Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Metabolic surgery for the treatment of Type 2 Diabetes and obesity in Adults in Ireland:

Protocol for a Health Technology Assessment

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1.1. Introduction

For the purposes of this assessment, metabolic surgery refers to the use of bariatric surgical procedures with the intention of treating patients with type 2 diabetes (T2D) and obesity. Despite increasing research activity, the clinical practice of metabolic surgery is not yet widely adopted. Numerous international guidelines for the management of T2D recommend metabolic surgery for patients with T2D and obesity.[1, 2] However, in Ireland access to metabolic surgery is not currently available as part of the T2D clinical care pathway. The increasing prevalence of T2D in Ireland[3] combined with the consequent rising economic burden,[4] indicates a critical need to revisit the current T2D treatment algorithms. A multifaceted approach, including lifestyle, pharmacological and surgical interventions, as appropriate, is needed.

At present, patients with obesity and any obesity-related comorbidity access surgery through the bariatric surgery service. According to HIPE data, between 2009 and 2019, 25% of bariatric surgery cases had a diagnosis of T2D prior to surgery. Although the burden of disease is not well defined, based on census projections for 2020, it is estimated that there are approximately 33,000 individuals with T2D and a BMI ≥35 kg/m^2.[5] While not all those who meet the eligibility criteria for metabolic surgery may want or require it, the apparent gap between the eligible population and those with T2D and obesity who undergo bariatric surgery at present suggests that supply within the bariatric surgery service is inadequate to meet the clinical needs of this population.

Following a request from the Clinical Lead of the National Clinical Programme for Diabetes in the Health Service Executive (HSE), with support from the National Clinical Programme for Obesity, this topic was prioritised for inclusion in the HIQA HTA work plan. Given the potential significant organisational and resource implications associated with introducing a metabolic surgery programme and the associated changes to the current T2D treatment pathway, a full health technology assessment (HTA) will be conducted to inform the decision-making process. This protocol aims to present the methods for estimating the burden of disease and assessing clinical-effectiveness, cost-effectiveness, budget impact, ethical and social aspects and any organisational changes associated with the introduction of a metabolic surgery programme for patients with T2D and obesity.

1.2. Aims and objectives

A HTA comprising systematic reviews of clinical-effectiveness and cost-effectiveness, a cost-effectiveness analysis (CEA) and budget impact analysis (BIA) will be carried out to inform policy decisions regarding the introduction of metabolic surgery services for patients with T2D and obesity in Ireland.

The overarching aim of this HTA is to estimate the clinical and cost-effectiveness of metabolic surgery for the treatment of T2D in adults with obesity within the diabetes clinical care pathway.

The specific objectives of this HTA are to:

- describe the treatment options for the management of T2D in Ireland
- describe the burden of disease associated with T2D in adults in Ireland
- carry out a systematic review of the clinical effectiveness and safety of metabolic surgery in patients with T2D and obesity with a clinical indication for surgery
- carry out a systematic review of the cost-effectiveness of metabolic surgery in patients with T2D and obesity with a clinical indication for surgery
- assess the cost-effectiveness and budget impact of introducing metabolic surgery for patients with T2D and obesity in the context of the Irish public healthcare system.
- consider the organisational changes and resource implications associated with the introduction of metabolic surgery services
- consider any ethical and social implications that the provision of metabolic surgery services may have for patients, the general public or the healthcare system in Ireland.

1.3. Establishment of the Expert Advisory Group

An appropriately represented Expert Advisory Group (EAG) has been convened as a source of expertise to inform interpretation of the evidence and development of the advice to the Minister for Health.

This group comprises nominees from a range of stakeholder organisations, including patient representation, healthcare providers and managers, as well as clinical, public health and methodological experts.

1.4. Description of the technology

A brief description of T2D, the methods and criteria for diagnosing T2D and a brief description of current approaches to disease management will be provided. The various types of metabolic procedures in current use include:

- adjustable gastric banding (AGB)
- sleeve gastrectomy (SG)
- roux-en-y gastric bypass (RYGB)
- biliopancreatic diversion with duodenal switch (BPD-DS).

Additional surgical procedures that have been newly adopted elsewhere, include:

- one anastomosis gastric bypass (OAGB), also known as single anastomosis gastric bypass (SAGB) or mini gastric by-pass (MGB)
- single anastomosis duodenal-ileal bypass with sleeve gastrectomy (SADI-S)
- single anastomosis sleeve ileal bypass (SASI).

The field of bariatric surgery is still evolving. New or refined procedures are currently under investigation in an attempt to achieve the optimal risk-benefit balance to guide surgical decision-making and informed consent. For example, in 2020, the Haute Autorité de Santé (HAS) in France identified 17 new techniques.[(6)] Procedures used in clinical practice in Ireland (that is, AGB, SG, RYGB, BPD-DS) or recently adopted elsewhere (OAGB, SADI-S, SASI) will be considered, where evidence is available for the target population of this assessment.

A brief description of usual care for the management of T2D will be provided for context and to inform the cost of treatment for the economic evaluation and budget impact analysis, including:

- lifestyle intervention (including increased physical activity and dietary changes)
- pharmacological treatments to:
  - improve glycaemic control (such as, oral anti-hyperglycaemic agents or insulin)
  - manage cardiovascular risk (such as, statins, anti-hypertensive agents)
  - improve both glycaemic control and cardiovascular risk factor reduction using newer anti-hyperglycaemic agents (for example, sodium-glucose co-transporter-2 (SGLT2) inhibitors)

  - manage diabetes-related complications (such as, fibrates for retinopathy; atypical analgesics for painful neuropathy)
- patient education to facilitate self-care
- regular screening for early detection and treatment of complications (for example, retinopathy screening).

1.5. Epidemiology of disease

A comprehensive description of the burden of disease attributable to T2D in patients with obesity in Ireland will be provided. This section will be informed by a review of national and international literature and databases.

The incidence and, or prevalence of T2D-related complications will be estimated to determine the burden on the Irish healthcare system. The review of epidemiological sources will be used to inform the inputs to the economic model (described in section 1.7) and the estimated resources required to provide the appropriate level of care to the target population (that is, patients with T2D and obesity).

In Ireland, there is no national diabetes register, database of electronic medical records or population-based survey of T2D to generate estimates of the burden of disease or the impact of interventions at a national level. Prevalence estimates rely on data from observational studies or national level datasets. Cross-sectional analyses of nationally representative datasets and individual studies will be used to estimate the prevalence of T2D and related complications in the Irish adult population. In the absence of Irish data, the best available estimates will be derived from the international literature.

Morbidity and mortality

In patients with T2D, vascular complications are the most serious manifestations of the disease; these include microvascular (that is, retinopathy, nephropathy, and neuropathy) and macrovascular (that is, diseases of the coronary arteries, peripheral arteries, and cerebrovasculature) disease. A description of morbidity (incidence and prevalence of vascular complications) and mortality (survival outcomes) associated with T2D and associated complications will be provided.

Estimation of the eligible population

According to recommendations from the 2nd Diabetes Surgery Summit (DSS-II) and the American Diabetes Association (ADA), metabolic surgery can be recommended as a treatment option for T2D in screened surgical candidates with a BMI ≥40 kg/m^2, and in adults with a BMI 35.0 to 39.9 kg/m^2 with T2D control above treatment targets despite best medical care. Metabolic surgery may be considered as

an option to treat T2D in adults with BMI 30.0 to 34.9 kg/m^2 with T2D control above treatment targets despite best medical care.[1, 2] There is no standardised definition of T2D control above target despite best medical care (also called refractory T2D, treatment-resistant T2D, suboptimally or inadequately controlled T2D).[7, 8] In clinical practice, targets for glycaemic control are typically determined at an individual patient level with consideration to the duration of diabetes, risk of hypoglycaemia, age and the presence of comorbidities. However, in general, the risk of vascular complications increases with increasing blood glucose levels above the normal range. A number of different measures of inadequately controlled T2D have been proposed, which typically consider comorbidity status and or indicators of glycaemic control.[9-12]

Based on a cross-sectional analysis of TILDA data, it has been estimated that 2.06% (95% CI: 1.70 to 2.49) of adults over 50 years of age may be eligible for bariatric surgery based on obesity status (BMI ≥35kg/m^2) and the presence of T2D. Given that international guidance now recommends consideration of access to surgery for those with a BMI ≥30 kg/m^2 and inadequate glycaemic control, and TILDA data is limited to those >50 years of age, there is considerable uncertainty regarding the size of the population eligible for metabolic surgery in Ireland. The input of the EAG will be required to support estimates of the eligible population.

1.6. Systematic review

Two systematic reviews relating to metabolic surgery in patients with T2D and obesity will be conducted: (1) a systematic review of clinical effectiveness and safety; and (2) a systematic review of the economic evaluations. Full details of each review will be outlined in a registered protocol on PROSPERO. The reporting of the systematic reviews will adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria and national guidelines.[13-15]

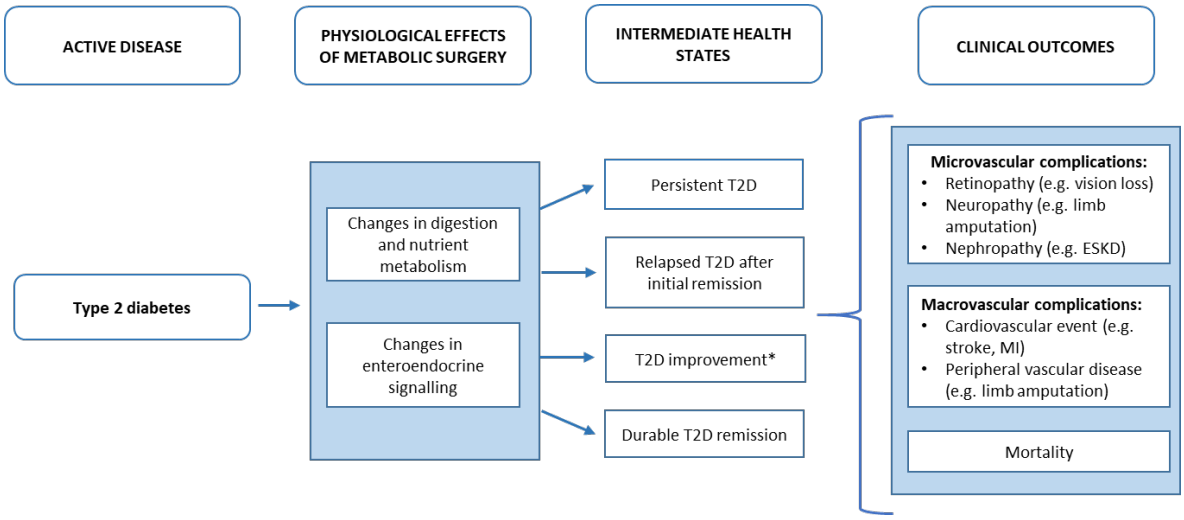
1.6.1. Clinical effectiveness and safety

The research question for the clinical effectiveness and safety of metabolic surgery in patients with T2DM with obesity has been formulated in line with the PICOS (population, intervention, comparator, outcome, study design) framework. Studies will be selected for inclusion based on the criteria outlined in Table 1. Clinical and safety outcomes are defined with consideration to core outcome sets for reporting outcomes of bariatric and metabolic surgery,[16, 17] with the addition of diabetes-related complications reported in diabetes-specific core outcome sets.[18, 19] Outcomes are presented in a conceptual framework in Figure 1.

Preliminary scoping identified many systematic reviews published in recent years,[20-25] and registered on PROSPERO.[26-28] The scope of systematic reviews already published or underway varies in terms of the population (for example, BMI category, patients with T2D, patients with non-alcoholic fatty liver disease (NAFLD), adolescents), the types of procedure, the range of outcomes (micronutrient status, microvascular or macrovascular disease) or methodological considerations (for example, study designs included, minimum duration of follow-up). No single systematic review in line with the PICOS for this research question has been identified.

Randomised controlled trials (RCTs) and non-randomised controlled trials (nRCTs) will be considered eligible for inclusion. As defined by the Cochrane Effective Practice and Organisation of Care (EPOC), nRCTs are defined as trials in which participants are allocated to different groups for comparison using a method that is not random (for example, chart number).[29] Observational study designs whereby participants were not allocated to a group by the study investigators will not be included.

Figure 1: Conceptual framework of clinical outcomes of metabolic surgery



Key: ESKD – End stage kidney disease; MI – myocardial infarction; T2D – type 2 diabetes.
* May include those with reduced use of diabetes medications, or decreased or sustained (in those with progressive deterioration of glycaemic control prior to surgery) HbA1c levels who do not achieve full remission.
Figure adapted from Adams et al. 2016.[30]

Table 1: PICOS for systematic review of clinical effectiveness and safety

Population	Adults ≥ 18 years of age with type 2 diabetes and obesity*
Intervention	Metabolic surgery procedures in current use, performed either as open or laparoscopic procedures
Comparator	▪ Optimal medical management (including oral or injectable antidiabetic agents and/or insulin) with or without a sham procedure ▪ Other metabolic surgical procedures in current use, performed either as open procedures or laparoscopically
Outcomes	**Primary outcomes:** ▪ Diabetes status o Glycaemic endpoints (e.g., HbA1c, T2D remission, T2D improvement) o T2D medication use (oral anti-hyperglycaemic medication and insulin) ▪ Safety outcomes: o Mortality (30 day and long-term) o Any major or minor technical complications associated with the surgery (e.g., leaks, fistula, strictures, ulcers at anastomosis, internal hernia, gastric band slippage or erosion, intra-operative organ injury, wound infection) o Any post-operative clinical complications (e.g., dysphagia/regurgitation, dumping syndrome, clinically significant nutritional deficiency†) o Any re-operation/re-intervention **Secondary outcomes:** ▪ Weight-related outcomes (BMI) ▪ Health-related quality of life indicators and diabetes-specific measures using a validated instrument (e.g., EQ-5D score, SF-36 score, KCCQ score, BAROS) ▪ Healthcare utilisation or resource use o Hospital length of stay o Outpatient care o Hospital admission/re-admission *Diabetes-related complications* ▪ Lower limb ulceration; major or minor amputation ▪ End-stage renal disease ▪ Cardiovascular risk reduction o Cardiovascular events (e.g., MI, stroke) o Medication use (e.g., antihypertensive agents, statins, aspirin) o Hypertension (diastolic blood pressure, systolic blood pressure) o Dyslipidaemia (triglycerides, LDL-c, HDL-c, total cholesterol) ▪ Microvascular complications o Incidence of microvascular complications of T2D (retinopathy, nephropathy, neuropathy) o Resolution or improvement in microvascular complications (e.g., reduction in albuminuria, interventional therapy for retinopathy such as anti-VEGF treatment or the use of medication for neuropathy or nephropathy)
Study design	Randomised controlled trials, non-randomised controlled trials

Key: BAROS – Bariatric Analysis and Reporting Outcome System; BMI – Body mass index; EQ-5D - EuroQoL-5 Dimension; HbA1c – Haemoglobin A1c; HDL – high density lipoprotein; KCCQ - Kansas City Cardiomyopathy Questionnaire; LDL – low density lipoprotein; MI – myocardial infarction; SF-36 – Short Form 36-item Survey; T2D – Type 2 Diabetes.

* Obesity as defined by the study author.

† Clinically significant nutritional deficiency is defined is any lack of essential vitamins and/or minerals secondary to post-operative intestinal malabsorption resulting in clinical manifestations including but not limited to microcytic anaemia, megaloblastic anaemia, neurologic abnormalities, osteoporosis, fractures, ocular xerosis, night blindness symptoms, ophthalmoplegia, peripheral neuropathy and easy bleeding as reported by the European Association for the Study of Obesity (EASO) and the British Obesity and Metabolic Surgery Society (BOMSS) (see appendix 1).[31, 32]

Exclusion criteria

- Reviews, conference abstracts, case reports, case series, case-control studies retrospective or prospective cohort studies.
- Before and after studies, not directly comparing surgery with a no-surgery group, will be excluded, due to the progressive nature of the disease over time.
- Studies in which only a sub-group of the population had a diagnosis of T2D.
- Studies that include revisional procedures (unless disaggregated data are available).
- Surgeries that remove fat (for example, liposuction or abdominoplasty), excess skin or any cosmetic procedures.
- Articles reporting data on participants <18 years of age (unless disaggregated data are available).

Search strategy, screening and data extraction

Electronic searches will be conducted in Embase, MEDLINE (via Ovid) and The Cochrane Library. Electronic database searches will be supplemented by a search of grey literature. The references lists of included studies will be searched to identify additional relevant studies.

Titles and abstracts of studies retrieved using the search strategy and those from additional sources will be screened independently by two reviewers. The full text of potentially eligible studies will be retrieved and independently assessed for eligibility by two reviewers according to the criteria outlined in table 1. Data extraction will be conducted independently by two reviewers using a standardised, pre-piloted electronic data extraction form. Disagreements in study selection or data extraction will be resolved through discussion, or if necessary, a third reviewer.

Data synthesis and analysis

Where appropriate, meta-analysis will be performed and presented via a forest plot. The choice between a fixed-effect and random-effects model will be made based on the level of statistical and clinical heterogeneity observed across studies. Where sufficient data are available, the following subgroup analyses will be performed: type of procedure, BMI category (that is, ≥30 to 34.9 kg/m^2, ≥35 to 39.9 kg/m^2, and ≥40 kg/m^2), length of follow-up and duration of diabetes.

Quality assessment

Two reviewers will independently assess the included studies for risk of bias, using validated critical appraisal tools. Disagreements will be resolved through discussion and, if necessary, a third reviewer.

The methodological quality of RCTs will be assessed using the Cochrane risk of bias 2 tool.[33] For non-randomised studies of interventions, the Risk Of Bias In Non-randomised Studies-of Interventions (ROBINS-I) tool will be used.[34]

The GRADE approach will be used to assess the quality of the overall body of evidence for primary outcomes.

1.6.2. Cost-effectiveness

Economic evaluations of bariatric or metabolic surgery may vary in terms of the costs (for example, antidiabetic medications) and outcomes (for example, T2D remission, T2D-related complications such as amputation, end-stage kidney disease) considered. Economic models of bariatric surgery for the treatment of obesity that do not consider T2D-specific outcomes may not capture the costs and consequences of metabolic surgery in patients with T2D and obesity, and therefore may not be representative of the target cohort considered in this HTA.

Two systematic reviews of cost effectiveness analyses of bariatric surgery in adults, adolescents or children with obesity have been identified that include data up to September 2018,[35, 36] both updating a previous systematic review.[37] However, no systematic review was identified that explicitly focussed on the cost-effectiveness of metabolic surgery in patients with obesity and T2D. Therefore, a de novo systematic review will be conducted. Where available, cost-effectiveness analyses with outcomes and cost data related to patients with obesity and T2D will be considered. Studies will be considered for inclusion in accordance with the following hierarchy of evidence:

1. cost-effectiveness analyses of metabolic surgery in patients with T2D and obesity

2. cost-effectiveness analyses of bariatric surgery in patients with obesity, where a sub-group of the population have T2D and obesity.

Initial scoping exercises identified a number of economic evaluations of bariatric/metabolic surgery, including patients with T2D published since the previous systematic reviews were carried out.[38-41]

The aim of the systematic review is to inform the model structure and inputs of an Irish-specific CEA. The specific question of the systematic review of cost-effectiveness is outlined in Table 2. Cost-utility analysis (that is, cost per quality-adjusted life-year gained (QALY)) and cost-effectiveness analyses (for example, cost per life-year gained) will be considered eligible for inclusion. The results will be synthesised narratively.[15]

Assessment of methodological limitations and transferability

Assessment of the methodological quality of economic evaluations will be carried out using the Consensus on Health Economics Criteria (CHEC)-list.[42] The ISPOR questionnaire will be used to assess the transferability potential (that is, applicability) of model-based economic evaluations to the Irish healthcare setting.[43]

Table 2: PICOS for systematic review of cost effectiveness analyses

Population	Adults ≥ 18 years of age with obesity (BMI ≥30 kg/m^2) and T2D
Intervention	Bariatric/metabolic surgery procedures in current use, performed either as open or laparoscopic procedures
Comparator	Non-surgical treatment (usual care*)
Outcomes	ICER or NMB
Study design	Full economic evaluations (CUA, CEA)

Key: BMI – Body mass index; CEA – cost-effectiveness analysis; CUA – cost-utility analysis; ICER – incremental cost-effectiveness ratio; NMB – net monetary benefit; T2D – Type 2 Diabetes.
* Usual care can include descriptions such as conservative treatment, conventional or intensive medical management.

Exclusion criteria

- cost-consequence analysis, cost-benefit analysis, other types of cost analyses and comparative resource use studies
- commentaries, letters, conference papers and abstracts where the full paper was not available
- partial economic evaluations or cost analyses
- studies for which an English translation could not be found.

1.7. Economic evaluation

An economic evaluation comprising a CEA and a BIA will be carried out from the perspective of the Health Service Executive (HSE). A summary of model characteristics for each of the analyses is presented in Table 3.

Table 3: Model characteristics for CEA and BIA

	CEA	BIA
Perspective	Publicly-funded health and social care system (HSE)	Publicly-funded health and social care system (HSE)
Time horizon	Lifetime†	Five year
Discounting rate	4% (costs and outcomes)‡ after the first year	N/A
Outcome	ICER or incremental net monetary benefit (INMB)	Incremental cost per annum
Sensitivity analysis	Probabilistic and deterministic	Probabilistic and deterministic

Key: BIA – budget impact analysis; CEA – cost-effectiveness analysis; HSE – Health Service Executive; ICER – incremental cost-effectiveness ratio; N/A – not applicable; QALY – quality-adjusted life year.
† The time horizon for the analysis may be dependent on availability of input parameters to support estimates of clinical effectiveness and safety over longer time horizons.
‡ Or the discount rate that applies at the time of publication.

1.7.1. Cost-effectiveness analysis

An economic evaluation will be conducted to estimate the cost-effectiveness of metabolic surgery in patients with obesity and T2D compared with usual care (that is, lifestyle intervention, best medical therapy and patient education and support) in accordance with national HTA guidelines and Consolidated Health Economic Evaluation Reporting Standards (CHEERS) reporting guidelines.[15, 44]

Economic evaluations that measure effectiveness of an intervention in life-years gained (LYG) are commonly referred to as cost-effectiveness analyses (CEA), whereas those measuring the effectiveness of an intervention in terms of quality-adjusted life years (QALYs) are called cost–utility analyses. CUA is the preferred type of economic evaluation for public healthcare interventions, such as metabolic surgery.[15] A CUA will be conducted from the perspective of the HSE in a hypothetical patient cohort over a lifetime period. The primary outcome of the CUA will be an incremental cost-effectiveness ratio (ICER) expressed in terms of the mean cost per quality-adjusted life year (QALY) gained. A discount rate of 4% will be applied to costs and outcomes occurring after the first year. There is currently no willingness-to-pay (WTP) threshold for non-pharmaceutical technologies in Ireland. However, WTP thresholds of €20,000/QALY and €45,000/QALY are generally employed to interpret cost-effectiveness.

The appropriate model structure will be informed by the results of the systematic review of cost-effectiveness analyses. A provisional list of model inputs and potential data sources are presented in Appendix 2, Table 1.

Estimates of relative effectiveness generated from the systematic review of clinical effectiveness and safety will be used to populate the economic model. Where possible, model inputs will be informed by national literature and data sources. In the absence of robust national data, data from countries considered generalisable to the Irish setting may be a potential source of model input values. Where data from the literature is lacking or subject to considerable uncertainty, the expert input of the EAG will be required to inform suitable model input parameters.

A comprehensive sensitivity analysis will be conducted to deal with uncertainty in the model to determine the impact on the ICER. Uncertainty regarding individual parameters will be investigated through probabilistic sensitivity analysis. Key drivers will be identified using deterministic sensitivity analysis. Based on the findings of the systematic review of CEA and input of the EAG, additional scenario analyses will be constructed (for example, increasing/decreasing the T2D remission rate).

1.7.2. Budget impact analysis

Although the initial budget impact of introducing a metabolic surgery programme for patients with T2D and obesity is likely to be substantial owing to high procedural costs, these may be partly offset by savings due to reduced costs associated with the ongoing management of T2D. The BIA will estimate the incremental direct cost to the HSE associated with the introduction of a metabolic surgery programme over a five-year time horizon.

Estimates of budget impact will be particularly sensitive to uptake rates for surgery. Many patients with obesity and T2D may not require metabolic surgery for disease management, may not be suitable candidates for surgery or may not wish to undergo surgery. A range of scenarios reflecting judgements on uptake rates for surgery will be considered in the BIA. For parameters unsupported by published evidence, input from the EAG will be required to inform plausible values.

While the proposed study will be carried out from the perspective of the publicly-funded health and social care system, an understanding of the overall (that is, public and private hospitals) current level of activity may be useful in generating estimates of future demand if access to metabolic surgery is established within the public sector. However, there would likely be considerable uncertainty surrounding these estimates, given that many patients who may require the surgery cannot afford to access services privately. Additionally, data from the National Treatment Purchase

Fund and Cross Border Directive may be requested in relation to the number of procedures carried out in Irish private hospitals or in another EU country, respectively, funded by the HSE to inform estimates of future demand for the surgery.

1.8. Organisational considerations

The assessment of necessary organisational changes will be carried out in accordance with the EUnetHTA Core Model.[45] The current clinical care pathway for patients with T2D and obesity will be described, in addition to any anticipated changes in the organisation of care as a result of the addition of metabolic surgery to the clinical care pathway and the impact on existing activities. The impact of the provision of metabolic surgery on various types of resources (such as equipment and supplies, facilities, and human resources) and any additional associated healthcare interventions (for example, additional patient education and support services or dietetic services) will be considered. Estimated resource use (with consideration to the size of the eligible population) will be used to inform the budget impact analysis.

1.9. Ethical considerations

The ethical analysis will consider key social and morals norms and values relevant to metabolic surgery. Key ethical issues outlined in the EUnetHTA Core Model will be used to guide the ethical analysis.[45]

Potential ethical issues may include issues related to:

- potential inequities in access between metabolic and bariatric surgery care pathways
- criteria for patient prioritisation (comorbidity-based vs BMI-based eligibility criteria) and the impact on access to care
- informed consent (procedure selection and long-term lifestyle changes)
- the availability of medically-indicated body contouring surgery following sustained weight loss
- adequate access to post-operative care
- impact of delays accessing surgery (early versus late utilisation)
- inequalities in outcomes of bariatric/metabolic surgery according to socioeconomic status (cultural and income differences)
- medical tourism in bariatric/metabolic surgery (lack of access for those who cannot afford private healthcare if metabolic surgery is not provided).

1.10. Conclusion

A metabolic surgery programme may represent a clinically and cost-effective intervention to reduce the burden of T2D on health services and the economy. This HTA is intended to inform a decision on whether or not to introduce a metabolic surgery programme for the treatment of T2D in adults with obesity in the Irish public healthcare system. Considering the anticipated high costs and potential benefits, a HTA comprising systematic reviews of clinical- and cost-effectiveness, an economic evaluation, BIA, organisational considerations and ethical analysis will be conducted to inform a decision to provide metabolic surgery services within the T2D clinical care pathway.

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Appendix 1

Table A1: Clinical manifestations of post-bariatric/metabolic surgery nutritional deficiencies*†

Deficiency	Clinical manifestation
Iron	microcytic anaemia
Vitamin B12	megaloblastic anaemia neurologic abnormalities (unexplained sensory and/or motor and gait symptoms)
Vitamin D (and calcium)	bone demineralisation osteoporosis fracture
Vitamin A	visual problems such as xerophthalmia and loss of night vision
Vitamin E	peripheral neuropathy muscle weakness ataxia
Vitamin K	easy bleeding
Thiamine	ataxia, confusion and coma (cerebral beriberi or Wernicke's encephalopathy) neuropathy and neuritis especially in lower limbs (dry beriberi) cardiac insufficiency with tachycardia and respiratory symptom (wet beriberi) Korsakoff's psychoses
Zinc	poor wound healing taste changes glossitis hair loss
Copper	anaemia leucopoenia thrombocytopenia neuromuscular abnormalities
Selenium	chronic diarrhoea metabolic bone disease unexplained anaemia unexplained cardiomyopathy
Vitamin B12, thiamine, copper or vitamin E	myeloneuropathy

*Clinical manifestations of post-operative nutritional deficiencies in patients undergoing bariatric/metabolic surgery according to the British Obesity and Metabolic Surgery Society (BOMSS) and European Association for the Study of obesity (EASO) guidelines.[31, 32]

† Not an exhaustive list.

Appendix 2

Table A2: Model inputs and data sources*

Model Input	Description of model input	Data sources
Costs	Healthcare costs incurred by the HSE to deliver bariatric surgery or usual care: ▪ procedure costs ▪ hospital admissions ▪ day cases ▪ outpatient appointments ▪ emergency department attendances ▪ medication costs ▪ follow-up consultations (primary care and specialist services).	HSE, HIPE, PCRS, DPS
Clinical outcomes	▪ change in BMI ▪ changes in HRQoL, ▪ early complications (<30 days) ▪ late complications ▪ number of revision operations (minor and major) ▪ T2D remission/relapse ▪ cardiovascular events (e.g. stroke, MI) ▪ diabetes-related complications (e.g. amputation, ESKD requiring dialysis or kidney transplant) ▪ mortality.	Systematic literature review
Transition probabilities	▪ remission of T2D ▪ persistent/relapsed T2D ▪ mortality.	International literature
Utilities	QALY values for health states	International literature
Demographic Information	Age Gender Prevalence and incidence	Central Statistics Office, Healthy Ireland Survey
Uptake	Scenario analysis	International literature, expert opinion

Key: BMI – Body mass index; DPS – Drugs payment scheme; ESKD – End-stage kidney disease; HIPE – Hospital in-patient enquiry; HRQoL – Health-related Quality of life; HSE – Health Service Executive; PCRS – Primary care reimbursement service; QALY – quality adjusted life year.
*This list is not exhaustive and only includes some of the most common model inputs required.

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