL + 1.2 mg Liraglutide; Liraglutide 1.8 mg	12 months (10-year CVD risk)	70
264633877 (economic)	Armstrong, 2018	DJBL (EndoBarrier)	DJBL + 1.2 mg Liraglutide; Liraglutide 1.8 mg	24 months	70
264636237 (economic)	Gupta, 2018	DJBL (EndoBarrier)	DJBL + 1.2 mg Liraglutide; Liraglutide 1.8 mg	24 months	70
264636238 (economic)	Gupta, 2016	DJBL (EndoBarrier)	DJBL + 1.2 mg Liraglutide; Liraglutide 1.8 mg	24 months	70
Non-randomised controlled studies (no. articles/no. studies): 0					

Duodenal–jejunal bypass liner in other combinations

TABLE 72 Duodenal–jejunal bypass liner in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 8/2					
264639656	Ruban, 2021	DJBL (EndoBarrier)	'Conventional medical therapy' + LSI	12 months (12 months DJBL)	170
264639652	Ruban, 2021	DJBL (EndoBarrier)	'Conventional medical therapy' + LSI	12 months (12 months DJBL)	170
264639657	Ruban, 2020	DJBL (EndoBarrier)	'Conventional medical therapy' + LSI	12 months (12 months DJBL)	170
264639658	Ruban, 2021	DJBL (EndoBarrier) + 'intensive medical care'	'Intensive medical care'	24 months	170 'inadequately controlled T2D'
930783667	Ruban, 2022	DJBL + 'intensive medical care'	'Intensive medical care'	24 months	170 'inadequately controlled T2DM'
264636055	Glaysher, 2021	DJBL	'Medical therapy' + LSI	12 months	140
930783069	Aldhwayan, 2022	DJBL (EndoBarrier) + LSI	'Standard conservative weight loss management'	NR	47
264634536	Caiazzo, 2020	DJBL	'Conventional medical care'	24 months	82 (metabolic syndrome)
Non-randomised controlled studies (no. articles/no. studies): 20/4					
264634151	Benes, 2015 (prelim results)	DJBL (EndoBarrier)	No implant	6 months	44
264633320	Benes, 2015 (prelim results)	DJBL (EndoBarrier)	No implant	10 months	57
264634162	Benes, 2015 (prelim results)	DJBL (EndoBarrier)	No implant	10 months	70
264634157	Benes, 2014 (interim results)	DJBL (EndoBarrier)	No implant	10 months	70
264634163	Benes, 2015 (interim results)	DJBL (EndoBarrier)	No implant	10 months	70
264634164	Benes, 2016 (final results)	DJBL (EndoBarrier)	No implant	10 months	70
264634158	Benes, 2016 (final results)	DJBL (EndoBarrier)	No implant	10 months	70
264634153	Benes, 2017 (final results)	DJBL (EndoBarrier)	No implant	10 months	70
264634154	Benes, 2018 (final results)	DJBL (EndoBarrier)	No implant	10 months	70
264634155	Benes, 2018 (id of factors contrib to EndoB effect)	DJBL (EndoBarrier)	No implant	10 months	70
264634152	Benes, 2018	DJBL (EndoBarrier)	No implant	10 months	70
264634159	Benes, 2018	DJBL (EndoBarrier)	No implant	10 months	70
264634160	Benes, 2018	DJBL (EndoBarrier)	No implant	10 months	70
264634161	Benes, 2019	DJBL (EndoBarrier)	No implant	10 months	70
264634489	Bujisic, 2017	DJBL	'Controls'	12 months	NR morbidly obese adolescents

continued

TABLE 72 Duodenal–jejunal bypass liner in other combinations (*continued*)

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
264637195	Klemencic, 2021	DJBL	'Conservative treatment'	24 months (12 months DJBL)	45 severely obese adolescents
264641385	Younus, 2015	DJBL (EndoBarrier)	No treatment	NR	14
264641386	Younus, 2017	DJBL (EndoBarrier)	No treatment	12 months	22
264641387	Younus, 2018	DJBL (EndoBarrier)	No treatment	12 months	22
264634206	Betzel, 2013	DJBL sedation	DJBL general anaesthetic	Very short term	56
264637220	Koehestanie, 2014	DJBL (EndoBarrier) sedation	DJBL (EndoBarrier) general anaesthetic	Very short term	56

Evidence for duodenal mucosal resurfacing

Duodenal mucosal resurfacing versus bariatric surgery

TABLE 73 Duodenal mucosal resurfacing vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 0					

Duodenal mucosal resurfacing versus sham procedures

TABLE 74 Duodenal mucosal resurfacing vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 1/1					
264637007	Kaur, 2021	DMR	Sham	6 months	32
Non-randomised controlled studies (no. articles/no. studies): 0					

Duodenal mucosal resurfacing versus lifestyle intervention

TABLE 75 Duodenal mucosal resurfacing vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 0					

Duodenal mucosal resurfacing versus other endoscopic interventions

TABLE 76 Duodenal mucosal resurfacing vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 0					

Duodenal mucosal resurfacing versus pharmacotherapy

TABLE 77 Duodenal mucosal resurfacing vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 0					

Duodenal mucosal resurfacing in other combinations

TABLE 78 Duodenal mucosal resurfacing in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 0					

Evidence for other forms of endoscopic treatment

Evidence for aspiration therapy

Aspiration versus bariatric surgery

TABLE 79 Aspiration vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 3/2					
264641182	Wilson, 2017	Aspiration	Bariatric surgery (RYGB)	12 months	106
264641183	Wilson, 2018	Aspiration	Bariatric surgery (RYGB)	36 months	106
264638056	Mathur, 2021	Aspiration	Sleeve; Band; Bypass; Stimulator; LSI	60 months	30

Aspiration versus sham procedures

TABLE 80 Aspiration vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 2/1					
930783309	Gether, 2022	Aspiration (AspireAssist)	Sham; no treatment	NR acute effects only for hormones	14 (7 within subject test of aspiration and sham visits: 7 controls)
264636003	Gether, 2021	Aspiration (AspireAssist)	Sham; no treatment	NR	14 (7 within subject test of aspiration and sham visits: 7 controls)

Aspiration versus lifestyle interventions

TABLE 81 Aspiration vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 7/2					
264637193	Klein, 2012	Aspiration (AspireAssist) + LSI	LSI	12 months	18
264640444	Sullivan, 2012	Aspiration (AspireAssist) + LSI	LSI	24 months	18
264640447	Sullivan, 2013	Aspiration (AspireAssist) + LSI	LSI	24 months	18
264640657	Thompson, 2016	Aspiration (AspireAssist) + LSI	LSI	12 months	171
264640656	Thompson, 2017	Aspiration (AspireAssist) + LSI	LSI	12 months	207
264640661	Thompson, 2018	Aspiration (AspireAssist) + LSI	LSI	48 months	55 (of 171)
264640658	Thompson, 2019	Aspiration (AspireAssist) + LSI	LSI	60 months	171
Non-randomised controlled studies (no. articles/no. studies): 1					
264638056	Mathur, 2021	Aspiration (AspireAssist)	Sleeve; Band; Bypass; Stimulator; LSI	60 months	30

Aspiration versus other endoscopic interventions

TABLE 82 Aspiration vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 1					
264633686	Almuhaidb, 2019	Aspiration	Endoscopic IGB; swallowable IGB; ESG	6 months	98

Aspiration versus pharmacotherapy

TABLE 83 Aspiration vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 0					

Aspiration in other combinations

TABLE 84 Aspiration in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 0					

Evidence for botox

Botox versus bariatric surgery

TABLE 85 Botox vs. bariatric surgery

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 1/1					
930783609	Ozdil, 2022	Botox	Bariatric surgery; LSI	6 months	72

Botox versus sham procedures

TABLE 86 Botox vs. sham procedures

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 6/5					
Hand searching	Foschi, 2007 (pilot study)	Botox	Sham (placebo)	8 weeks	24
264639822	Sanchez-Torralvo, 2021	Botox	Sham (placebo)	6 months	52
930783689	Sachez-Torralvo, 2022	Botox	Sham (placebo)	8 months	46

continued

TABLE 86 Botox vs. sham procedures (*continued*)

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
264638276	Mittermair, 2007	Botox	Sham (placebo)	6 months	10
264635151	de Moura, 2019	Botox	Sham (placebo)	6 months	32
264636211	Gui, 2006 (pilot)	Botox (two different doses)	Sham (placebo)	5 weeks	18
Non-randomised controlled studies (no. articles/no. studies): 2/2					
264635760	Foschi, 2008	Botox	Sham	8 weeks	30
264633434	Abu Dayyeh, 2016	Botox; endoscopic IGB; DJBS; ESG	Sham (placebo); LSI	6 months	118

Botox versus lifestyle interventions

TABLE 87 Botox vs. lifestyle interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 4/4					
930783376	Hsu, 2022	Botox + LSI	LSI	4 months	71
264635638	Ferhatoglu, 2020	Botox + LSI	LSI; botox	NR	87
930783609	Ozdil, 2022	Botox	Bariatric surgery; LSI	6 months	72
264633434	Abu Dayyeh, 2016	Botox; endoscopic IGB; DJBS; ESG	Sham; LSI	6 months	118

Botox versus other endoscopic interventions

TABLE 88 Botox vs. other endoscopic interventions

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 2/1					
264637608	Li, 2012	Botox 200U dose	Botox 300U dose	3 months	20
264637609	Li, 2012	Botox 200U dose	Botox 300U dose	3 months	20
Non-randomised controlled studies (no. articles/no. studies): 4/4					
930783755	Tayyem, 2022	Botox	Endoscopic IGB	6 months	176
264635353	Durmus, 2019	Botox + LSI	Endoscopic IGB + LSI	3 months	52
264636939	Kanlioz, 2020	Botox	Endoscopic IGB + botox; endoscopic IGB	6 months	121
264633434	Abu Dayyeh, 2016	Botox	Endoscopic IGB; DJBS; ESG; sham; LSI	6 months	118

Botox versus pharmacotherapy

TABLE 89 Botox vs. pharmacotherapy

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 0					

Botox in other combinations

TABLE 90 Botox in other combinations

ID	Author, date	Intervention(s)	Comparator(s)	Follow-up	*N*
RCTs (no. articles/no. studies): 0					
Non-randomised controlled studies (no. articles/no. studies): 0					

Appendix 2 Clinical effectiveness evidence to inform models

Evidence map

In order to inform model parameters on relative effectiveness of ESG versus LSG, ESG versus semaglutide and IGB versus semaglutide, comparative studies were sought from the evidence map.

Endoscopic sleeve gastroplasty versus laparoscopic sleeve gastrectomy

There were no RCTs directly comparing ESG with LSG. A systematic review from 2022[100] was identified, which included seven controlled studies (five retrospective and two prospective cohort studies). The same seven studies were also identified in the evidence map, and no additional controlled studies were identified (searches to January 2023).

The systematic review was quality assessed using the A MeaSurement Tool to Assess systematic Reviews 2 checklist[121] as a guide and was found to be of good methodological quality. Independent data extraction of the seven studies was performed and there were no discrepancies with the data reported in the systematic review. The pooled summary mean differences from random-effects meta-analyses (mean %TBWL at 6, 12 and 24 months) were therefore used to inform model 1. The %TBWL was significantly greater with LSG compared with ESG [6 months: MD −7.48 (95% CI −10.44 to −4.52, $p < 0.00001$); 12 months: MD −9.90 (95% CI −10.59 to −9.22, $p < 0.00001$); 24 months: MD −7.63 (95% CI −11.31 to −3.94, $p < 0.0001$)]. As the evidence is from observational studies, and the 12- and 24-month pooled estimates are based on only four and two studies, respectively, there is uncertainty associated with these estimates.

Endoscopic sleeve gastroplasty or intragastric balloon versus semaglutide

There were no RCTs or controlled studies identified within the evidence map that directly compared ESG or IGB to semaglutide.

Indirect comparisons

In the absence of direct comparisons of ESG versus semaglutide and IGB versus semaglutide, indirect comparisons were undertaken. This required identification of RCTs with similar populations, interventions and comparators in common.

Randomised controlled trials of ESG versus any comparator and IGB versus any comparator were identified from the evidence map. RCTs of semaglutide versus any comparator were not sought as part of the main searches as this comparison was beyond the remit of the report. Therefore, systematic reviews identified as part of the evidence map screening were checked to identify any existing NMAs that may have included controlled studies of ESG, IGB or semaglutide with comparators in common. Only two systematic reviews including a NMA were identified (Ding *et al.*,[122] Sung Hoon Jung *et al.*)[123] and neither were useful in providing such studies. Additional targeted searches for systematic reviews of semaglutide were therefore conducted in order to identify RCTs within these (Focused search strategies for systematic reviews of semaglutide). Fifteen systematic reviews were identified, and included RCTs were mapped according to number of included RCTs, interventions, comparators and population. Additionally, recent RCTs focusing on semaglutide were sought from Cochrane CENTRAL (n = 144 records identified and screened).

Indirect comparisons rely on RCTs being similar in patient and study characteristics other than the treatment comparison of interest. Across all RCTs identified within the systematic reviews and those identified from Cochrane CENTRAL, seven RCTs were selected that were deemed most similar in terms of the comparator treatment, included populations and outcome assessment. The most common comparator identified across all RCTs was LSI alone, with both intervention and comparator arms receiving LSI. Follow-up periods were mostly up to 12 months, and the outcome of interest to inform the model was %TBWL.

Two RCTs comparing ESG with LSI,[85,124] *Appendix 1*, *Table 90*, three RCTs comparing IGB with LSI[125–127] (*Appendix 2*, *Table 91*) and two RCTS comparing semaglutide with LSI[128,129] (*Appendix 2*, *Table 92*) were included in the analysis. Follow-up was at 6 and/or 12 months. Sample sizes ranged from *n* = 31 to *n* = 1232. Data were extracted on patient numbers in the different treatment arms and mean [standard deviation (SD)] %TBWL at 6 and 12 months. Where a SD was not reported, this was estimated from the SE (multiplying by square root of sample size) or from the 95% CI.[130] The analysis at 6 months included all seven RCT, and at 12 months included five RCTs where 12-month data were reported.

TABLE 91 Randomised controlled trials comparing ESG with LSI

Trial name, Author, date, reference	Population *N*/age/sex Baseline BMI	Baseline comorbidities no. (%)	Length of follow-up	Details of lifestyle intervention	Effects and time points measured	Effect sizes for %TBWL
MERIT trial ESG + LSI vs. LSI alone Abu Dayyeh, 2022[85] *Lancet* 2022;**400**: 441–51	*N* = 209 ESG 85: LSI 124 Actual *N* ESG 77: LSI 110. Mean age (y) ESG 47.3 (9.3) LSI 45.7 (10.0) Female ESG *n* = 68 (88%) LSI *n* = 92 (84%) Based on ESG 77: LSI 110 Mean BMI ESG 35.5 (2.6) LSI 35.7 (2.6)	Hypertension ESG 38 (49%) LSI 58 (53%); T2DM ESG 18 (23%) LSI 36 (33%)	52 weeks (104 weeks for ESG group)	For first 12 months of study treatment, a standard moderate-intensity LSI adjusted according to each participants needs. Low-calorie diet plan. Physical activity, including 150 minutes aerobic exercise/week, was encouraged and assessed for compliance during the study Transitional diet for ESG group to allow for suture healing. Dietary supplements for ESG group Programme based on The Mayo Clinic HEALTH Program, a behavioural approach for weight management	% EWL, proportion of patients with 25% or more EWL, %TBWL, proportion of patients with 5% or more and 10% or more of TBWL. AEs and SAEs Absolute WL, waist circumference. QoL: SF-36 and the Impact of Weight on Quality of Life (IWQOL) tool. Three-factor eating, depression (PHQ-9), and satisfaction with treatment	Mean %TBWL at 52 weeks ESG 13.6% (8.0) LSI 0.8% (5.0) ($p < 0.0001$) After adjusting for age, sex, T2DM, hypertension, and baseline BMI in a modified ITT analysis with mixed-effects models, participants in the ESG group had a mean difference of 12.6% (10.7–14.5) TBWL, compared with the control group at 52 weeks ($p < 0.0001$ using LOCF and $p < 0.0001$) using mixed-model imputations for missing data 24m data cannot be used, as control group could crossover to ESG after 12 months (contingent on meeting certain attendance criteria)
ESG + LSI vs. LSI alone Huberty, 2021[124] *Gut* 2021;**70**: 1479–85	*N* = 71 ESG 49: LSI 22 Mean age (y) ESG 37.6 (9.9) LSI 45.3 (11.7) $p = 0.005$ Female ESG *n* = 46 (94%) LSI *n* = 20 (91%) $p = 0.651$ Mean BMI ESG 34.8 (2.7) LSI 34.2 (2.5) $p = 0.367$	Not reported or not reported for separate arms	6 months	Low-calorie high-protein diet and lifestyle counselling based on Belgian Association for the Study of Obesity (BASO) 2010 and American Society of Metabolic and Bariatric Surgery (ASMBS) 2013 guidelines. Physical activity was promoted. Psychological support was added on a case-by-case basis when needed. Transitional diet for ESG patients after procedure	Mean EWL, %TBWL at 6 months, BMI, absolute WL, QoL. AEs and SAEs	%TBWL at 6 m ESG 11.0 (8.86–13.15) LSI 2.7 (0.14–5.44) 12 m data given but not relevant due to crossover of LSI patients to ESG at 6 months

LOCF, last observation carried forward; PHQ-9, Patient Health Questionnaire-9 items; T2DM, type 2 diabetes mellitus.

TABLE 92 Randomised controlled trials comparing IGB with LSI

Trial name, Author, date, reference	Population N/age/sex Baseline BMI	Baseline comorbidities no. (%)	Length of follow-up	Details of lifestyle intervention	Effects and time points measured	Effect sizes
IGB + LSI vs. LSI alone Abu Dayyeh, 2021[125] *Lancet* 2021;**398**: 1965–73	*N* = 288 IGB 187: LSI 101 Mean age (y) IGB 44.4 (8.9) LSI 44.0 (8.9) Female IGB *n* = 162 (87%) LSI *n* = 90 (89%) Mean BMI IGB 35.8 (2.6) LSI 35.8 (2.7)	Dyslipidaemia IGB 41 (22%) LSI 23 (23%) Hypertension IGB 41 (22%) LSI 32 (32%) Obstructive sleep apnoea IGB 1 (1%) LSI 1 (1%) T2DM IGB 13 (7%) LSI 4 (4%)	32 weeks	Diet to create a deficit of 500–1000 kcal/day for each patient. Diet plans reviewed and adjusted as needed. Dietary education provided. Exercise plan with three stages that were phased in over the 32-week follow-up period, with increasing levels of activity/intensity. Tailored to patients' capabilities to prevent injury	%TBWL %EWL Absolute WL, AEs and SAEs.	Multiple imputed ITT population: mean %TBWL at 32 weeks IGB 15.0% (95% CI 13.9 to 16.1) LSI 3.3% (2.0 to 4.6) ($p < 0.0001$) The difference in mean %TBWL at week 32 between the adjustable IGB and control groups was 11.7% (9.9 to 13.5) The per-protocol population showed a mean of 15.2% TBWL at 32 weeks in the aIGB group and 4.1% in the control group ($p < 0.0001$) Percentage of participants with TBWL at week 32 ≥ 5%: IGB 91.7; LSI 31.8 ≥ 10%: IGB 72.4; LSI 15.2 ≥ 15%: IGB 46.7; LSI 5.6
The BIB or IB-005 study IGB + LSI vs. LSI alone Courcoulas, 2017[126] *International Journal of Obesity* 2017;**41**:427–33	*N* = 255 IGB 125: LSI 130 Mean age (y) IGB 38.7 ± 9.37 LSI 40.8 ± 9.61 Female IGB *n* = 112 (89.6%) LSI *n* = 117 (90.0%) Mean BMI < 30 IGB *n* = 2 (1.6%) LSI *n* = 1 (0.8%) ≥ 30 to < 35 IGB *n* = 63 (50.4%) LSI *n* = 57 (43.8%) ≥ 35 to ≤ 40 IGB *n* = 56 (44.8%) LSI *n* = 70 (53.8%) > 40 IGB *n* = 4 (3.2%) LSI *n* = 2 (1.5%)	Type 2 diabetes IGB 9 (7%) LSI 8 (6%) Hypertension IGB 33 (26) LSI 37 (28) Dyslipidaemia IGB 49 (39) LSI 39 (30)	IGB for 6 months. Followed up for 12 months	Both study groups participated in a 12-month lifestyle programme that incorporated the following elements: a low-calorie (1000–1500 calories per day) diet, daily food and exercise diary, encouragement to exercise and emphasis on behavioural change during a total of 21 visits (9 visits in months 1–6, 12 visits in months 7–12).	%TBWL; %EWL; AEs, QoL. Absolute WL also given. Reported at 6, 9 and 12 months.	At 6 months %TBWL mean (SD) range IGB −10.2 (6.56) −29.2 to 9.6 LSI − 3.3 (5.02) −19.0 to 5.4 ($p < 0.001$) At 9 months (3 months post-balloon removal) %TBWL IGB −9.1 (6.86) −28.0 to 14.0 LSI −3.4% (5.33) −19.8 to 5.7 ($p < 0.001$) At 12 months, −3.1% (−2.9 kg) vs. −7.6% (−7.4 kg, $p < 0.001$) Adjusted means and mean differences in %TBWL: 6 months %TBWL IGB −9.1 (−10.1 to −8.2) (95% CI) LSI −3.3 (−4.3 to −2.4). MD −5.8 (−7.1 to −4.5) $p < 0.001$. 9 and 12 months also reported

continued

DOI: 10.3310/PWKQ2310

Health Technology Assessment 2025 Vol. 29 No. 68

TABLE 92 Randomised controlled trials comparing IGB with LSI (*continued*)

Trial name, Author, date, reference	Population *N*/age/sex Baseline BMI	Baseline comorbidities no. (%)	Length of follow-up	Details of lifestyle intervention	Effects and time points measured	Effect sizes
IGB + LSI vs. LSI alone Fuller, 2013[127] *Obesity* 2013;**21**:1561–70	*N* = 66 IGB 31: LSI 35 Mean age (yr ± SD) IGB 43.4 ± 9.4 LSI 48.1 ± 7.3 Female IGB *n* = 21 (68%) LSI *n* = 23 (66%) Mean BMI ± SD IGB 36.0 ± 2.7 LSI 36.7 ± 2.9	NR	6 months IGB with 12 months behavioural modification OR 12 months behavioural modification	The same behavioural modification programme was employed for both groups, based on the Type 2 Diabetes Lifestyle Intervention Program. Written guide to the specific types of foods and the quantities which could be consumed. Tailored exercise programme. Each subject also received a pedometer and was encouraged to walk at least 10,000 steps daily. Patients were instructed to remain inactive for 3 days post insertion and to comply with a transitional diet up to day 20	Given for 3, 6, 9 and 12 months. Change in weight from baseline as % of initial WL; absolute WL; %EWL; BMI; proportion with a ≥ 5%, ≥ 10%, or ≥ 15% weight reduction Waist circumference Remission of metabolic syndrome Exercise tolerance. QoL. Eating behaviours. Safety. Primary end point for the study was % WL at month 6	3 and 9 months also reported. Mean % WL at 6 months: IGB −14.2 vs. LSI −4.8; $p < 0.0001$. Mean % WL at 12 months: IGB −9.2 vs. LSI −5.2; $p = 0.007$

IGB, intragastric balloon; T2DM, type 2 diabetes mellitus.

TABLE 93 Randomised controlled trials comparing semaglutide with LSI

Trial name, Author, date, reference	Population *N*/age/sex Baseline BMI	Baseline comorbidities no. (%)	Length of follow-up	Details of lifestyle intervention	Effects and time points measured	Effect sizes
STEP 1 SG + LSI vs. Placebo + LSI	*N* = 1961 SG 1306: Placebo 655	Dyslipidaemia SG 499 (38.2)	68 weeks	Individual counselling sessions every 4 weeks to help them adhere to a reduced-calorie diet (500-kcal deficit per day relative to the energy expenditure estimated at the time they underwent randomisation) and increased physical activity (with 150 minutes per week of physical activity, such as walking, encouraged)	Every 4–20 weeks then every 8–68 weeks. Observed in trial and on treatment data given. Percentage body weight and BMI change. Participants with body-weight reduction at different thresholds. Waist circumference, absolute body weight, SF-36 physical functioning and IWQOL-Lite-CT physical function scores also given. AEs and SAEs	Percentage body-weight change from Baseline to week 68 SG −14.85: Placebo −2.41. Difference between SG and Placebo (95% CI) −12.44 (−13.37 to −11.51).
Wilding, 2021[129] *New England Journal of Medicine* 2021;**384**: 989–1002	Mean age (y) SG 46 ± 13 Placebo 47 ± 12 Female SG *n* = 955 (73.1%) Placebo *n* = 498 (76.0%) Mean BMI SG 37.8 ± 6.7 Placebo 38.0 ± 6.5 BMI distribution no. (%) ≥ 30 to < 35: SG 436 (33.4); Placebo 207 (31.6) ≥ 35 to < 40: SG 406 (31.1); Placebo 208 (31.8) ≥ 40: SG 383 (29.3) Placebo 204 (31.1)	Placebo 226 (34.5) Hypertension SG 472 (36.1) Placebo 234 (35.7) Coronary artery disease SG 32 (2.5) Placebo 17 (2.6) Obstructive sleep apnoea SG 159 (12.2) Placebo 71 (10.8) Asthma or COPD, non-alcoholic fatty liver disease and number of coexisting conditions at screening also given				

continued

DOI: 10.3310/PWKQ2310

TABLE 93 Randomised controlled trials comparing semaglutide with LSI (*continued*)

Trial name, Author, date, reference	Population *N*/age/sex Baseline BMI	Baseline comorbidities no. (%)	Length of follow-up	Details of lifestyle intervention	Effects and time points measured	Effect sizes
STEP 5 SG + LSI vs. Placebo + LSI Garvey, 2022[128] *Nature Medicine* 2022;**28**: 2083–91	Three hundred and four participants were randomly assigned to semaglutide 2.4 mg (*n* = 152) or placebo (*n* = 152) SG 47.3 years (11.7) Placebo 47.4 years (10.3) Female SG 123 (80.9%) Placebo 113 (74.3%) Mean BMI SG 38.6 (6.7) Placebo 38.5 (7.2)	Dyslipidaemia SG 58 (38.2%) Placebo 49 (32.2%) Hypertension SG 56 (36.8%) Placebo 62 (40.8%) Coronary artery disease SG 2 (1.3%) Placebo 3 (2.0%) Obstructive sleep apnoea SG 27 (17.8%) Placebo 24 (15.8%)	104 weeks	Longer running STEP trial. Not reported but LSI will be same as other trials	Observed in trial and on treatment data given. Percentage body-weight and BMI change from baseline. Percentage of participants with body-weight reduction at different thresholds. Waist circumference, absolute body weight. AEs and SAEs	Percentage body-weight change from baseline [estimated mean (SE)] to week 104 SG −15.2 (0.9): Placebo −2.6 (1.1). Difference between SG and Placebo (95% CI) −12.6 (−15.3 to −9.8); $p < 0.0001$

COPD, chronic obstructive pulmonary disease; IWQOL, Impact of Weight on Quality of Life; SG, semaglutide.

Data for indirect comparisons

TABLE 94 Endoscopic sleeve gastroplasty + LSI vs. LSI alone

		ESG + LSI				LSI			
Study	***N* at baseline**	***N***	**Mean**	**SD**	**95% CI**	***N***	**Mean**	**SD**	**95% CI**
%TBWL at 6 months									
Abu Dayyeh 2022[85]	77 ESG: 110 LSI	NR	14.722	NR	(14.166 to 15.277)	NR	1.427	NR	(0.891 to 2.036)
Huberty 2021[124]	49 ESG: 22 LSI	45	11.0	NR	(8.86 to 13.15)	21	2.7	NR	(0.14 to 5.44)
%TBWL at 12 months									
Abu Dayyeh 2022[85]	77 ESG: 110 LSI	68	13.6	8	NR	89	0.8	5	NR

TABLE 95 Intragastric balloon + LSI vs. LSI alone

		IGB + LSI				LSI			
Study	***N* at baseline**	***N***	**Mean**	**SD**	**95% CI**	***N***	**Mean**	**SD**	**95% CI**
%TBWL at 6 months									
Abu Dayyeh 2021[125]	187 IGB: 101 LSI	156	15.0	NR	(13.9 to 16.1)	75	3.3	NR	(2.0 to 4.6)
Courcoulas 2017[126]	125 IGB: 130 LSI	119	10.2	6.56	NR	121	3.3	5.02	NR
Fuller 2013[127]	31 IGB: 35 LSI	29 (31 in analysis)	Least squares means 14.2	NR	(12.079 to 16.187)	30 (35 in analysis)	Least squares means 4.8	NR	(2.854 to 6.774)
%TBWL at 12 months									
Abu Dayyeh 2021[125]	187 IGB: 101 LSI	144	NR	NR	NR	NR	NR	NR	NR
Courcoulas 2017[126]	125 IGB: 130 LSI	98	7.6	7.48	NR	93	3.1	5.9	NR
Fuller 2013[127]	31 IGB: 35 LSI	23 (31 in analysis)	9.2	NR	(7.009 to 11.32)	22 (35 in analysis)	5.2	NR	(3.183 to 7.173)

Stata was used to run the analysis. For each of the three pairwise comparisons, random-effects meta-analyses were performed fit using restricted maximum likelihood estimation[131] using the Knapp–Hartung adjustment to the SE.[132] These were each performed separately at 6 months and at 12 months. Results from pairwise meta-analyses were used to perform indirect comparisons using the method of Bucher *et al.*[133]

The indirect comparison found little evidence of a difference in mean %TBWL (95% CI) between ESG and semaglutide at 6 months [2.15 (−29.47 to 33.76)] and 12 months [0.54 (−2.05 to 3.14)], *Appendix 2*, *Table 96*, though CIs at 6 months are extremely wide. The mean difference between IGB and semaglutide was 0.54 (−2.05 to 3.14) at 6 months and −7.91 (−11.14 to −4.67) at 12 months, thus finding little difference at 6 months but good statistical evidence of a difference in favour of greater WL with semaglutide at 12 months.

TABLE 96 Semaglutide + LSI vs. placebo + LSI

Study	*N* at baseline	Semaglutide + LSI				Placebo + LSI			
		N	Mean	SD	95% CI	*N*	Mean	SD	95% CI
%TBWL at 6 months									
Wilding 2021[129]	1306 SG: 655 Placebo	1232	11.715	SE 11.526, 11.905	NR	592	2.859	SE 2.635, 3.083	NR
Garvey 2022[128]	152 SG: 152 Placebo	152	12.052	SE 11.555, 12.578	NR	133	2.666	SE 2.169, 3.105	NR
%TBWL at 12 months									
Wilding 2021[129]	1306 SG: 655 Placebo	1203	15.51	SE 15.242, 15.780	NR	549	3.295	SE 3.026, 3.563	NR
Garvey 2022[128]	152 SG: 152 Placebo	149	15.863	SE 15.083, 16.667	NR	129	3.314	SE 2.730, 3.899	NR

There are some limitations to this analysis. Despite selecting the most similar RCTs, there were some differences in the comparator as the semaglutide trials included a placebo in addition to LSI, while the ESG and IGB trials included only LSI with no placebo/sham treatment. This is due to the nature of the interventions, with blinding more difficult to undertake for the surgical interventions compared with pharmacotherapy. As a result, the transitivity assumption required for indirect comparisons is in doubt and results should be treated with extreme caution. There were also some differences between the LSIs, though all included dietary and physical activity components, and some slight differences in mean baseline BMI (where reported). Suitable trial data beyond a 12-month follow-up period were not identified.

The time horizon for the economic models was 5 years; therefore, effectiveness data up to 5 years were required to inform model parameters. Based on the controlled studies identified from the evidence map, and the indirect comparisons, there were data up to 24 months for ESG versus LSG, and up to 12 months for ESG versus semaglutide and IGB versus semaglutide.

The evidence map was therefore searched for single-arm studies with follow-up beyond 12 months (IGB) or beyond 24 months (ESG). Targeted searches were performed for longer-term semaglutide and LSG studies, and clinical experts from the steering group also highlighted studies with potentially longer follow-up for all interventions.

Appendix 2, *Table 97* shows the studies identified and highlights those where estimates informed model parameters as well as reasons for why study estimates were not considered suitable. Overall, the evidence on long-term effectiveness (> 24 months) was very limited. Only 10 potentially relevant studies were identified, and of these, only 3 were used to inform model parameters. The main concerns with the long-term studies were substantial losses to follow-up over time, high or unknown proportions of patients undergoing revision therapy or switching to other treatments if WL was insufficient, or selection of patients for further follow-up based on initial WL targets.

Long-term effectiveness (weight loss) data

Evidence for longer-term effectiveness of ESG came from the Alqahtani 2022 study,[110] a large propensity score-matched comparative study of ESG and LSG with a follow-up of 36 months (*n* = 3018 patient pairs). Only a small proportion (< 4%) underwent revision or further surgery in the ESG arm and the proportion remaining in follow-up was around 33% at 36 months. Baseline BMIs were between 27.5 and 35, which includes a slightly lower BMI than that of the population modelled. Further evidence for LSG came from the study by Wölnerhanssen (2021),[111] which had data on around 200 LSG patients followed up over 5 years.

DOI: 10.3310/PWKQ2310

TABLE 97 Indirect comparison results

Comparison type	T1	T2	MD	Lower95	Upper95	SeMD	Number of trials	Total sample size (direct comparisons)
6 months								
Direct	ESG and LSI	LSI	11.084	−20.441	42.608	16.08393	2	122 ESG + LSI, 131 LSI
Direct	SG and LSI	LSI and Placebo	8.937	6.519	11.354	1.233418	2	1384 Semaglutide + LSI, 725 LSI
Indirect	ESG and LSI	SG and LSI	2.15	−29.47	33.76	16.13	–	–
Direct	IGB and LSI	LSI	9.303	3.142	15.464	3.143367	3	306 IGB + LSI, 231 LSI
Direct	SG and LSI	LSI and Placebo	8.937	6.519	11.354	1.233418	2	1384 Semaglutide + LSI, 725 LSI
Indirect	IGB and LSI	SG and LSI	0.37	−6.25	6.98	3.38	–	–
12 months								
Direct	ESG and LSI	LSI	12.8	10.633	14.967	1.105612	1	68 ESG + LSI, 89 LSI
Direct	SG and LSI	LSI and Placebo	12.258	10.833	13.683	0.727041	2	1352 Semaglutide + LSI, 678 LSI
Indirect	ESG and LSI	SG and LSI	0.54	−2.05	3.14	1.32	–	–
Direct	IGB and LSI	LSI	4.352	1.451	7.253	1.480102	3	273 IGB + LSI, 203 LSI
Direct	SG and LSI	LSI and Placebo	12.258	10.833	13.683	0.727041	2	1352 Semaglutide + LSI, 678 LSI
Indirect	IGB and LSI	SG and LSI	−7.91	−11.14	−4.67	1.65	–	–

Kotzampassi (2012)[113] provided long-term effectiveness estimates for IGB. This was a single-arm study (n = 500) with a follow-up of up to 5 years. The proportion remaining in follow-up after 5 years was 39%. There were some concerns around follow-up bias, as only patients with > 20% WL could continue after 6 months, and a proportion also had additional interventions. However, rate of weight regain only was used from years 1 to 5, so it was not expected that biases in the follow-up would impact the rate of regain significantly.

Lincoff (2023)[114] provided long-term effectiveness data for semaglutide. This was a placebo-controlled RCT with n = 8803 randomised to semaglutide with a follow-up of up to 48 months. At 48 months, only 13% remained in follow-up. Eligibility for the study was a BMI 27 or over and pre-existing cardiovascular disease, and no diabetes, which differs from the population modelled. Further, semaglutide was given for the whole trial duration, whereas the model assumes discontinuation of semaglutide after 2 years. However, this study was only used in the 5-year analysis for assuming continuity of WL.

Given the limited evidence on long-term effectiveness and the uncertainty around the effect estimates, sensitivity analyses were undertaken around all long-term effectiveness estimates used in the model.

The model included costs and disutilities associated with SAEs. It was not possible to estimate AEs rates for ESG, IGB and LSG based on studies included in the evidence map as the volume of studies was too substantial. Instead, targeted searches for systematic reviews were undertaken and clinical experts from the steering group also highlighted potentially useful reviews and primary studies. For ESG, LSG and IGB, SAEs were defined as any AE requiring hospitalisation. This did not include revision or redo procedures due to weight regain. For semaglutide, SAEs were defined as per a recent model developed as part of a NICE Single Technology Appraisal.[36]

There were several concerns with SAE reporting across studies (*Appendix 2*, *Tables 98–101*). Some studies/systematic reviews did not report AEs, or did not distinguish by severity so could not be used. Where studies did report SAEs, these were frequently not the same ones for the same intervention and/or there were differences in classifications for defining 'serious' or 'severe'. The study definition for SAE did not always overlap with our definition of 'requiring hospitalisation' and the overlap between SAEs, reoperations and hospital re-admissions was often unclear. It was thus not possible to estimate the proportion of those with SAEs requiring surgical interventions. Further, there were differences in length of follow-up, different methods of calculating summary estimates (e.g. pooled effect estimate from meta-analysis or crude incidence) and potentially some double counting of the same studies included in different reviews.

Serious adverse events and mortality

For ESG, the SAE rate from the systematic review and meta-analysis by Docimo[104] was used in the base case (*Appendix 2*, *Table 98*). This was based on a review of previous systematic reviews as well as primary studies and, as such, was the most comprehensive. This estimated the overall SAE rate as 2–3% and mortality at 0%. There was no single definition for SAEs; the main ones noted were bleeding and abscess formation.

For LSG, findings from the systematic review by Beran (2022)[100] were used, which reported a 0.51 lower risk of overall AEs for ESG compared with LSG, and a 4% LSG AE rate.

For IGB, the SAE rate of 0.6% was estimated from four previous systematic reviews,[105,117–119] a large case series[116] (*Appendix 2*, *Table 99*) and clinical advice. A mortality rate of 0.1% was applied based on the systematic review by Singh *et al.* (2020).[105]

For semaglutide, no studies reported SAEs or mentioned hospitalisations (*Table 101*). However, a recent model for semaglutide[36] used a SAE rate of 4.9%. As this is a pharmacological intervention, the SAE profile used in the NICE model for semaglutide is clearly distinct from SAEs associated with surgery. Therefore, severe gastrointestinal events as defined by the NICE model were considered, which had a lower cost and disutility than the SAEs associated with surgery. Assumptions regarding the rate and severity of SAEs were tested in the model extensively.

TABLE 98 Long-term studies

Study and source	Intervention	Months FU	Mean %TBWL	SD	95% CI	*n* (%) in FU	Caveats
Alqahtani 2022[110]	ESG *n* = 3018	6	15.1	6.1	NR	2855	BMIs between 27.5 and 35. Eighty patients (2.7%) underwent revision to LSG for insufficient WL or weight regain after an average of 10 months, and 28 (0.9%) had a second ESG after a mean of 19 months. No weight-related revision was performed in LSG group **USED TO INFORM MODEL**
		12	19.2	7.7	NR	2637	
		24	16.2	9.7	NR	2442	
		36	14	12.1	NR	1005	
	LSG *n* = 3018	6	18.0	7.3	NR	2294	
		12	28.9	8.2	NR	2354	
		24	22.2	8.2	NR	2102	
		36	18.8	7.5	NR	746	
Bhandari 2022[134]	ESG *n* = 612	6	18.68	4.52	(18.31 to 19.06)	612	Twenty-two (3.6%) patients had revision or redo ESG and 19 (3.1%) were revised to sleeve gastrectomy Seventy per cent self-funded patients who may be more motivated than those in other settings. Unclear if patients had post-procedural pharmacotherapy. Eligibility criteria for follow-up unclear
		12	21.20	4.70	(20.81 to 21.59)	570	
		24	20.05	5.23	(19.61 to 20.48)	552	
		36	18.74	4.06	(18.31 to 19.12)	466	
		48	18.19	5.02	(17.72 to 18.57)	254	
Sander 2022[135]	ESG *n* = 189	12	%AWL −16.54	NR	(−17.78 to −15.87)	189	No numbers of secondary interventions reported. Very low patient numbers at 36 and 48 months. Definition of %AWL unclear though likely to be equivalent to %TBWL
		24	%AWL −20.15	NR	(−21.60 to −18.92)	149	

continued

DOI: 10.3310/PWKQ2310

Health Technology Assessment 2025 Vol. 29 No. 68

TABLE 98 Long-term studies (*continued*)

Study and source	Intervention	Months FU	Mean %TBWL	SD	95% CI	*n* (%) in FU	Caveats
		36	%AWL −19.77	NR	(−22.73 to −17.49)	51	
		48	%AWL −21.09	NR	(−26.27 to −16.24)	16	
Lopez-Nava 2021[136]	ESG *N* = 199	6	16.8	NR	(15.6 to 18.0)	NR	No numbers of secondary interventions reported
		12	18.6	NR	(17.3 to 20.0)	135	
		18	19.4	NR	(17.4 to 21.4)	NR	
		24	18.5	NR	(16.6 to 20.5)	46	
	LSG *n* = 61	6	26.5	NR	(24.8 to 28.2)	NR	
		12	28.4	NR	(26.6 to 30.2)	43	
		18	29.2	NR	(27.1 to 31.3)	NR	
		24	28.3	NR	(26.2 to 30.4)	34	
Abu Dayyeh 2022[85]	ESG *n* = 77	12	13.6	8.0	NR	68	None had secondary intervention before 24 months. Numbers taken from graph (using webplot digitiser)
		24	11.86	NR	(11.28 to 12.32)	44	
Lind 2023[137]	LSG *n* = 1263	12	−26.2	9.4	NR	846	Numbers taken from graph (using webplot digitiser)
		24	−23.29	NR	(−22.37 to −24.06)	569	
		36	−21.79	NR	NR	448	
		48	−19.20	NR	(−18.59 to −19.97)	359	
		60	−17.23	NR	(−16.31 to −18.15)	277	

Study and source	Intervention	Months FU	Mean %TBWL	SD	95% CI	*n* (%) in FU	Caveats
Wölnerhanssen 2021[111]	LSG *n* = 228	12	28.2	NR	(22.3 to 34.1)	218	Results based on two trials comparing LSG with LRYGB
							Results were adjusted for sex, age, baseline BMI and baseline diabetes status, and study and centre were used as random factors
							USED TO INFORM MODEL
		36	26.5	NR	(22.1 to 30.9)	212	
		60	23.7	NR	(19.9 to 27.6)	199	
Genco 2013[138]	IGB *n* = 261	6	%EWL	33.0 (Rome)	NR	39 (Rome)	BMI 27–30. No loss to follow-up from the Rome and Madrid centres. No secondary intervention within 3 years at the Rome centre
			59.9 (Rome)	34.2 (Madrid)		101 (Madrid)	For Madrid *N* = 6 out of 101 with post-IGB surgery [4 (4–48 months post-BIB removal), 2 (9–12 months post-IGB removal)].
			65.0 (Madrid)				
		36	%EWL	77.2 (Rome)	NR	39 (Rome)	
			38.9 (Rome)	49.9 (Madrid)		101 (Madrid)	
			34.9 (Madrid)				
Kotzampassi 2012[113]	IGB *n* = 500	6	%EWL	19.07	NR	395	Selection bias: at 6 months only those with over 20% WL could continue (76 removed). Follow-up bias: a further 43 removed; of these, 12 had regained weight at 6 months and another 2 had a second balloon insertion, 11 were operated on for obesity, and 18 were lost to follow-up
			42.3				No numbers of secondary interventions reported
							Balloon removed at 6 months
							USED TO INFORM MODEL
		12	%EWL 42.73	18.87	NR	387	
		18	%EWL 27.71	13.4	NR	352	
		30	%EWL 17.11	8.4	NR	352	

continued

TABLE 98 Long-term studies (*continued*)

Study and source	Intervention	Months FU	Mean %TBWL	SD	95% CI	*n* (%) in FU	Caveats
		66	%EWL 12.97	8.54	NR	195	
Lincoff 2023[114]	Semaglutide 2.4 mg *n* = 8803	12	−9.27	NR	(−9.17 to −9.47)	7290	BMI 27 or over and pre-existing cardiovascular disease defined as previous myocardial infarction, previous stroke, or symptomatic peripheral arterial disease, and no diabetes Some numbers taken from graph (using webplot digitiser) Discontinuation of semaglutide after 4 years **USED TO INFORM MODEL**
		24	−9.37 or −9.39 from text	NR 0.09 SE from text	NR	7474	
		36	−9.17	NR	(−9.42 to −8.87)	5085	
		48	−10.21	NR	(−9.57 to −10.81)	921	
Garvey 2022[128] STEP 5 trial	Semaglutide 2.4 mg *n* = 152	12	−15.6	0.7 SE	NR	149	Adjunct to behavioural intervention, BMI ≥ 30, or with overweight ≥ 27 kg and at least one weight-related comorbidity, without diabetes
		24	−15.2	0.9 SE	NR	144	No numbers reported for secondary interventions

AWL, absolute weight loss; FU, follow-up; LRYGB, laparoscopic Roux-en-Y gastric bypass.

TABLE 99 Severe adverse events with ESG

Study	Study design	Type of severe AE	Time point	SAE rate	Proportion of SAE needing surgery	Mortality
Docimo 2023[104]	SR/MA of 29 primary studies or SRs (includes the 3 SRs below + additional SRs)	Not defined – as reported by individual studies or SRs.	Not defined	Where reported:	Unclear	Where reported:
Most compre-hensive summary		Not always clear if 'none' or 'not reported'.		Deviere 2008 – 0%; Abu Dayyeh 2013 – 25% hospitalisation rate due to nausea; Miller 2017 – 0%; Kumar 2018 – 0%; Cohen 2019 SR 2–10% (pooled data); Fayad 2019 – 5.2%; Gys 2019 – 1%; De Miranda Neto 2020 – 0.8% *(as below)*; Hedjoudje 2020 – 2.2% (pooled data); Li 2020 – 1%; Singh 2020 – 2.26% (pooled data – NB differs from Singh estimate below); Alquatani 2022 – 0.5%; Brunaldi 2022 – 2.2% (+ 2.4% re-admission rate); Abu Dayyeh 2022 – 2% (as below); Singh 2022 – 2.8%		Gys 2019 – 0%
		Bleeding or abscess formation noted in summary as SAEs		***'Serious adverse events, such as bleeding or abscess formation, occurred in 2%–3% of patients across most studies'***		Abu Dayyeh 2022 – 0%
de Miranda Neto *et al.* 2020[139]	SR/MA of 11 studies (mainly observational); studies with at least 15 participants, minimum FU 1 month	*'Gastrointestinal bleeding (n = 13) and perigastric collections (n = 10) were the most common major adverse events reported. Other events included severe abdominal pain (n = 8), fever (n = 5), deep vein thrombosis (n = 1) and pneumo-thorax (n = 1)'.* NB four events specifically designated 'severe' (*'Mainly GI bleeding and perigastric fluid collection'*)	Studies report-ing SAEs: up to 12-month follow-up	**Pooled incidence 0.8% (95% CI 0.3 to 2.0)**	Unclear.	*'None reported in any included studies'*
				Based on four events (*'Mainly GI bleeding and perigastric fluid collection'*)	*'3 people with perigas-tric collections needed surgical interventions (including closure of a gastric fistula and 1 reversal of ESG)'*	

continued

DOI: 10.3310/PWKQ2310

Health Technology Assessment 2025 Vol. 29 No. 68

TABLE 99 Severe adverse events with ESG (*continued*)

Study	Study design	Type of severe AE	Time point	SAE rate	Proportion of SAE needing surgery	Mortality
Singh 2020[105]	SR/MA of 28 studies	***'Serious adverse events included gastrointestinal bleeding (0.61%), perigastric fluid collection (0.45%), perforation (0.10%), post-procedure fever (0.25%), and pulmonary embolism and DVT (0.10%)'***	FU up to 24 months	**Crude incidence 1.52%** (no measure of uncertainty)	Unclear	*'No deaths associated with the procedure were reported'*
	ESG: 1 comparative, 9 observational				Overall incidence of reversal of ESG due to persistent symptoms was 0.15%	
	Minimum FU 12 months					
Marincola 2021[140]	SR/MA of 16 studies	Clavien–Dindo grade III, IV and V considered as major AEs	FU 12 months	No pooled estimate presented. Rates in individual studies: **0%** (0/53), **0%** (0/148), **0%** (0/154), **0.6%** (6/1000), **0.95%** (1/105), **1.04%** (2/193), **2%** (2/100), **8%** (2/25)	Unclear as specific AEs not described	Unclear – grade V is death but not stated if any deaths occurred
	ESG: 8 observational studies			Overall crude incidence (***not calculated in Marincola 2021***): 0.73% (13/1778)		
Abu Dayyeh 2022[85]	RCT (MERIT) *n* = 209	Abdominal abscess, grade 3 managed endoscopically (*n* = 1); upper gastrointestinal bleed, managed conservatively without transfusion (*n* = 1); malnutrition requiring endoscopic reversal of the ESG (*n* = 1)	FU up to 2 years	**2.3%** (3/131)	None of the three required surgery	No mortality
	ESG + LSI vs. LSI			However, *'Six (4%) of 150 participants required subsequent* ***hospital admission*** *for medical management of accommodative symptoms'. (Includes those crossing over to ESG). So potentially 9/150 SAEs* ***(6%)***		
Bhandari 2023[134]	Prospective cohort, *n* = 612	No details on how serious AE defined	FU up to 4 years	**0%** (no SAEs)	N/A	No mortality
				22 (3.6%) underwent revision or redo ESG during the study period – however, this appears to be due to weight regain. No emergency interventions		

Study	Study design	Type of severe AE	Time point	SAE rate	Proportion of SAE needing surgery	Mortality
Sharaiha 2021[141]	Prospective cohort, *n* = 216	AEs were categorised according to the standard American Society for Gastrointestinal Endoscopy lexicon as mild, moderate, severe and fatal	FU up to 5 years	Two cases of perigastric leak (managed as inpatient with antibiotics in 1 case and percutaneous drainage in other). Therefore, it meets our criteria for 'severe'	None	No mortality
		'There was an overall rate of 1.3% moderate AEs, without any severe or fatal AEs according to American Society for Gastrointestinal Endoscopy definitions'		**0.93%** (2/216)		
Gudur 2023[42]	Unmatched analysis, *n* = 603,517 (*n* = 6054 for ESG)	*'Major AEs were a composite variable including any of the following: skin infections, wound disruptions, postoperative anastomosis leak, pneumonia, pulmonary embolism, progressive renal insufficiency, acute renal failure, cerebrovascular accidents, cardiac arrest, myocardial infarction, blood transfusion within 72 hours of procedure, sepsis, septic shock, unplanned admission to the intensive care unit, GI tract bleeding, or bowel obstruction, as defined by previous studies'.*	30 days	Major AEs **1.4%** (86/6054) – does not appear to include all reoperations. Also does not appear to include all re-admissions within 30 days. Unclear if this includes deaths	Reoperation within 30 days **1.4%** (86/6054). Reasons for reoperation: intestinal obstruction (10%), GI perforation (10%), abdominal pain (10%), strictures/luminal obstruction (8%), N/V, fluid, electrolyte or nutritional depletion (7%), GI leak (6%), infection/fever/sepsis (4%), gallbladder disease (4%), bleeding (3%), bile reflux gastritis (3%), ulcer (3%), fistula (1%)	Death within 30 days 0.066% (4/6054), deaths likely related to procedure **0.033%** (2/6054).
				Re-admission within 30 days was **3.8%** (231/6054) – unclear how many of these linked to major AE (main causes of re-admission were N/V, fluid, electrolyte or nutritional depletion (26%), abdominal pain (17%) and GI leak (6%), bleeding (5%)		

GI, gastrointestinal; MA, meta-analysis.

DOI: 10.3310/PWKQ2310

Health Technology Assessment 2025 Vol. 29 No. 68

TABLE 100 Severe adverse events with IGB

Study	Study design	Type of severe AE	Time point	SAE rate	Proportion of SAE needing surgery	Mortality
Wiggins 2024[116]	Case series, *n* = 1149	Gastric perforation and obstruction	Median 11.96 months	**0.17%** 'severe complications' (two cases, one each of perforation and obstruction)	4.35% early removal due to intolerance	None reported
Ulger 2022[117]	SR with 24 IGB studies (unclear how many randomised)	Authors did not define any AEs as severe By our definition, 'severe' includes GI bleeds, obstruction, perforation, ulcers, early removal due to intolerance and mortality	Treatment period either 4 or 6 months	Reported in four studies: **0.5%, 0.74%, 0.89%, 3.32%** (not including early removal)	Early removal reported in five studies: 2.2%, 5.4%, 6%, 8.3% and 18.8%. (unclear what overlap with SAEs is)	None reported
Singh 2020[105]	SR/MA of 28 studies IGB: 4 RCTs, 14 observational Minimum FU 12 months	Authors did not define any AEs as severe. By our definition, 'severe' includes GI bleeds, obstruction, perforation, ulcers, early removal due to intolerance and mortality	FU up to 24 months	Crude incidence **0.65%** (no measure of uncertainty) to include GI bleeds, obstruction, perforation, ulcers. If include mortality: **0.75%**	Unclear Removal due to intolerance **5.92%** (unclear what overlap with SAEs is)	**0.10%** (*n* = 3, 2 gastric perforation, 1 cardiac arrest at 4 weeks)
Saber 2017[118]	SR/MA of 20 RCTs IGB vs. sham, LSI or no treatment	Authors did not define any AEs as severe. By our definition, gastric ulcers, mucosal erosions, obstruction, perforation and hypoxia classified as severe	Treatment with IGB between 12 weeks and 6 months	**12.5%** gastric ulcer, **4.07%** mucosal erosion. Further rare complications reported at time of IGB removal including small bowel obstruction, hypoxia with IGB extraction and oesophageal perforation (no numerical data)	Unclear	No mortality
Yorke 2016[119]	SR/MA 1 RCT, 25 case-series	AEs described as serious were: mortality, gastric ulcers, gastric perforation and balloon migration	6 months	Crude incidence 0.49% (no measure of uncertainty) to include gastric ulcers, gastric perforation and balloon migration. If include mortality: **0.54%**	Early removal due to AEs **3.5%**. Unclear if overlaps with SAEs	**0.05%**

GI, gastrointestinal.

DOI: 10.3310/PWKQ2310

TABLE 101 Severe adverse events with LSG

Study	Study design	Type of severe AE	Time point	SAE rate	Proportion of SAE needing surgery	Mortality
Zhao 2020[142]	SR/MA – 11 RCTs comparing LSG against LRYGB	Variously defined in studies	30 days	'Early major complications' reported in one study: 6.67% Re-admission within 30 days reported in three studies: 3.31%, 18.2% ('overall re-admission'), 2.63%	Reoperation within 30 days reported in five studies: 2.48%, 0.93%, 0%, 0%, 0%	0% in 10 studies (at 30 days)
Marincola 2021[140]	SR/MA of 16 studies LSG: 1 RCT and 7 observational	Clavien–Dindo grade III, IV and V considered as major AEs	FU 12 months	No pooled estimate presented. Rates in individual studies: 1.2% (3/252), 0% (0/122), 7.9% (66/836), 0% (0/32), 0% (0/90), 0% (0/218), 6.76% (5/74), 0% (0/300) Overall crude incidence (*not calculated in SR/MA*): 3.85% (74/1924)	Unclear as specific AEs not described	Unclear – grade V is death but not stated if any deaths occurred
Gudur 2023[42]	Unmatched analysis, *n* = 603,517 (*n* = 597,463 for SG)	*'Major AEs were a composite variable including any of the following: skin infections, wound disruptions, postoperative anastomosis leak, pneumonia, pulmonary embolism, progressive renal insufficiency, acute renal failure, cerebrovascular accidents, cardiac arrest, myocardial infarction, blood transfusion within 72 hours of procedure, sepsis, septic shock, unplanned admission to the intensive care unit, GI tract bleeding, or bowel* obstruction *as defined by previous studies'*	30 days	Major AEs 1.3% (7609/597,463) – does not appear to include all reoperations. Also does not appear to include all re-admissions within 30 days. Unclear if this includes deaths. Re-admission within 30 days was 2.8% (16,546/597,463) – unclear how many of these linked to major AE (main causes of re-admission were N/V, fluid, electrolyte or nutritional depletion (31%), abdominal pain (12%) and GI leak (6%)	Reoperation within 30 days 0.8% (86/6054). Reasons for reoperation: GI bleed (25%), staple line leak (15%), gallbladder disease (8%), infection/fever/sepsis (6%), intestinal obstruction (6%), abdominal pain (5%), hernia (5%)	Death within 30 days 0.055% (331/597,463), deaths likely related to procedure 0.029% (176/597,463)

continued

Health Technology Assessment 2025 Vol. 29 No. 68

TABLE 101 Severe adverse events with LSG (*continued*)

Study	Study design	Type of severe AE	Time point	SAE rate	Proportion of SAE needing surgery	Mortality
Kumar 2018[143]	Analysis of registry data *N* = 93,062 for LSG	'Morbidity' was defined as any of the following: deep surgical site infection, organ space infection, wound disruption, leak, intensive care admission, sepsis, renal failure, transfusion, cardiac arrest, myocardial infarction, cerebrovascular accident, coma, pneumonia, > 48 hours on ventilator, unplanned intubation, pulmonary embolism, venous thromboembolism, or intervention, reoperation, or re-admission within 30 days Leak was defined as any of the following: leak outcome, drain present > 30 days, organ space surgical site infection, leak-related 30-day admission, or leak-related 30-day reoperation or intervention	30 days	'Serious morbidity' in 5.8% Leaks in 0.8% (appears to be included in overall serious morbidity estimate)	Unclear	0.10%
Kapur 2021[144]	Analysis of registry data *N* = 447,326 for LSG	Clavien–Dindo grades used	30 days	Clavien–Dindo grade III: 3.3%, grade IV: 0.36%, grade V (death): 0.07% Re-admission within 30 days 3.0% Re-peration within 30 days 0.8% (considered grade III) *NB these likely contained within grade III to V*	Reoperation within 30 days 0.8%, but unclear what overlap with SAEs is	All cause 0.07% Procedure related 0.04%

GI, gastrointestinal; LRYGB, laparoscopic Roux-en-Y gastric bypass.

Summary of severe adverse event rates

TABLE 102 Severe adverse events with semaglutide

Study	Study design	Type of severe AE	Time point	SAE rate	Proportion of SAE needing surgery	Mortality
Qin 2023[145]	SR with six RCTs, including all STEP ones (*n* = 3962)	Not defined but may include hypoglycaemic incidents, acute pancreatitis or psychiatric disorders. ***Not the same as our definition***	Between 20 and 104 weeks	8.94% (pooled rate)	N/A	Three studies: 0% Two studies reported one death in each group (not associated with treatment); one study reported one death in semaglutide arm (not associated with treatment)
Wilding 2021[129] STEP 1 SG + LSI vs. placebo + LSI	RCT (*n* = 1306 semaglutide, *n* = 655 placebo)	'Severe' defined as preventing normal everyday activities, **that is *not the same as our definition*** Serious AEs include serious GI disorders and hepatobiliary disorders	68 weeks FU	9.8% in semaglutide group – but unclear if any leading to hospitalisation (hospitalisation not mentioned in article)	N/A	One death in each arm not considered to be treatment related
Garvey 2022[128] STEP 5 SG + behavioural intervention vs. placebo + behavioural intervention	RCT (*n* = 152 semaglutide, *n* = 152 placebo)	'Severe' defined as preventing normal everyday activities, **that is *not the same as our definition***	104 weeks FU	7.9% in semaglutide group – but unclear if any leading to hospitalisation (hospitalisation not mentioned in article) None *'requiring temporary or permanent interruption'* of semaglutide treatment	N/A	One death in semaglutide arm not considered to be treatment related
Lincoff 2023[114] SG vs. placebo ***NB patients with pre-existing cardiovascular disease***	RCT (*n* = 8803 semaglutide, *n* = 8801 placebo)	SAEs include: cardiac disorders, infections and infestations, nervous system disorders, surgical and medical procedures, neoplasms benign, malignant and unspecified, and gastrointestinal disorders	Mean 40 months FU	33.4% in semaglutide group – but unclear if any leading to hospitalisation (hospitalisation not mentioned in article). AEs regardless of seriousness leading to permanent discontinuation of semaglutide in 16.6% (*n* = 1461) SAEs related to GI disease, acute kidney failure, pancreatitis, cancers, or psychiatric disorders and were not more frequent with semaglutide than with placebo	N/A	Primary cardiovascular end point was a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke in a time-to-first-event analysis

GI, gastrointestinal.

DOI: 10.3310/PWKQ2310

Health Technology Assessment 2025 Vol. 29 No. 68

Focused search strategies for systematic reviews of semaglutide

Database: Ovid MEDLINE(R) and In-Process, In-Data-Review and Other Non-Indexed Citations <1946 to 28 March 2023>

Search Strategy:

----
1 glucagon-like peptide-1 agonist*.ti,ab. (267)
2 GLP-1 agonist*.ti,ab. (682)
3 GLP-1 receptor agonist*.ti,ab. (2443)
4 glucagon-like peptide-1 receptor agonist*.ti,ab. (2918)
5 semaglutide.ti,ab. (920)
6 Ozempic.ti,ab. (8)
7 Wegovy.ti,ab. (6)
8 Rybelsus.ti,ab. (10)
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (6117)
10 (systematic review or meta-analys*).ti,ab. (376786)
11 9 and 10 (625)
12 limit 11 to yr='2020 –Current' (351)
13 exp Obesity/ (255860)
14 (obes$ or overweight).ti,ab. (380064)
15 13 or 14 (432111)
16 12 and 15 (31)

****

Database: EMBASE <1974 to 28 March 2023>

Search Strategy:

----
1 exp semaglutide/ (3335)
2 semaglutide.ti,ab. (1950)
3 Wegovy.ti,ab. (6)
4 Ozempic.ti,ab. (18)
5 Rybelsus.ti,ab. (17)
6 1 or 2 or 3 or 4 or 5 (3454)
7 exp obesity/ (646299)
8 (obes* or overweight).ti,ab. (579769)
9 7 or 8 (767877)
10 6 and 9 (1088)
11 limit 10 to 'reviews (maximizes specificity)' (63)
12 limit 11 to yr='2020 – 2023' (60)
13 (systematic review or meta-analys$).ti,ab. (506200)
14 10 and 13 (72)
15 limit 14 to yr='2020 –Current' (67)
16 12 or 15 (67)

****

29 records in Epistemonikos:

(semaglutide or wegovy or Ozempic or rybelsus) AND (obesity or obese or overweight)

Appendix 3 Additional information for review of cost-effectiveness

TABLE 103 List of review of cost-effectiveness excluded studies

#	Author, year, setting	Title	Study type	Population	Intervention/comparators	Outcomes	Reason for exclusion
1	Armstrong, 2018, UK	A UK CEA of the EndoBarrier device in patients with T2D and obesity	Trial-based CEA	Patients with obesity with T2DM	Endobarrier device/ Endobarrier + Liraglutide; Liraglutide alone	QALYs; ICERs	Conference poster
2	Gupta, 2018, UK	CEA of the EndoBarrier device in patients with T2D	Trial-based CEA	Obese patients with T2DM	Endobarrier device/ Endobarrier + Liraglutide; Liraglutide alone	QALYs; ICERs	Conference poster (same authors as above)
3	Chiang, 2016, USA	Cost–utility analysis of obesity therapy: a comparison of lifestyle intervention to surgical and endoscopic strategies	State-transition microsimula-tion model	Cohort of 100,000 35-year-old Caucasian females with a BMI of 40, diabetes, and hypertension	IGB, RYGB, LSG and LAGB/LSI	QALYs; ICER	Conference abstract
4	Jirapinyo, 2018, USA	CEA of two endoscopic bariatric and metabolic therapeutic approaches: IGB vs. ESG	State transition model/CEA	100,000 US non-African Americans aged 35years and BMI 32.5kg/m^2 without obesity-related comorbidities	IGB/ESG	QALYs; ICERs	Conference abstract
5	Jirapinyo, 2020, USA	Incremental cost-effectiveness of aspiration therapy vs. bariatric surgery and no treatment for morbid obesity					Commentary on Mital *et al.*, 2019
6	Kim, 2016, USA	The cost-effectiveness of bariat-ric treatments in overweight and obese patients	State transition Monte Carlo microsim-ulation model/CUA	Overweight ($25 \leq BMI < 30$) and mildly obese ($30 \leq BMI < 35$) patients	IGB/lifestyle intervention pharmacotherapy	QALYs; ICERs	Conference abstract
7	Oster, 2021, Germany	Efficacy, safety and cost-effectiveness of IGB therapy compared to a multidisciplinary WL programme in a real-world population propensity score matching analysis	Trial-based CEA	Participants aged 18–70 years with a BMI of 30–55 kg/m^2	IGB/weight loss program (PPTIFAST)	Cost analysis	Full text not available
8	Saumoy, 2017, The Netherlands	A cost–utility analysis comparing endoscopic, surgical and lifestyle management of obesity	Markov CEA	A 20-year-old patient with obesity and without T2DM	ESG/IGB, SG and LSI	ICERs; QALYs	Conference abstract

DOI: 10.3310/PWKQ2310

Health Technology Assessment 2025 Vol. 29 No. 68

TABLE 104 Quality assessment checklist for model-based economic evaluation studies

	Philips criteria (for modelling studies)	Kelly 2023	Mital 2021	Mital 2019
S1	Is there a clear statement of the decision problem?	Y	Y	Y
	Is the objective of the evaluation and model specified and consistent with the stated decision problem?	Y	Y	Y
	Is the primary decision-maker specified?	Y	Y	Y
	Is the perspective of the model stated clearly?	Y	Y	Y
S2	Are the model inputs consistent with the stated perspective?	Y	Y	Y
	Has the scope of the model been stated and justified? (i.e. Have any choices or assumptions been explained sufficiently, in the context of available evidence?)	N	N	N
	Are the outcomes of the model consistent with the perspective, scope and overall objective of the model?	Y	Y	Y
S3	Has the evidence regarding the model structure been described?	Y	Y	Y
	Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	Y	Y	Y
	Are the sources of data used to develop the structure of the model specified?	Y	Y	Y
	Are the causal relationships described by the model structure justified appropriately?	N	N	N
S4	Are the structural assumptions transparent and justified?	N	N	N
	Are the structural assumptions reasonable given the overall objective, perspective and scope of the model?	N	N	N
S5	Is there a clear definition of the options under evaluation?	Y	Y	Y
	Have all feasible and practical options been evaluated?	N	N	N
	Is there justification for the exclusion of feasible options?	Y	Y	Y
S6	Is the chosen model type appropriate given the decision problem and specified causal relation-ships within the model?	Y	Y	Y
S7	Is the time horizon of the model sufficient to reflect all important differences between options?	Y	Y	Y
	Is the time horizon of the model, the duration of treatment and the duration of treatment effect described and justified?	Y	Y	Y
S8	Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological process of the disease in question and the impact of interventions?	Y	Y	Y
S9	Is the cycle length defined and justified in terms of the natural history of disease?	Y	Y	Y

continued

TABLE 104 Quality assessment checklist for model-based economic evaluation studies (*continued*)

	Philips criteria (for modelling studies)	Kelly 2023	Mital 2021	Mital 2019
D1	Are the data identification methods transparent and appropriate given the objectives of the model?	Y	N	N
	Where choices have been made between data sources, are these justified appropriately?	N	N	N
	Has particular attention been paid to identifying data for the important parameters in the model?	Can't tell	Can't tell	Can't tell
	Has the process of selecting key parameters been justified and systematic methods used to identify the most appropriate data?	N	N	N
	Has the quality of the data been assessed appropriately?	N/S	N/S	N/S
	Where expert opinion has been used, are the methods described and justified?	N	N/A	N/A
D2	Is the pre-model data analysis methodology based on justifiable statistical and epidemiological techniques?	Y	Y	Y
	Is the choice of baseline data described and justified?	Y	Y	Y
	Are transition probabilities calculated appropriately?	Y	Y	N/S
	Has a half cycle correction been applied to both cost and outcome? If not, has this omission been justified?	Y	N	N
	If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques?	N/A	N/A	N/A
	Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified?	N	N/A	N/A
	Have alternative extrapolation assumptions been explored through sensitivity analysis?	Y	N/A	N/A
	Have assumptions regarding the continuing effect of treatment once treatment is complete been documented and justified?	Y	Y	Y
	Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis?	Y	Y	Y
	Are the utilities incorporated into the model appropriate?	Y	Y	Y
	Is the source for the utility weights referenced?	Y	Y	Y
	Are the methods of derivation for the utility weights justified?	Y	Y	Y
D3	Have all data incorporated into the model been described and referenced in sufficient detail?	N	N	N
	Has the use of mutually inconsistent data been justified (i.e. are assumptions and choices appropriate)?	N/A	N/A	N/A
	Is the process of data incorporation transparent?	Y	N	N

	Philips criteria (for modelling studies)	Kelly 2023	Mital 2021	Mital 2019
	If data have been incorporated as distributions, has the choice of distribution for each parameter been described and justified?	N	N	N
	If data have been incorporated as distributions, is it clear that second order uncertainty is reflected?	N	N	N
D4	Have the four principal types of uncertainty been addressed? If not, has the omission of particular forms of uncertainty been justified?	N	N	N
	Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?	Y	Y	Y
	Is there evidence that structural uncertainties have been addressed via sensitivity analysis?	N	N	N
	Has heterogeneity been dealt with by running the model separately for different sub-groups?	N	N	N
	Are the methods of assessment of parameter uncertainty appropriate?	Y	Y	Y
	If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified?	N	N	N
C1	Is there evidence that the mathematical logic of the model has been tested thoroughly before use?	Y	N	N
C2	Are the conclusions valid given the data presented?	Y	Y	Y
	Are any counterintuitive results from the model explained and justified?	N/A	N/A	N/A
	If the model has been calibrated against independent data, have any differences been explained and justified?	N/A	N/A	N/A
	Have the results of the model been compared with those of previous models and any differences in results explained?	Y	Y	Y

Source
Reproduced with permission from Philips *et al.*[77]. This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The text below includes minor additions and formatting changes to the original text.

DOI: 10.3310/PWKQ2310

Health Technology Assessment 2025 Vol. 29 No. 68

Appendix 4 Additional information for economic models

Targeted searches to inform model parameters

Targeted literature searches were undertaken for treatments for obesity beyond endoscopic procedures, such as bariatric surgery and pharmacotherapy that could serve as potential comparator treatments. These additional searches aimed to identify relevant model structures that could be adapted to the decision problem, and further sources for model parameters.

Data extraction

Data were extracted from 20 studies. Information was extracted on model structure, range of health states utilised in any models and types of model inputs relating to patient transitions, resource use, QoL measures and outcomes.

Narrative synthesis

Descriptions of the study characteristics and other additional aspects are provided in *Tables 105* and *106*.

DOI: 10.3310/PWKQ2310

TABLE 105 Characteristics of selected studies included in purposive review

#	Author, year, country	Study population (obesity definition/ eligibility)	Interventions	Health states/ diseases modelled	Model type	Time horizon	Cycle length	Perspective	Benefit measure
Bariatric surgery									
1	Alsumali, 2018,[86] USA	Adults aged 18–74 years with BMI ≥ 35 kg/m². Initial BMI ranged between 35 and 69, and 78% were female	Laparoscopic Roux-en-Y gastric bypass (LRYGB), LAGB and LSG vs. no surgery	5 BMI health states that reflected their current BMI level: not obese (BMI ≤ 30 kg/m²), obese (BMI 30–34.9 kg/m²), morbidly obese I (BMI 35–39.9 kg/m²), morbidly obese II (BMI 40–49.9 kg/m²), and super obese (BMI ≥ 50 kg/m²)	Individual Markov microsimulation model	Lifetime	12 months	US Healthcare	QALY
2	Avenell, 2018,[43] UK	A representative population of all adults with a BMI of ≥ 35 kg/m²	Weight management programmes (WMP), RYGB vs. WMP	CHD, stroke, hyper-tension, T2DM, knee osteoarthritis and BMI-related cancers, including breast, colorectal, endome-trial, oesophageal, pancreatic and renal	UK Health Forum microsimulation model	30 years	12 months	NHS	QALY
3	Borisenko, 2015,[146] Sweden	Patients aged 25–65 years (mean 41) with a BMI range of 30–60 (mean 42.8)	Gastric bypass, sleeve gastrectomy and adjustable gastric banding vs. non-surgical usual care (consisting of drug therapy, diet and physical exercise)	Surgery and post-surgery, post-surgery complications, T2D, angina pectoris, myocardial infarction, stroke, transient ischaemic attack, heart failure and peripheral arterial disease states	Markov	Lifetime	12 months	Swedish Health care	QALY (outcomes of interest – cost, life-years gained and QALYs gained)
4	Borisenko, 2018,[147] UK	Patients aged 25–65 years (mean 45.4) with a BMI range of 30–60 (mean 50.5)	Gastric bypass, sleeve gastrectomy and adjustable gastric banding vs. non-surgical usual care (consisting of drug therapy, diet and physical exercise)	Postoperative complications or no complications, T2DM or obesity-associated cardiovascular diseases (angina, myo-cardial infarction, stroke, heart failure and peripheral artery disease), have T2D remission or die	Markov	10 years and lifetime	1 month	NHS	QALY

continued

TABLE 105 Characteristics of selected studies included in purposive review (*continued*)

#	Author, year, country	Study population (obesity definition/ eligibility)	Interventions	Health states/ diseases modelled	Model type	Time horizon	Cycle length	Perspective	Benefit measure
5	Borisenko, 2018,[148] Belgium	Morbidly obese patients	Gastric bypass, sleeve gastrectomy, and adjustable gastric banding vs. conventional medical management (CMM)	Surgery or post-surgery complications, T2DM, CVDs, or death.	Markov	10 years and lifetime	1 month	Third-party payer	QALY
6	Borisenko, 2017,[149] Denmark	Patients aged 22–57 years (mean 40) with a BMI range of 20–68 (mean 42)	Gastric bypass, sleeve gastrectomy and adjustable gastric banding vs. optimal medical management	Surgery, post-surgery complications, T2DM, CVDs or death	Markov	10 years and lifetime	1 month	Third-party payer	QALY
7	Borisenko, 2017,[150] Germany	Patients aged 25–65 years (mean 40.4) with a BMI range of 30–60 (mean 48.8)	Gastric bypass, sleeve gastrectomy and adjustable gastric banding vs. medical management	Surgery, post-surgery complications, T2DM, CVDs or death	Markov	10 years and lifetime	1 month	Health care	QALY
8	Campbell, 2010,[87] USA	Adults aged 18–74 years who satisfied the clinical eligibility criteria for bariatric surgery: BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with comorbid conditions	LAGB and LRYGB vs. no treatment	Five BMI health states: not obese (BMI < 30 kg/m^2); obese (BMI 30–34.9 kg/m^2); morbidly obese I (BMI 35–39.9 kg/m^2); morbidly obese II (BMI 40–49.9 kg/m^2); and super obese (BMI > 50 kg/m^2)	Markov	Lifetime	12 months	Third-party payer	QALY
9	Elliot, 2021,[151] UK	Female patients with active IIH and no other significant comorbidity, aged 18–55 years, with a BMI > 35 kg/m^2	Bariatric surgery vs. community WMP	Three BMI health states: severe obesity (Class III) (BMI 40 kg/m^2), obesity (BMI 30–39.9 kg/m^2), or no obesity (BMI 30 kg/m^2), or into an	Markov	5, 10 and 20 years	12 months	NHS	QALY

#	Author, year, country	Study population (obesity definition/ eligibility)	Interventions	Health states/ diseases modelled	Model type	Time horizon	Cycle length	Perspective	Benefit measure
10	Gulliford, 2017,[75] UK	A random sample of 50,000 participants from each BMI category:18.5–25, 25–29, 30–34, 35–39, 40–44, and 45 kg/m^2 or higher	Bariatric surgery, including equal proportions of adjustable gastric banding, gastric bypass and sleeve gastrectomy vs. standard non-surgical management	101 states were included in the model across two treatment conditions. DM, CHD, stroke, or cancer, depression, with substates representing 'not depressed' and 'depressed' BMI category	Markov	Lifetime	12 months	NHS	QALY and LY
11	Klebanoff, 2017,[152] USA	228 patients from the Teen-LABS study with a mean age of 17 (1.6) years, and an initial BMI of 53 (34–88)	Bariatric surgery vs. no surgery	Alive (same weight), alive (losing weight) dead	Markov	3 years	1 month	Patient	QALY
12	Lauren, 2022,[153] USA	Severe obesity and T2D, stratified by T2D severity	SG, and RYGB vs. medical therapy	Five BMI health states (normal, 18–24.9; overweight, 25–29.9; mild obesity, 30–34.9; moderate obesity, 35–39.9; and severe obesity, 40), T2D status (baseline severity, remission, and relapse to baseline severity), surgery complications and mortality	Patient-level Microsimulation Model	5 years (10 and 30 years in SA)	1 month	Health care sector	QALY
13	Lucchese, 2017,[154] Italy	Patients aged 21–56 years (mean 40.6) with a BMI range of 23–58 (mean 46.2)	Gastric bypass, sleeve gastrectomy and adjustable gastric banding vs. optimal medical management	Surgery, post-surgery complications, T2DM, CVDs or die	Markov	10 years and lifetime	1 month	Third-party payer	QALY
14	Maklin, 2011,[155] Finland	Patients aged 33–63 years (mean 43) with a baseline BMI of 38–59 (mean 47)	Bariatric surgery (gastric bypass, sleeve gastrectomy and gastric banding) vs. ordinary treatments	Alive (no abdominoplasty nor reoperation), abdominoplasty, reoperation and dead.	Decision tree and Markov	10 years	12 months	Healthcare provider	QALY

continued

DOI: 10.3310/PWKQ2310

Health Technology Assessment 2025 Vol. 29 No. 68

TABLE 105 Characteristics of selected studies included in purposive review *(continued)*

#	Author, year, country	Study population (obesity definition/ eligibility)	Interventions	Health states/ diseases modelled	Model type	Time horizon	Cycle length	Perspective	Benefit measure
15	Meads, 2014,[156] UK	Adults with a mean age of 47 years (SD = 13.9) and BMI of 36.8 (SD = 6.7). Of the sample, 11.5% were overweight, 62.2% had a BMI between 30 and 39.9, and 25.6% had BMI ≥ 40	12-week primary care referral 12-week primary care referral to a commercial weight loss programme (CWLP) vs. usual care	Five BMI groups ['Normal' – < 25; 'Overweight' – 25–29.9; 'Moderately obese' – 30–34.9; 'Severely obese' – 35–39.9; 'Very severely obese' – ≥ 40) T2D, stroke, myocardial infarction (MI)] and death	Markov	Lifetime	12 months	Personal Health and Social Services	QALY
16	Picot, 2012,[157] UK	Mild (class I, BMI 30–34.99) or moderate (class II, BMI 35–39.99) obesity	Bariatric surgery vs. non-surgical treatment	No comorbidity T2D, CHD, stroke, dead	Markov	20 years	12 months	NHS and PSS	QALY
17	Wentworth, 2017,[158] USA	Overweight but not obese adults with T2DM, aged 18–65 years and a BMI of 25–30 kg/m^2	Gastric band surgery	N/S	Microsimulation model using UK Prospective Diabetes Outcome Model	10 years	12 months	Societal	QALY
Pharmacotherapy									
18	Kim, 2022,[159] USA	Adult patients with obesity (i.e. BMI ≥ 30) and overweight (i.e. BMI 27–29.9) with one or more weight-related comorbidities	Semaglutide 2.4 mg vs. no treatment, diet and exercise (D&E), and three branded AOMs (liraglutide 3 mg, phentermine-topiramate, and naltrexone-bupropion)	No comorbidity (i.e. normal glucose tolerance or prediabetes), single comorbidity (i.e. post-acute coronary syndrome, T2D, poststroke and cancer), dual comorbidity, multicomorbidity and death.	Markov	30 years	3 months in year 1 and annual cycles thereafter	Third-party payer	QALY
19	Lee, 2022,[160] USA	People with mild obesity (BMI 30–35). BMI of at least 30 or a BMI of at least 27 with weight-related comorbidities was eligible	Intensive lifestyle intervention, orlistat, phentermine, phentermine/topiramate, lorcaserin, liraglutide and semaglutide vs. no treatment		Microsimulation Model	1, 3 and 5 years	1 month	Health care system	QALY

#	Author, year, country	Study population (obesity definition/ eligibility)	Interventions	Health states/ diseases modelled	Model type	Time horizon	Cycle length	Perspective	Benefit measure
20	Veerman, 2011,[161] Australia	Obese Australian adults free of obesity-related disease	1-year pharmacological interventions with sibutramine and orlistat vs. no intervention	Stroke, ischaemic heart disease, hypertensive heart disease, diabetes mellitus, osteoarthritis, post-menopausal breast cancer, colon cancer, endometrial cancer and kidney cancer	Multistate life table-based Markov	Lifetime	12 months	Health Sector	DALY

AOM, anti-obesity medications; IIH, idiopathic intracranial hypertension; T2DM, type 2 diabetes mellitus.

DOI: 10.3310/PWKQ2310

Health Technology Assessment 2025 Vol. 29 No. 68

TABLE 106 Additional Information on studies

#	Author, year, country	Primary clinical treatment effects modelled/assessed	Level and source of effectiveness evidence	Uncertainty	Model validation	Currency base	Discount rate	ICER/QALY	WTP threshold
Bariatric surgery and pharmacotherapy									
1	Alsumali, 2018,[86] USA	Cumulative change in BMI	Prospective RCT Angrisiani *et al.*, 2007, Angrisiani *et al.*, 2013, Lim *et al.*, 2014, Gadiot *et al.*, 2017	DSA and PSA	No formal validation reported	2016 US$	3%	ICERs for LSG vs. no surgery, LRYGB vs. no surgery and LAGB vs. no surgery were below $10,000 per QALY LRYGB was the optimal bariatric technique and most cost-effective compared to LSG, LAGB, and no surgery options	$100,000/QALY
2	Avenell, 2018,[43] UK	Change in BMI	RCT and meta-analyses of RCTs/ Look AHEAD Research Group	DSA	Previous validated model	2016 GBP	1.5%; 0%, 3.5% and 6%		£30,000/QALY
3	Borisenko, 2015,[146] Sweden	Absolute BMI reduction	Clinical trials Scandinavian Obesity Surgery Registry (SOREG)	One-way DSA, 11 additional scenarios analysis and PSA	Face, internal and external validation	2012 €	3%	Bariatric surgery was cost-saving in comparison with conservative management. Over a lifetime, surgery led to savings of €8408 and generated an additional 0.8 years of life and 4.1 QALYs per patient, which translates into gains of 32,390 quality-adjusted person-years and savings of €66million for the cohort, operated in 2012	€35,526/QALY
4	Borisenko, 2018,[147] UK	Absolute BMI reduction	UK Second National Bariatric Surgery Registry (NBSR) report (data available as a reduction in excess weight (% EWL) and was transformed into a relative reduction in BMI). Change in BMI [Swedish Obese Subjects (SOS) Study]	DSA and PSA	Face, internal and external validation	2015 GBP	3.50%	Base-case analysis over 10 years, bariatric surgery vs. usual care ICER of €3294 (£2336)	£30,000/QALY
5	Borisenko, 2018,[148] Belgium	Absolute BMI reduction	Scandinavian Obesity registry report	DSA and PSA	Face, internal and external validation	2012 €	3% for costs, 1.5% for health outcomes	Base-case analysis over a 10-year time horizon, bariatric surgery vs. CMM: ICER of €2809 per QALY	€30,000/QALY
6	Borisenko, 2017,[149] Denmark	Absolute BMI reduction	Danish obesity Surgery registry report	DSA and PSA	Face, internal and external validation	2012 DKK	3%	In the 10-year base-case analysis, bariatric surgery was cost-effective with an ICER of 17,818 DKK per QALY and was dominant over conservative management during a lifetime.	223,000 DKK/QALY
7	Borisenko, 2017,[150] Germany	Absolute BMI reduction	German Quality Assurance in Bariatric Surgery Registry. SOS	DSA and PSA	Face, internal and external validation	2012 €	3%	Over 10 years, bariatric surgery was cost-effective at 10 years with an ICER of €2457 per QALY vs. medical management	€35,000/QALY

#	Author, year, country	Primary clinical treatment effects modelled/ assessed	Level and source of effectiveness evidence	Uncertainty	Model validation	Currency base	Discount rate	ICER/QALY	WTP threshold
8	Campbell, 2010,[87] USA	Decreases in BMI	Head-to-head RCTs/Angrisani *et al*, 2007, O'Brien *et al.*, 2006	DSA and PSA	No formal validation reported	2006 US$	3.00%	ICER discounted LAGB vs. no treatment: US$9300/LYS; LRYGB vs. no treatment: US$10,200/LYS; LRYGB vs. LAGB: US$12,900/LYS ICER discounted LAGB vs. no treatment: US$5400/QALY; LRYGB vs. no treatment: US$5600/QALY; LRYGB vs. LAGB: US$6200/QALY	$50,000/QALY
9	Elliot, 2021,[151] UK	Change in BMI	Multicentre RCT IIH: WT/Mollan *et al.*, 2021	PSA	No formal validation reported	2017–8 GBP	3.50%	Base-case analysis: over a 20-year time horizon, bariatric surgery was 'dominant', led to cost savings of £49,500, and generated an additional 1.16 QALYs vs. community weight management intervention	£20,000–30,000/QALY
10	Gulliford, 2017,[75] UK	Reduction in disease incidence and mortality	Published literature and data from the Clinical Practice Research Datalink	DSA	No formal validation reported	2013 GBP	3.5%. Undiscounted values and values discounted at 1.5% are also shown as SA	Cost per QALY gained is £7129 (range £6775–7506)	£20,000–30,000/QALY
11	Klebanoff, 2017,[152] USA	Total WL	Single study/Inge *et al.*, 2016	One-way DSA and PSA	No formal validation reported	2015 US$	N/S	At 3 years, surgery vs. no surgery ICER of $154,684. Extrapolation to 4 years ICER $114,078, 5 years $91,032	$100,000/QALY
12	Lauren, 2022,[153] USA	BMI decrease and Total body weight lost	Clinical trials, large cohort studies/ Schauer *et al.*, 2017; McTigue *et al.*, 2020; Hoerger, 2019; Dennett *et al.*, 2008; Klebanoff *et al.*, 2017	DSA and PSA	Internal and external validation	2020 US$	3.00%	RYGB vs. Med treatment ICER, $46,877 per QALY for the overall population; and when stratified by baseline T2D severity: mild: ICER, $36,479 per QALY; moderate: ICER, $37,056 per QALY; and severe ICER, $98,940 per QALY	$100,000/QALY
13	Lucchese, 2017,[154] Italy	Absolute BMI reduction	SOReg 2011	DSA and PSA	Internal and external validation	2015 €	3.00%	Bariatric vs. optimal med management EUR 2412/QALY at 10 years	EUR50,000/QALY
14	Maklin, 2011,[155] Finland	Excess WL	Meta-analysis	DSA	No formal validation reported	2010 EUR	3.00%	ICER discounted LAGB vs. medical management: €–37,380/QALY; LRYGB vs. medical management: €–27,441/QALY; LSG vs. medical management: €–29,684/QALY	Not specified

continued

DOI: 10.3310/PWKQ2310

TABLE 106 Additional Information on studies (*continued*)

#	Author, year, country	Primary clinical treatment effects modelled/assessed	Level and source of effectiveness evidence	Uncertainty	Model validation	Currency base	Discount rate	ICER/QALY	WTP threshold
15	Meads, 2014,[156] UK	Change in BMI	Targeted literature searches	One-way, scenario and threshold DSA	No formal validation reported	GBP	3.50%	At 12 months CWLP vs. usual care ICER was £6906.10	£20,000–30,000/QALY
16	Picot, 2012,[157] UK	% BMI change, %weight reduction	RCT	DSA and PSA	No formal validation reported	GBP 2010	3.50%	For people with class I or II obesity and T2D, the ICER at 2 years is £20,159, reducing to £4969 at 5 years and £1634 at 20 years	£20,000–30,000/QALY
17	Wentworth, 2017,[158] USA	N/C	Trial-based study	DSA	No formal validation reported	US$ 2015	3%	ICER for GB surgery at 2 years exceeded $90,000 per QALY gained but decreased to $52,000, $29,000 and $22,000 when the health benefits of surgery were assumed to endure for 5, 10 and 15 years, respectively	$50,000/QALY
Pharmacotherapy									
18	Kim, 2022,[159] USA	% Change in BMI	4 RCTs/STEP 1, SCALE, COR II and CONQUER	DSA and scenario analyses	Internal and external validation	2021 US$	3.00%	Semaglutide vs. current standard care $122,549; Semaglutide vs. no treatment ($27,113) and other AOMs ($144,296)	$150,000 (based on the value assessment framework of the Institute for Clinical and Economic Review
19	Lee, 2020,[160] USA	Change in BMI	RCTs	DSA and PSA	No formal validation reported	2019 US$	3.00%	At all the three follow-up points, phentermine remained the most cost-effective option, with an ICERs of $46,258 per QALY after 1 year, $20,157 per QALY after 3 years, and $17,880/QALY after 5 years. Semaglutide proved to be the most effective option for the 3- and 5-year time frames, providing total QALYs of 2.224 and 3.711, respectively. However, its ICERs were significantly higher, reaching $1437 340 per QALY after 3 years and $576 931 per QALY after 5 years	$100,000/QALY
20	Veerman, 2011,[161] Australia	Mean reduction in body weight	Meta-analysis	DSA	No formal validation reported	Aus $2003	3%	The ICERs are A$130,000/DALY [95% uncertainty interval (UI) 93,000–180,000] for sibutramine and A$230,000/DALY (170,000–340,000) for orlistat.	Not specified

Note
Exchange rate of 1 US$ = 0.75 GBP, as of 25 April 2025.
Exchange rate of 1€ = 0.85 GBP, as of 25 April 2025.

Setting

Of the 20 selected studies, 6[43,76,147,151,156,157] were conducted in the UK while 7[87,88,152,153,158–152] were in the USA. Six studies[146,148,149,150,154,155] were set in various European countries and one was carried out in Australia.[161]

Interventions and comparators

The 20 studies assessed various interventions which can be grouped into three broad categories: bariatric surgery,[75,86,87,146–155,157] pharmacotherapy[158,160,161] and a mix of other interventions.[43,148] These interventions were typically compared with no treatment, usual care or medical therapy.

Bariatric surgery

There were 15 studies[75,86,87,146–155,157,158] that focused on a range of bariatric surgeries of which 5 were by the same authors in different settings.[146–150] The bariatric interventions were mostly LSG, laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic adjustable gastric banding (LAGB).

Pharmacotherapy interventions

Three studies[159–161] focused on obesity pharmacotherapy including semaglutide, liraglutide, sibutramine and orlistat. Semaglutide was recently recommended by NICE for the management of obesity in adults with at least one weight-related comorbidity and BMI of at least 35 kg/m^2, and exceptionally, a BMI of 30.0–34.9 kg/m^2 if they are referred to tier 3 services based on NICE's criteria.[36]

Mixed Interventions

Avenell *et al.*[43] assessed five different weight management programmes (WMPs) including dietary and lifestyle interventions and bariatric surgery, while the other study[156] focused on a commercial WL programme.

Study population

With regards to the age of participants, 19 studies modelled adult patients with an age range of between 18 and 75 years, while 1 study,[152] which was carried out in the USA, focused on adolescent patients with a mean age of 17 years. For patient disease state (*Appendix 3*, *Table 105*), 11 studies[43,86,87,146–151,154,157] estimated the cost-effectiveness of WL interventions for obesity for patients with a BMI of ≥ 35 kg/m^2.

The UK studies[43,162] were mostly consistent with respect to the definition of the population with obesity for whom surgical intervention is recommended according to NICE guidelines. Borisenko *et al.*[147] carried out a study in the UK and reported that patients were selected following the NICE eligibility criteria for bariatric surgery. Two studies assessed patients with T2D; while one study[153] focused on patients with obesity, the other[158] modelled overweight patients (but not patients with obesity) with T2D.

Of the three pharmacotherapy studies, Veerman *et al.*[161] assessed adults with obesity that had no obesity-related disease while the others[159,160] focused on adults with BMI ≥ 30 or BMI 27–29.9 with at least one weight-related comorbidity. Three studies[75,152,157] assessed patients with different BMI categories.

Model type

In terms of the types of models used to assess the cost-effectiveness of interventions, the majority of the studies used a state transition (Markov) model while one study[155] used both a decision tree and Markov model (*Table 105*).

Of the studies that used Markov models, 12 were cohort Markov models,[75,86,146–151,154,156,159] of which 6 studies across Europe were by the same authors that used the same model. Five studies[43,86,153,157,158,160] used an individual-level microsimulation model, while one study,[161] which assessed different pharmacological interventions, used a multistate life table-based Markov model.

Of the five studies that used individual STM, a UK-based study[43] adapted an existing model – the UK Health Forum Microsimulation Model (a dual-module modelling process developed by the UK Foresight working group),[43] while a US-based study[158] used the UK Prospective Diabetes Outcome Model.

The majority of the model-based studies did not justify their model choice.

Time horizon

The time horizon ranged from 1 year to a lifetime with most papers evaluating more than one time horizon (*Table 105*). The majority of the studies on bariatric surgery applied a 10-year[155] and lifetime[86,146–150,154] time horizon. Two of the UK studies used either a 20-year[157] time horizon or 30 years.[43] However, Klebanoff *et al.*,[152] which focused on adolescents, used a 3-year time horizon. The three papers that assessed pharmacotherapy interventions all used different time horizons. Kim *et al.*[159] used a 30-year time horizon, Lee[160] used a 1-, 3- and 5-year horizon while Wentworth[158] used a 10-year time horizon.

Health states and cycle length

Studies modelled a range of health states associated with obesity including BMI categories (6), obesity-related comorbidities (5) and post-surgical complications (7). Two studies[158,160] did not describe the health states used.

The studies that modelled BMI status typically included two[153,156] categories [no obesity (BMI ≤ 30 kg/m^2), class, 1 obesity (BMI 30–34.9 kg/m^2), class 2 obesity (BMI 35–39.9 kg/m^2), class 3 obesity (BMI≥ 40 kg/m^2)] while some papers[86,87] included a fifth category [super obesity (BMI ≥ 50 kg/m^2)]. Elliot *et al.*[151] assessed the impact of bariatric surgery and used three BMI categories.

The cycle lengths ranged from 1 to 12 months (*Table 105*). Kim *et al.*[159] evaluated the impact of semaglutide with a 30-year time horizon and used a 3-month cycle length for the first year and a 12-month cycle length thereafter.

Perspective and costs

Most of the studies (12) adopted the perspective of the health system and 5 studies[87,148,149,157,159] used the third-party payer perspective. Wentworth *et al.*[158] focused on gastric band (bariatric) surgery among overweight adults with T2DM and adopted a societal perspective.

Measures of effectiveness

With respect to effectiveness measures (*Table 106*), most of the models used either BMI or WL. Thirteen studies used various BMI measures such as change in BMI,[43,86,87,151,156,160] the percentage change in BMI[159] or absolute BMI reduction.[146–150,154] Two studies used a WL measure such as percentage total[152] or excess[155] WL. Two studies[153,157] used both a change in BMI and WL, Veerman *et al.*[161] used a mean reduction in body weight while Wentworth *et al.*[158] was not explicit about the effectiveness measure used.

Sources of clinical evidence for weight change

For model parameters on effectiveness, the studies used data from various sources (*Appendix 3*, *Table 106*). The majority of the studies used either clinical trials[87,151,153,155,157,159,160] only or different approaches.[43,75,86,146–150,154] Two studies[155,161] used data from a systematic review and meta-analysis of studies.

Borisenko *et al.*[146–150,154] conducted studies across Europe, using absolute BMI reduction and sourced effectiveness data from the various Obesity Surgery Registry Reports within Europe. The UK study[147] used data from the UK Second National Bariatric Surgery Registry (NBSR) expressed as a percentage excess weight loss (%EWL) combined with data on BMI obtained from the Swedish Obese Subjects (SOS) study.

Sensitivity analysis

Fifteen studies performed both one-way DSA and PSAs, eight studies conducted one-way DSA only, and one study[151] conducted PSA only.

TABLE 107 Summary of results from DSA based on ICER (cost per QALY)

Strategy	ICER of endoscopic therapy and comparators (£/QALY)					
	ESG vs. LSG		ESG vs. semaglutide		IGB vs. semaglutide	
Base case	£10,593.28		£7267.07		Semaglutide dominant	
Sensitivity analysis	Lower value	Upper value	Lower value	Upper value	Lower value	Upper value
1. Varying SAE incidence rates from base-case values selected based on evidence and clinical advice						
ESG-SAE rate	£10,626.00	£10,256.30	£6663.86	£9173.88	N/A	N/A
LSG-SAE rate	£10,347.91	£11,492.00	N/A	N/A	N/A	N/A
IGB-SAE rate	N/A	N/A	N/A	N/A	Semaglutide dominant	Semaglutide dominant
Semaglutide-SAE rate	N/A	N/A	£7294.49	£7233.58	Semaglutide dominant	Semaglutide dominant
2a. Increasing/decreasing surgery disutilities by 20%						
ESG disutility	£10,285.38	£10,921.09	£8326.05	£6447.08	N/A	N/A
LSG disutility	£11,037.25	£10,184.43	N/A	N/A	N/A	N/A
IGB disutility	N/A	N/A	N/A	N/A	Semaglutide dominant	Semaglutide dominant
2b. Increasing/decreasing surgery disutilities by 10%						
ESG disutility	£10,435.00	£10,757.28	£7768.25	£6826.65	N/A	N/A
LSG disutility	£10,809.73	£10,390.57	N/A	N/A	N/A	N/A
IGB disutility	N/A	N/A	N/A	N/A	Semaglutide dominant	Semaglutide dominant
3. Applying a higher semaglutide disutility based on evidence	N/A	N/A	£4927.29	N/A	Semaglutide dominant	N/A
4a. Increasing/decreasing SAE disutilities by 20%						
ESG-SAE disutility	£10,587.27	£10,600.15	£7285.88	£7248.37	N/A	N/A
LSG-SAE disutility	£10,606.61	£10,580.84	N/A	N/A	N/A	N/A

DOI: 10.3310/PWKQ2310

Strategy	ICER of endoscopic therapy and comparators (£/QALY)					
	ESG vs. LSG		ESG vs. semaglutide		IGB vs. semaglutide	
IGB-SAE disutility	N/A	N/A	N/A	N/A	Semaglutide dominant	Semaglutide dominant
Semaglutide-SAE disutility	N/A	N/A	£7265.20	£7268.95	Semaglutide dominant	Semaglutide dominant
4b. Increasing/decreasing SAE disutilities by 10%						
ESG-SAE disutility	£10,590.49	£10,596.93	£7276.46	£7257.71	N/A	N/A
LSG-SAE disutility	£10,600.15	£10,587.27	N/A	N/A	N/A	N/A
IGB- SAE disutility	N/A	N/A	N/A	N/A	Semaglutide dominant	Semaglutide dominant
Semaglutide-SAE disutility	N/A	N/A	£7266.14	£7268.01	Semaglutide dominant	Semaglutide dominant
5a. Increasing/decreasing SAE costs by 20%						
ESG-SAE costs	£10,618.00	£10,569.00	£7163.63	£7370.52	N/A	N/A
LSG-SAE costs	£10,545.00	£10,642.00	N/A	N/A	N/A	N/A
IGB-SAE costs	N/A	N/A	N/A	N/A	Semaglutide dominant	Semaglutide dominant
Semaglutide- SAE costs	N/A	N/A	£7294.97	£7238.97	Semaglutide dominant	Semaglutide dominant
5b. Increasing/decreasing SAE costs by 10%						
ESG-SAE costs	£10,606.00	£10,582.00	£7215.35	£7318.80	N/A	N/A
LSG-SAE costs	£10,569.00	£10,618.00	N/A	N/A	N/A	N/A
IGB-SAE costs	N/A	N/A	N/A	N/A	Semaglutide dominant	Semaglutide dominant
Semaglutide-SAE costs	N/A	N/A	£7280.97	£7252.97	Semaglutide dominant	Semaglutide dominant
6. Aligning CHD prevalence rate with disease severity to account for mortality bias in the literature	£10,530.20		£7278.50		Semaglutide dominant	

continued

TABLE 107 Summary of results from DSA based on ICER (cost per QALY) (*continued*)

	ICER of endoscopic therapy and comparators (£/QALY)					
Strategy	**ESG vs. LSG**		**ESG vs. semaglutide**		**IGB vs. semaglutide**	
7a. Increasing/decreasing intervention costs by 20%						
ESG cost	£14,363.70	£6701.80	ESG dominant	£23,521.31	N/A	N/A
LSG cost	£4482.70	£16,582.86	N/A	N/A	N/A	N/A
IGB cost	N/A	N/A	N/A	N/A	£6030.39	Semaglutide dominant
Semaglutide cost	N/A	N/A	£14,376.32	£175.52	Semaglutide dominant	Semaglutide dominant
7b. Increasing/decreasing intervention costs by 10%						
ESG cost	£12,448.20	£8617.30	ESG dominant	£15,394.19	N/A	N/A
LSG cost	£7507.70	£13,557.80	N/A	N/A	N/A	N/A
IGB cost	N/A	N/A	N/A	N/A	Semaglutide dominant	Semaglutide dominant
Semaglutide cost	N/A	N/A	£10,826.121	£3725.72	Semaglutide dominant	Semaglutide dominant
8. Varying the disease severity in the baseline population (lower value – more severe, upper value – less severe)	£8045.20	£13,169	£11,972.20	£6236.00	Semaglutide dominant	Semaglutide dominant
9a. Increasing/decreasing health-state utilities by 20%	£13,708.40	£8701.9	£7413.71	£7196.04	Semaglutide dominant	Semaglutide dominant
9b. Increasing/decreasing health-state utilities by 10%	£11,774.40	£9530.90	£7411.52	£7198.11	Semaglutide dominant	Semaglutide dominant
10a. Increasing/decreasing comorbidity costs by 20%	£10,718.50	£10,468.90	£7361.60	£7172.55	Semaglutide dominant	Semaglutide dominant
10b. Increasing/decreasing comorbidity costs by 10%	£10,656.10	£10,531.00	£7314.34	£7219.81	Semaglutide dominant	Semaglutide dominant

Strategy	ICER of endoscopic therapy and comparators (£/QALY)					
	ESG vs. LSG		**ESG vs. semaglutide**		**IGB vs. semaglutide**	
11. Varying long-term transition probabilities based on optimistic (upper value) and pessimistic (lower value) scenarios informed by clinical advice						
ESG transition probabilities	£8484.80	£11,499.6	£7849.50	£4641.32	N/A	N/A
LSG transition probabilities	£28,762.16	£9628.51	N/A	N/A	N/A	N/A
IGB transition probabilities	N/A	N/A	N/A	N/A	Semaglutide dominant	Semaglutide dominant
Semaglutide transition probabilities	N/A	N/A	£3679.28	£26,299.03	Semaglutide dominant	Semaglutide dominant

TABLE 108 Model transition probabilities and associated distributions

Model 1 Transition probabilities and alpha/beta values for PSA						
ESG				LSG		
Transition	Alpha	Beta	Transition probability	Alpha	Beta	Transition probability
Baseline > 6 months						
0 > 0						
0 > 1						
0 > 2						
0 > 3						
1 > 0						
1 > 1						
1 > 2						
1 > 3						
2 > 0	244.79	565.21	0.30	370.80	369.20	0.50
2 > 1	487.84	322.16	0.60	323.03	416.97	0.44
2 > 2	75.78	734.22	0.09	44.44	695.56	0.06
2 > 3	1.59	808.41	0.00	1.74	738.26	0.00
3 > 0	2.05	271.95	0.01	15.42	234.58	0.06
3 > 1	68.08	205.92	0.25	87.58	162.42	0.35
3 > 2	114.34	159.66	0.42	83.13	166.87	0.33
3 > 3	89.52	184.48	0.33	63.88	186.12	0.26
6 > 12 months						
0 > 0	246.85	0.00	1.00	386.22	0	1
0 > 1	0.00	246.85	0.00	0	386.22	0
0 > 2	0.00	246.85	0.00	0	386.22	0
0 > 3	0.00	246.85	0.00	0	386.22	0
1 > 0	186.27	369.66	0.34	347.71	62.88	0.85

Model 1 Transition probabilities and alpha/beta values for PSA

	ESG			LSG		
Transition	**Alpha**	**Beta**	**Transition probability**	**Alpha**	**Beta**	**Transition probability**
1 > 1	369.59	186.34	0.66	62.89	347.71	0.15
1 > 2	0.07	555.85	0.00	0	410.60	0
1 > 3	0.00	555.92	0.00	0	410.60	0
2 > 0	0.00	190.12	0.00	0.60	126.96	0.01
2 > 1	68.51	121.61	0.36	115.28	12.28	0.90
2 > 2	121.09	69.03	0.64	11.68	115.89	0.09
2 > 3	0.52	189.60	0.00	0	127.56	0
3 > 0	0.00	91.11	0.00	0	65.62	0
3 > 1	0.00	91.11	0.00	0.99	64.63	0.02
3 > 2	20.66	70.45	0.23	34.07	31.54	0.52
3 > 3	70.45	20.66	0.77	30.55	35.06	0.47
12 > 24 months						
0 > 0	354.22	78.89	0.82	503.40	231.1345	0.69
0 > 1	78.89	354.22	0.18	231.13	503.4048	0.31
0 > 2	0.00	433.11	0.00	0	734.5393	0
0 > 3	0.00	433.11	0.00	0	734.5393	0
1 > 0	1.36	436.74	0.00	0	179.1558	0
1 > 1	339.84	98.25	0.78	103.06	76.09931	0.56
1 > 2	96.89	341.20	0.22	76.10	103.0564	0.42
1 > 3	0.00	438.10	0.00	0	179.16	0
2 > 0	0.00	141.82	0.00	0	45.75	0
2 > 1	0.20	141.62	0.00	0	45.75	0
2 > 2	105.73	36.09	0.75	24.13	21.62	0.53

continued

TABLE 108 Model transition probabilities and associated distributions (*continued*)

Model 1 Transition probabilities and alpha/beta values for PSA						
ESG				LSG		
Transition	Alpha	Beta	Transition probability	Alpha	Beta	Transition probability
2 > 3	35.89	105.93	0.25	21.62	24.13	0.47
3 > 0	0.00	70.97	0.00	0	30.55	0
3 > 1	0.00	70.97	0.00	0	30.55	0
3 > 2	0.09	70.88	0.00	0	30.55	0
3 > 3	70.88	0.09	1.00	30.55	0	1
24 > 36 months						
0 > 0	264.53	37.36	0.88	365.72	74.60	0.83
0 > 1	37.36	264.53	0.12	74.32	366.01	0.17
0 > 2	0.00	301.89	0.00	0.29	440.04	0.00
0 > 3	0.00	301.89	0.00	0	440.33	0
1 > 0	0.95	318.03	0.00	72.37	187.06	0.28
1 > 1	257.79	61.19	0.81	169.96	89.47	0.66
1 > 2	60.24	258.74	0.19	16.96	242.47	0.07
1 > 3	0.00	318.98	0.00	0.14	259.29	0.00
2 > 0	0.00	318.98	0.00	0.78	258.65	0.00
2 > 1	0.10	112.54	0.00	22.52	25.17	0.47
2 > 2	85.86	26.77	0.76	21.94	25.74	0.46
2 > 3	26.67	85.96	0.24	2.45	45.23	0.05
3 > 0	0.00	23.50	0.00	0	9.56	0
3 > 1	0.00	23.50	0.00	0.43	9.13	0.05
3 > 2	0.01	23.49	0.00	2.60	6.96	0.27
3 > 3	23.49	0.01	1.00	6.53	3.03	0.68

DOI: 10.3310/PWKQ2310

Model 1 Transition probabilities and alpha/beta values for PSA						
	ESG			LSG		
Transition	Alpha	Beta	Transition probability	Alpha	Beta	Transition probability
36 > 48 months						
0 > 0	125.36	7.38	0.94	212.04	7.39	0.97
0 > 1	7.38	125.36	0.06	7.39	212.04	0.03
0 > 2	0.00	132.74	0.00	0	219.43	0
0 > 3	0.00	132.74	0.00	0	219.43	0
1 > 0	2.51	145.11	0.02	0.51	133.10	0.00
1 > 1	120.45	27.17	0.82	131.49	2.12	0.98
1 > 2	24.67	122.95	0.17	1.61	132.00	0.01
1 > 3	0.00	147.62	0.00	0	133.61	0
2 > 0	0.00	73.06	0.00	0	20.89	0
2 > 1	0.33	72.73	0.00	0.10	20.79	0.00
2 > 2	55.08	17.98	0.75	20.47	0.42	0.98
2 > 3	17.66	55.40	0.24	0.32	20.57	0.02
3 > 0	0.00	25.08	0.00	0	4.56	0
3 > 1	0.00	25.08	0.00	0	4.56	0
3 > 2	0.06	25.02	0.00	0.01	4.55	0.00
3 > 3	25.02	0.06	1.00	4.55	0.00	1.00
48 > 60 months						
0 > 0	105.03	22.85	0.82	205.83	6.73	0.97
0 > 1	22.85	105.03	0.18	6.73	205.83	0.03
0 > 2	0.00	127.87	0.00	0	212.56	0
0 > 3	0.00	127.87	0.00	0	212.56	0
1 > 0	0.00	128.15	0.00	0	138.98	0
1 > 1	106.41	21.74	0.83	137.02	1.96	0.99

continued

TABLE 108 Model transition probabilities and associated distributions (*continued*)

Model 1 Transition probabilities and alpha/beta values for PSA						
ESG				LSG		
Transition	Alpha	Beta	Transition probability	Alpha	Beta	Transition probability
1 > 2	21.74	106.41	0.17	1.96	137.02	0.01
1 > 3	0.00	128.15	0.00	0	138.98	0
2 > 0	0.00	79.81	0.00	0	22.09	0
2 > 1	0.00	79.81	0.00	0	22.09	0
2 > 2	68.16	11.65	0.85	21.73	0.36	0.98
2 > 3	11.65	68.16	0.15	0.36	21.73	0.02
3 > 0	0.00	42.67	0.00	0	4.87	0
3 > 1	0.00	42.67	0.00	0	4.87	0
3 > 2	0.00	42.67	0.00	0	4.87	0
3 > 3	42.67	0.00	1.00	4.87	0	1

Model 2 Transition probabilities and alpha/beta values for PSA						
	ESG			Semaglutide (also for model 3)		
Transition	Alpha	Beta	Transition probability	Alpha	Beta	Transition probability
Baseline > 6 months						
0 > 0						
0 > 1						
0 > 2						
0 > 3						
1 > 0	1187.81	164.19	0.88	391.07	44.93	0.90
1 > 1	161.63	1190.37	0.12	44.93	391.07	0.10
1 > 2	2.51	1349.49	0.00	0	436	0
1 > 3	0.05	1351.95	0.00	0	436	0
2 > 0	288.98	670.02	0.30	32.69	373.31	0.08
2 > 1	582.28	376.72	0.61	351.15	54.85	0.86
2 > 2	86.90	872.10	0.09	22.15	383.85	0.05
2 > 3	0.85	958.15	0.00	0	406	0
3 > 0						
3 > 1						
3 > 2						
3 > 3						
6 > 12 months						
0 > 0	1476.73	0.06	1.00	423.77	0	1
0 > 1	0	1476.79	0	0	423.77	0
0 > 2	0	1476.79	0	0	423.77	0
0 > 3	0	1476.79	0	0	423.77	0
1 > 0	264.46	479.45	0.36	221.25	174.83	0.56
1 > 1	477.92	265.98	0.64	174.83	221.24	0.44
1 > 2	1.52	742.39	0.00	0	396.08	0
1 > 3	0	743.91	0	0	396.08	0
2 > 0	0	89.41	0	0	22.15	0
2 > 1	27.93	61.47	0.31	21.12	1.03	0.95
2 > 2	60.65	28.76	0.68	1.03	21.12	0.05
2 > 3	0.83	88.58	0.01	0	22.15	0
3 > 0	0	0.90	0	0	0	0
3 > 1	0	0.90	0	0	0	0
3 > 2	0	0.90	0	0	0	0
3 > 3	0	0.90	0	0	0	0

Model 2 Transition probabilities and alpha/beta values for PSA

	ESG			Semaglutide (also for model 3)		
Transition	**Alpha**	**Beta**	**Transition probability**	**Alpha**	**Beta**	**Transition probability**
12 > 24 months						
0 > 0	1534.28	206.91	0.88	322.51	0	1
0 > 1	206.91	1534.28	0.12	0	322.51	0
0 > 2	0	1741.19	0	0	322.51	0
0 > 3	0	1741.19	0	0	322.51	0
1 > 0	0	505.86	0	8.48	89.50	0.09
1 > 1	405.72	100.14	0.80	89.50	8.48	0.91
1 > 2	100.14	405.72	0.20	0	97.98	0
1 > 3	0	505.86	0	0	97.98	0
2 > 0	0	62.17	0	0	0.52	0
2 > 1	0	62.17	0	0.24	0.28	0.46
2 > 2	42.67	19.50	0.69	0.28	0.24	0.54
2 > 3	19.50	42.67	0.31	0	0.52	0
3 > 0	0	0.83	0	0	0	
3 > 1	0	0.83	0	0	0	
3 > 2	0	0.83	0	0	0	
3 > 3	0	0.83	0	0	0	
24 > 36 months						
0 > 0	1492.64	189.47	0.89	115.75	49.74	0.70
0 > 1	189.47	1492.64	0.11	46.01	119.48	0.28
0 > 2	0.00	1682.11	0.00	3.65	161.84	0.02
0 > 3	0.00	1682.11	0.00	0.07	165.42	0.00
1 > 0	0.00	539.52	0.00	1.31	43.56	0.03
1 > 1	432.78	106.75	0.80	21.57	23.30	0.48
1 > 2	106.75	432.78	0.20	18.79	26.08	0.42
1 > 3	0.00	539.52	0.00	3.20	41.67	0.07
2 > 0	0.00	539.52	0.00	0.00	44.87	0.00
2 > 1	0.00	105.30	0.00	0.00	0.14	0.00
2 > 2	81.62	23.67	0.78	0.00	0.14	0.00
2 > 3	23.67	81.62	0.22	0.14	0.00	1.00
3 > 0	0.00	12.85	0.00	0.00	0.00	0.00
3 > 1	0.00	12.85	0.00	0.00	0.00	0.00
3 > 2	0.00	12.85	0.00	0.00	0.00	0.00
3 > 3	12.85	0.00	1.00	0.00	0.00	1.00

Model 2 Transition probabilities and alpha/beta values for PSA						
	ESG			Semaglutide (also for model 3)		
Transition	Alpha	Beta	Transition probability	Alpha	Beta	Transition probability
36 > 48 months						
0 > 0	673.76	72.57	0.90	38.72	19.81	0.66
0 > 1	72.57	673.76	0.10	19.81	38.72	0.34
0 > 2	0.00	746.32	0.00	0.00	58.53	0.00
0 > 3	0.00	746.32	0.00	0.00	58.53	0.00
1 > 0	0.19	310.93	0.00	0.00	33.79	0.00
1 > 1	246.27	64.85	0.79	22.78	11.01	0.67
1 > 2	64.66	246.46	0.21	11.01	22.78	0.33
1 > 3	0.00	311.12	0.00	0.00	33.79	0.00
2 > 0	0.00	94.19	0.00	0.00	11.22	0.00
2 > 1	0.00	94.19	0.00	0.00	11.22	0.00
2 > 2	66.75	27.43	0.71	8.29	2.93	0.74
2 > 3	27.43	66.75	0.29	2.93	8.29	0.26
3 > 0	0.00	18.26	0.00	0.00	1.71	0.00
3 > 1	0.00	18.26	0.00	0.00	1.71	0.00
3 > 2	0.00	18.26	0.00	0.00	1.71	0.00
3 > 3	18.26	0.00	1.00	1.71	0.00	1.00
48 > 60 months						
0 > 0	613.35	60.60	0.91	10.33	9.03	0.53
0 > 1	60.60	613.35	0.09	9.03	10.33	0.47
0 > 2	0.00	673.95	0.00	0.00	19.36	0.00
0 > 3	0.00	673.95	0.00	0.00	19.36	0.00
1 > 0	0.00	318.83	0.00	0.00	21.30	0.00
1 > 1	282.83	36.01	0.89	13.56	7.74	0.64
1 > 2	36.01	282.83	0.11	7.74	13.56	0.36
1 > 3	0.00	318.83	0.00	0.00	21.30	0.00
2 > 0	0.00	131.41	0.00	0.00	19.80	0.00
2 > 1	0.00	131.41	0.00	0.00	19.80	0.00
2 > 2	118.89	12.52	0.90	13.99	5.80	0.71
2 > 3	12.52	118.89	0.10	5.80	13.99	0.29
3 > 0	0.00z	45.70	0.00	0.00	2.32	0.00
3 > 1	0.00	45.70	0.00	0.00	2.32	0.00
3 > 2	0.00	45.70	0.00	0.00	2.32	0.00
3 > 3	45.70	0.00	1.00	2.32	0.00	1.00

Model 3 Transition probabilities and alpha/beta values for PSA			
IGB			
Transition	**Alpha**	**Beta**	**Transition probability**
Baseline > 6 months			
0 > 0	0.00	0.00	
0 > 1	0.00	0.00	
0 > 2	0.00	0.00	
0 > 3	0.00	0.00	
1 > 0	105.00	17.00	0.86
1 > 1	16.94	105.06	0.14
1 > 2	0.06	121.94	0.00
1 > 3	0.00	122.00	0.00
2 > 0	15.12	70.88	0.18
2 > 1	62.16	23.84	0.72
2 > 2	8.69	77.31	0.10
2 > 3	0.03	85.97	0.00
3 > 0	0.00	0.00	
3 > 1	0.00	0.00	
3 > 2	0.00	0.00	
3 > 3	0.00	0.00	
6 > 12 months			
0 > 0	42.50	8.18	0.84
0 > 1	0.00	50.68	0.00
0 > 2	0.00	50.68	0.00
0 > 3	0.00	50.68	0.00
1 > 0	0.00	33.37	0.00
1 > 1	30.21	3.16	0.91
1 > 2	3.16	30.21	0.09
1 > 3	0.00	33.37	0.00
2 > 0	0.00	3.69	0.00
2 > 1	0.00	3.69	0.00
2 > 2	3.65	0.04	0.99
2 > 3	0.04	3.65	0.01
3 > 0	0.00	0.01	0.00
3 > 1	0.00	0.01	0.00
3 > 2	0.00	0.01	0.00
3 > 3	0.01	0.00	1.00

Model 3 Transition probabilities and alpha/beta values for PSA			
IGB			
Transition	Alpha	Beta	Transition probability
12 > 24 months			
0 > 0	14.65	6.60	0.69
0 > 1	6.11	15.14	0.29
0 > 2	0.49	20.76	0.02
0 > 3	0.00	21.25	0.00
1 > 0	1.41	13.70	0.09
1 > 1	6.64	8.46	0.44
1 > 2	5.63	9.48	0.37
1 > 3	1.43	13.68	0.09
2 > 0	0.00	3.41	0.00
2 > 1	0.00	3.41	0.00
2 > 2	0.89	2.52	0.26
2 > 3	2.52	0.89	0.74
3 > 0	0.00	0.06	0.00
3 > 1	0.00	0.06	0.00
3 > 2	0.00	0.06	0.00
3 > 3	0.06	0.00	1.00
24 > 36 months			
0 > 0	14.66	1.39	0.91
0 > 1	1.39	14.66	0.09
0 > 2	0.00	16.06	0.00
0 > 3	0.00	16.06	0.00
1 > 0	0.00	12.75	0.00
1 > 1	11.66	1.10	0.91
1 > 2	1.10	11.66	0.09
1 > 3	0.00	12.75	0.00
2 > 0	0.00	12.75	0.00
2 > 1	0.00	7.00	0.00
2 > 2	6.52	0.48	0.93
2 > 3	0.48	6.52	0.07
3 > 0	0.00	4.01	0.00
3 > 1	0.00	4.01	0.00
3 > 2	0.00	4.01	0.00
3 > 3	4.01	0.00	1.00

Model 3 Transition probabilities and alpha/beta values for PSA			
IGB			
Transition	**Alpha**	**Beta**	**Transition probability**
36 > 48 months			
0 > 0	14.31	0.36	0.98
0 > 1	0.36	14.31	0.02
0 > 2	0.00	14.66	0.00
0 > 3	0.00	14.66	0.00
1 > 0	0.00	13.05	0.00
1 > 1	12.80	0.25	0.98
1 > 2	0.25	12.80	0.02
1 > 3	0.00	13.05	0.00
2 > 0	0.00	7.61	0.00
2 > 1	0.00	7.61	0.00
2 > 2	7.48	0.13	0.98
2 > 3	0.13	7.48	0.02
3 > 0	0.00	4.49	0.00
3 > 1	0.00	4.49	0.00
3 > 2	0.00	4.49	0.00
3 > 3	4.49	0.00	1.00
48 > 60 months			
0 > 0	13.94	0.37	0.97
0 > 1	0.37	13.94	0.03
0 > 2	0.00	14.31	0.00
0 > 3	0.00	14.31	0.00
1 > 0	0.00	13.15	0.00
1 > 1	12.85	0.31	0.98
1 > 2	0.31	12.85	0.02
1 > 3	0.00	13.15	0.00
2 > 0	0.00	7.73	0.00
2 > 1	0.00	7.73	0.00
2 > 2	7.59	0.14	0.98
2 > 3	0.14	7.59	0.02
3 > 0	0.00	4.62	0.00
3 > 1	0.00	4.62	0.00
3 > 2	0.00	4.62	0.00
3 > 3	4.62	0.00	1.00

EME
HSDR
HTA
PGfAR
PHR

Part of the NIHR Journals Library
www.journalslibrary.nihr.ac.uk

This report presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care

Published by the NIHR Journals Library