NETSCC, HTA

17 January 2012

1. Project title

SurgiCal Obesity Treatment Study (SCOTS)

3. Planned investigation

3.1 Research objectives

The SurgiCal Obesity Treatment Study (SCOTS) will establish the clinical outcomes and adverse events of different bariatric surgical procedures, their impact on quality of life and nutritional status, and the effect on co-morbidities in both the short and long term in a cohort of over 2000 patients.

Specific objectives:

To establish in a cohort of obese patients who are undergoing bariatric surgery:

1. All cause and cause specific mortality over a mean of 10 years since bariatric surgery.

2. Incidence of cardiovascular disease, cancer and diagnosis of diabetes over a mean of 10 years since bariatric surgery.

3. Incidence of acute and chronic postoperative complications. Acute complications, defined as up to three months post surgery, will include surgical site infection; chronic complications will include revisional surgery, plastic surgery and chronic pain.

4. Change in health related quality of life, anxiety and depression over time pre- and post-operatively for a mean of 10 years from date of bariatric surgery.

5. The micronutrient and weight status pre and post-operatively for a mean of 10 years since bariatric surgery.

6. The glycaemic control, lipids, blood pressure, medication prescription, and rate of diabetes complications (microalbuminuria and renal disease, retinopathy and foot ulceration) in those that have pre-existing diabetes or develop diabetes during a mean of 10 years follow up since bariatric surgery.

   All the above objectives are due to be achieved by July 2026
   (Start Jan 2012, 2 years development, 5 years recruitment finishing Jan 2019, mean 10 year follow-up finishing July 2026)

3.2 Existing Research

The efficacy of bariatric surgery for large scale, long term weight loss is well established[1]. However, many questions remain over the long term benefits of that weight loss for health, particularly when accounting for the potential complications of surgery. Given that the proportions of the population who are obese is increasingly rapidly, further information is required as to who benefits most from bariatric surgery and what the best pathways of care for delivering bariatric surgery are.

Clinical Outcomes

There are some pre-existing data on clinical outcomes with 10 year mortality rates being the best known. Overall mortality was found to be 29-40% lower in patients receiving bariatric surgery compared to BMI-matched subjects not receiving surgery[2;3]. Although impressive, these figures are from studies which initially recruited in the 1980s and early 1990s and further work is required to update the mortality rate in the current population, now that primary prevention measures for

cardiovascular disease, such as statins and ACE-inhibitors, have lowered the risk of premature mortality in at risk subjects, including those who are obese or have diabetes.

Diabetes improvement post bariatric surgery has also been of interest. Dixon et al conducted a randomised controlled trial of laparoscopic gastric banding in patients with newly diagnosed type 2 diabetes resulted in a 73% remission rate after 2 years [4]. Similar results have been shown for gastric bypass using meta-analysis of heterogeneous, mainly retrospective, cohort studies[5]. Whether remission is maintained beyond the first few years post surgery is unknown. However, the main outcomes of interest are the longer term effects on the development of diabetes complications such as retinopathy, nephropathy and cardiovascular disease and those are not established.

The effect of bariatric surgery on cardiovascular outcomes has not been ascertained. It is known that HDL cholesterol is less likely to be low and hypertriglycerideamia is less common after surgery[6], as expected by a procedure which will reduce intra-abdominal adiposity and thus insulin resistance, but a reduction in cardiovascular events has not been shown. Hypertension, which would be presumed to decrease, in fact shows no difference 8 years post surgery, once the initial antihypertensive effects of acute weight loss in the first few years post-surgery are accounted for[6]. Many have used cardiovascular risk factors measured during the acute weight loss phase, applied a population based cardiovascular risk score and stated a reduction in cardiovascular risk; this is of course a flawed use of such a score based on temporarily reduced cardiovascular risk factors. So, while the general population and the majority of physicians may assume that weight loss with bariatric surgery reduces the risk of a cardiovascular event, this is currently unknown.

What is established is that health related quality of life (HR-QoL) is increased compared to pre-operative levels[7]. When patients who decide to proceed to surgery are compared to those who opt for non-surgical treatment only, the baseline HR-QoL is far lower in those who select surgery, showing at least a perception of reduced quality of life in these individuals[8]. To what extent the improvements seen in HR-QoL correlate with weight loss, complications and clinical outcomes is not known.

The complication rates of bariatric surgery are poorly reported in the literature, leading to polarised views on their true incidence. Mortality rates in the first year post surgery have been reported as being similar to those of BMI-matched controls[3]; however, the same results may not be found today due to the decreased mortality rates as a result of primary preventative. There is little report of specific wound complications and re-operation rates, with a general belief that the low rates reported by the few studies releasing this data would not be replicated in routine practice.

The bariatric surgery pathway – evidence for pre and post operative care

Despite being a substantial proportion of the overall cost of a bariatric surgical procedure, there is little evidence to guide as to the most efficacious pre- and post-operative follow-up and monitoring. Pathways vary across the UK and throughout the world, with varying pre-operative and post-operative dietary advice, access to psychology, and filling of gastric bands. This lack of evidence has made it impossible for agencies such as NICE and SIGN to give any guidance in this area. In the absence of evidence as to the true risk of nutritional deficiency with each procedure type, the current nutritional monitoring guidance has been cautious and based largely on expert opinion.

The major unanswered questions for bariatric surgery are not only what clinical outcomes can be achieved, but how these are best achieved, in the safest, most cost effective manner. It may be that different pre-and post-operative care pathways work best for different patient groups. It is also important to know which patient groups are most likely to gain the maximum absolute benefit: for example, is it the younger, lighter patients recently diagnosed with diabetes, or the older severely obese individual with established diabetic nephropathy? The full benefits of bariatric surgery may accrue over many years. Given the scale of the obesity epidemic, it is unlikely that bariatric surgery will be available for all who fit the current criteria and these will need to be refined to provide the maximum benefit and cost efficiency.

A large prospective cohort study collecting comprehensive outcome data, including weight, clinical outcomes and surgical complications, from a variety of sources in the NHS and private sector, each using slightly different selection criteria, pre-

operative care and post-operative long term follow up regimes, will provide the wealth of data required to answer these important questions. Not only would such a study ascertain the true complication rate from routine bariatric surgery in the UK and the effects on clinical outcomes such as cardiovascular events, diabetes complications and cancer incidence, but it would help determine which pre-operative care and follow-up was most effective and which patient groups had the greatest long-term clinical benefits, thereby leading to significant cost-benefits. These data could then be directly applied to the writing of evidence based clinical guidelines for bariatric surgery.

3.3 Research methods

We plan to conduct a prospective cohort study of patients undergoing bariatric surgical procedures in Scotland recording mortality, morbidity including diabetes complications and cardiovascular disease, nutritional deficiencies, quality of life and surgical complications, both immediate and long term.

The cohort shall be populated through a clinical information system for use by bariatric surgeons in Scotland. This will supply information for research purposes through electronic data linkage with pre-existing NHS Scotland IT systems, including SCI-Store which is a database of blood results, and SCI-dc which is the database of all diabetes patients and their treatment in Scotland, in additional to providing a useful clinical tool for the recording and collation of patient data for clinical use.

A flow diagram summarising the proposal can be seen in figure 2.
The outcome measures and their sources are summarised in table 1.
The timetable for the project is summarised in figure 1.

3.4 Planned interventions

This 10 year prospective cohort study will collect data on the long term outcomes of bariatric surgery in a minimum of 2000 individuals. All patients due to have a bariatric surgical procedure in Scotland will be invited to participate - both NHS and private sector.

A bariatric surgical procedure is defined as a surgical intervention which has the primary purpose of large scale weight loss in a patient who is obese. Currently that includes gastric bypass, sleeve gastrectomy and laparoscopic gastric banding. The inclusion of emerging techniques in this definition will be decided by the steering committee.

This study will be based on data linkage of novel and existing clinical information systems in NHS Scotland.

3.4.1 Recruitment

Patients will be recruited from both NHS and private bariatric surgical practice in Scotland. They will be recruited by a member of the surgical team prior to undergoing a bariatric surgical procedure, including any significant pre-operative weight loss (such as a very low energy diet for liver shrinkage or use of an intra-gastric balloon) which is considered part of the surgical pathway. They will be asked to give fully informed consent for clinical data linkage, the use of anonymised clinical data for research purposes and to be contacted by Glasgow University by post or phone about future research and their details will be entered onto the bariatric clinical information system.

3.4.2 Bariatric Clinical Information System

The Bariatric Clinical Information system will operate as a clinical tool for use by bariatric surgical teams in the everyday management of their patients; it will provide the backbone to research data collection and data linkage with other NHS clinical data. This will be a custom-made system which will be used to record all patients who are undergoing bariatric surgery (subject to consent), will coordinate nutritional blood and weight monitoring in the community and allow details of surgery, subsequent follow-up and complications to be recorded.

In the first 18 months of the project, we will work with bariatric surgeons in Scotland to refine, and ensure completion of the clinical information system for bariatric surgical procedures in NHS and private settings. The system will be designed to maximise surgeon participation by ensuring it can generate clinical letters, audit data and statistics required for revalidation. All bariatric surgeons in Scotland are aware of this proposal and have declared an interest in using the system and contributing to the study.

The system will be designed and maintained by the Robertson Centre for Biostatistics, with full support available and a system update in year 8 (assuming a hardware/software lifecycle of around 6 years, the major update at year 8 will ensure technical compatibility for the remainder of the project, complementing the yearly IT/database maintenance plan).

Nutritional blood and weight monitoring

A major component of bariatric surgical follow-up is nutritional blood monitoring. In all of the UK, patients can have their operation in an area other than their local health board or primary care trust and this makes the transfer of blood results checked locally difficult and generally these are repeated at the surgical follow-up clinic.

We propose a system of **automated blood and weight monitoring** for patients who have undergone surgery funded by the NHS:

- Blood test monitoring will be based on SIGN guidance, which is in keeping with other guidance in this area (refs): At baseline, six months after and then annually post-operatively, FBC, Ca, Mg, Phos, Ferritin, B12, Folate, Vit D, albumin, HbA1c and CRP will be measured.
  If an abnormality is detected a full micronutrient screen will be performed: Vit A, B1, B2 and B6, C, E and K, Selenium, Zinc and Copper.

- A centrally generated blood form will be sent to the patient. They will attend their GP practice for phlebotomy and their weight will be recorded on the blood form. These blood tests will be analysed at their local laboratory and the weight entered into the local laboratory IT system.

- In Scotland, all blood test results are currently transferred from local NHS laboratory IT systems to health board central databases known collectively as Sci-store. Each Health Board's Sci-store will be interrogated for relevant blood test results for each person on the Bariatric Surgery Information System and the results will be transferred. We have met with the company who runs Sci-store for the NHS and they have given us the details required to do this.

Nutritional blood and weight results handling

A computer algorithm will decide whether to generate a blood form for a full micronutrient screen and send an urgent email alert to the relevant surgeon if weight has decreased at a rate faster than expected or if any of the blood test results are out with normal limits. The surgeon will also receive an urgent email if weight has increased significantly.

Otherwise, results will be sent to the surgeon via a non-urgent email and be available on the Bariatric Clinical Information System.

If at any stage the HbA1c is found to be ≥6.5% a letter will be sent to the patient and to the GP to arrange formal diabetes testing and follow-up.

This is summarised in the figure 2.

3.4.3 Clinical data linkage

Via the patients' unique community health index (CHI) numbers the Bariatric Clinical Information System will be linked with the following NHS Scotland Clinical Systems:

Sci-dc: a clinical information system of all patients diagnosed with diabetes in Scotland. It links GP and secondary care data, retinal screening data, podiatry data, blood results, renal and cardiovascular risk factor monitoring (BP, microalbumin, creatinine, lipids) and medications.

The Sci-dc system includes data from all but 5 of over 1000 general practices in Scotland. Recent work cross referencing the Sci-dc database to diabetes diagnosis from routine records suggests that the register is detecting 99.4% of eligible patients in Scotland.

Mortality and Morbidity Records: hospital discharge records (Scottish Morbidity Record) and General Register Office death records (held by the Information and Statistical Division of NHS Scotland). This technique demonstrates similar qualitative findings to event adjudication by endpoint committee[9].

3.4.4 Post-operative complications

A combination of patient self-report (post, online, phone) and data linkage will be used for measurement of post-operative complications.

This will take 5 forms, with overlap likely to safeguard against missing data from any one source:

1. Postoperative complications at 30 days: These will be patient reported outcomes. Patients will be contacted 30 days post-operatively and asked standard questions on superficial/deep surgical site infection; gastric-related symptoms; bodily pain, acute & chronic postoperative pain; other adverse postoperative events.

2. Hospital length of stay, 30-day mortality, readmission for further surgery and other clinically relevant adverse events (ie admissions or death) will be recorded from data linkage with NHS morbidity and mortality records.

3. If hospital discharge records show that that a patient has been admitted to hospital, or they declare such on their questionnaire, they (or their nominated contact) will be contacted by phone/post to find out if it is a bariatric surgery related complication and for a detailed complications interview.

4. A section will exist on the Bariatric Clinical Information system to document any revisional or plastic surgical procedures.
5. Patients will be asked (at the time of quality of life questionnaires) if they have had any hospital admissions related to their operation, revisional or plastic surgery and also other medical problems potentially related to bariatric surgery (e.g. gallstones or fractures).

3.4.5 Quality of life, anxiety and depression, employment status

Change in health related quality of life, anxiety and depression and employment status will be assessed by patient questionnaire pre-operatively and at 30 days, 6/12, 1, 3, 5, 7 & 10 yrs post-operatively.
This will consist of Short-form 36, EuroQoL EQ-5D and Hospital Anxiety and Depression Scale questionnaires.

During the first year of recruitment different methods of questionnaires will be piloted, namely postal and online, but also phone and text reminder systems. Patients will also be given the opportunity to request a particular method of contact. Patient incentives will not be offered at time of first recruitment, however, if return rates appear low within the first year of recruitment, or return rates decrease during the latter stages of the study, incentives may be offered to increase return rates. These would be in the order of a £20 shopping voucher for each participant.

3.4.6 Health Economics

We plan to collect sufficient data during the study to support health economic analyses of bariatric surgery procedures, including an annual question on employment status. We believe there is opportunity for many health economics related analyses (including assessment of lifetime costs of care, burden of side effects, cost per QALY from the different procedures, assessment of heterogeneity in costs and health outcomes, for example by BMI, by level of weight loss etc.) and we have the expertise within the team to do this. In particular, there will be important synergies between this team and the work being conducted around the health economic burden of diabetes in the Sci-dc data being undertaken for the Wellcome Trust funded Scottish Health Informatics Programme (SHIP). Recognising the length of the proposed study, at this stage we are requesting only modest support for health economist time to design data collection, conduct exploratory analyses and prepare future grant applications..

3.4.7 Maintaining a high rate of follow-up

The use of data linkage to pre-existing NHS records allows a large number of the outcomes to be collected even if the patient does not attend their bariatric surgical follow up or reply to questionnaire requests – these include mortality, hospital admissions and diabetes data.

The need for patient incentives will be assessed throughout the study particularly during the first year of recruitment. Funds have been requested to provide patient incentives for participating in questionnaires. We will work with patient representatives to ensure that the questionnaires and other material are as accessible and understandable as possible.

In order to ensure a high rate of recruitment, we will involve the bariatric surgeons and their teams in the initial design of the Bariatric Clinical information System so that it is practical for routine use. It is likely that bariatric specialist nurses will be initially consenting patients for inclusion and as such we propose to run information events and sponsored study days for this staff group, where we can educate and update them on the study, ensuring their continued interest. This will be coordinated via Bariatric Scotland, a group of nurses and allied health professionals in Scotland – this was co-founded by JM who is an applicant on this grant and will lead the nursing liaison. Funds will be available for private surgeons as incentive for recruitment and/or to cover administrative costs; the need for these will be assessed as recruitment commences.

3.4.7 Reference populations

We will compare outcomes with the IT based non-surgical weight management database in Greater Glasgow & Clyde (treatment seeking population with current data on 10,000 patients and 3,000 new referrals per year) which has prospective consent for research allowing data linkage for morbidity and mortality along with adjustment for smoking, deprivation, BMI, age and sex.

Standardised mortality ratios are available for a BMI matched cohort from the Scottish Health Survey.

The Scottish diabetes database allows an anonymous control group matched for key demographics to be created with prospective follow up of diabetes care and complications compared to those with diabetes who had bariatric surgery.

3.5 Planned inclusion/ exclusion criteria

Inclusion and exclusion criteria are guided by the Scottish Intercollegiate Guideline Network (SIGN) guidance, but each local health board and private surgeon has their own criteria in addition to this (e.g. patients with diabetes only). Local health board and private surgeon's criteria for bariatric surgery will be recorded at that start of the study and at any time they are updated.

It should be noted that there are no major differences between SIGN and NICE criteria for surgery. The main difference is that co-morbidities are required to be present for all patients regardless of BMI in Scotland, with NICE allowing surgery for those with a BMI >40 but no co-morbidity. However, there are few patients that do not have an obesity-related health

problem at BMI >40 (including depression) and most local PCT bariatric eligibility criteria in England require the presence of a co-morbidity or a far higher BMI than NICE dictates.

SIGN guidance:

Include this as part of the overall clinical plan for adults. Consider this following individual assessment of risk/benefit in patients with:

- BMI ≥35 kg/m^2
- presence of one or more severe comorbidities which are expected to improve significantly with weight reduction (e.g. severe mobility problems, arthritis, type 2 diabetes)

AND

- evidence of completion of a structured weight management programme involving diet, physical activity, psychological and drug interventions, not resulting in significant and sustained improvement in the co-morbidities.

New Bariatric Surgeons

Given the potential for a surgical learning curve[10], new surgeon's data will be recorded but not analysed for the primary outcome until they have performed 50 operations. Collection of this early data will provide important information on the effects of the learning curve on patient outcomes.

3.6 Ethical arrangements

Before they are entered onto the Bariatric Clinical Information System, every patient will give fully informed consent for clinical data linkage, the use of anonymised clinical data for research purposes and to be contacted by Glasgow University by post or phone about future research by the clinical team using an information sheet and consent form approved by the research ethics committee. Fully informed consent will be gained before patients participate in complication and quality of life questionnaire based follow-up.

The use of anonymised clinical information for research requires favourable ethical opinion to be gained along with the consent of the Caldicott Guardian of that data. In Scotland each health board has a Caldicott guardian who would have to approve the use of data in Bariatric Clinical Information System for research. To help streamline this process, we have had preliminary talks with the Caldicott Guardian for NHS Greater Glasgow and Clyde, Richard Copland, who has discussed with his colleagues in Scotland, and a Lead Caldicott Guardian arrangement will be organised whereby one Caldicott Guardian take responsibility for reflecting the views their colleagues.

The Clinical information system will be hosted within NHS Greater Glasgow and Clyde. Data will be transferred in anonymised format to the Robertson Centre for Biostatistics. Linkage to Sci-dc, Scottish Morbidity Records, and General Register Office death records will be done by staff at NHS Information Services Division Scotland.

We cannot foresee any risks to participants in this study.

Study documentation and data will be retained for a minimum of 5 years after the study completes (JN to comment).

3.7 Proposed sample size

Currently 230 operations are funded in NHS Scotland each year (of which approx 60 are bypass). Bariatric surgeons perform an additional 270 private procedures per year and they are already willing to commit to entering data (approx 80

bypass). Therefore 500 procedures per year are expected to be entered into the database with a belief that as numbers of people with severe obesity (BMI >40) are rising rapidly, this number will increase despite financial constraints. New surgeons' data will be entered but will not be included in primary analysis until they have performed 50 operations. From previous studies[2;3] we expect 10-year mortality of around 5% (100 deaths). This sample size will allow the mortality rate to be estimated with 95% confidence to within +/- 1% (i.e. for a 5% 10-year death rate, the 95% confidence interval will be between 4% and 6%). We will compare this mortality rate with an age-sex matched healthy population from the Registrar General of Scotland's life tables (assumed known with no sampling error). 100 deaths will be sufficient to allow us to build a predictive model for death post surgery (conventionally one requires around 10 events per prognostic covariate considered). A sample size of 2000 will easily provide adequate power for the other important outcomes under investigation (full details will be specified in the Statistical Analysis Plan which will govern all statistical activities and be agreed by the Study Steering Committee in advance of analyses). We will conduct comprehensive follow-up on the first 2000 patients recruited to the cohort study but will continue recruitment beyond this for data-linkage at minimal additional cost.

3.8 Statistical analysis

All statistical analyses will follow a comprehensive Statistical Analysis Plan which will be agreed by the Steering Committee. It is intended that the SCOTS database will become a very substantial and valuable research resource, and that both within the current research project the research questions and their statistical analysis will develop as the database grows and the surgical interventions are modified and expanded. There will also be requests from external researchers to utilise the database. The Steering Committee will play an active and experienced role in advising on the scientific proposals for the use of the SCOTS database, and facilitating the safe and secure use of the database, during the lifetime of the study, and to put in place processes that will assist in these goals after the initial study period (for example, using similar secure access protocols to bona fide researchers as per those developed for the Safe Haven record linkage centre managed by the Robertson Centre for Biostatistics).

An important goal within the funded period is a to build various predictive models to use accumulating information to predict good and bad outcomes, so that clinicians can identify treatment opportunities and make better informed intervention management decisions. Generically, these prediction models will relate potentially predictive information – both on entry into the SCOTS database on and around diagnosis, and from subsequent visits and at surgical and other treatment interventions – to outcomes of interest. The mainstay will be Cox proportional hazards time-to-event models, incorporating demographic, clinical, laboratory and life event data (e.g. hospitalisations, strokes, cancers, non weight loss surgery, and so on) as both fixed and time varying covariates. The influence of missing data on the robustness of predictions in these models will be assessed. Importantly, a hierarchy of models will be built, with ease of use for the clinician in mind, from very simple models built from easy to obtain information, through to more complex models with very many and possibly some difficult and/or expensive to measure covariates.

3.9 Proposed outcome measures

Primary Outcome

10 year mortality – recorded via data linkage (using CHI number) with General Register Office death records (held by the Information and Statistical Division of NHS Scotland).

Secondary Outcomes
In the 10 years following bariatric surgery:

1. Change in weight/BMI from pre-bariatric surgery weight
2. Rate of incident type 2 diabetes
3. Incidence of fatal and non-fatal coronary heart disease, cardiovascular disease, cancer and fractures
4. Incidence of incidence of nutritional deficiencies
5. Change in incidence of depression and anxiety compared to baseline level pre-operatively
6. Incidence of complications immediately post-operatively and the need for readmission for revisional procedures
7. Change in health-related quality of life compared to baseline level pre-operatively
8. Change in glycaemic control, cardiovascular risk factors, CKD, retinopathy and medications prescribed in patients with diabetes compared to equally obese patient with diabetes who did not have bariatric surgery
9. Cost of the procedure and follow-up (to inform cost-effectiveness analysis)

Outcomes, including their source and frequency of measurement, are summarised in table 1.

3.10 Research governance

This study will be sponsored by NHS Greater Glasgow and Clyde.

The Study Management Group (SMG) will consist of the principal investigator, other co-applicants, project manager and representatives from the clinical trials unit. It will be responsible for the day to day running of the trial and budget. It will meet at least 6 monthly, with more meetings initially and as required, and provide information to the steering committee as to the progress of the study.

A steering committee (SC) will be established to provide overall supervision of the study and ensure adherence to GCP. It will have an independent Chair, a patient representative (LM), and at least two other independent academics along with the principal investigator. Observers from the HTA programme will be invited to SC meetings, and all SC papers will be supplied to the HTA programme. The SC will meet at the start of the study, and annually thereafter.
RW, Clinical Lead for Bariatric surgery at an internationally recognised Centre of Excellence for Bariatric Surgery, co-founder of the National Bariatric Surgery Registry (NBSR) and investigator in the recently funded HTA BYBAND study, has agreed to chair the steering committee. It is hoped that this link will help promote uniformity and excellence in bariatric surgical data collection in the UK, via the NBSR, BYBAND and other studies.

Arrangements for sharing anonymised data

Following the example of, and with expertise from, the Scottish Diabetes Research Network Epidemiology Group we plan to make our data fully available for use in an anonymous form by other researchers. We will ensure that the initial patient consent procedure covers the sharing of data for future research by external researchers. We will follow the NHS code of Practice on Protecting Patient Confidentiality issued by NHS Scotland. We will require a written request/proposal for data to be made to our steering committee and we will endeavour to respond within 4 weeks. The steering committee will need to be satisfied that all ethical approvals are in place and that funds are available to cover any costs of collating the necessary data. Regular reports of progress with the research will be required. The steering committee should receive any draft manuscripts using our data at least four weeks before the proposed submission data. The collaboration with the SCOTS study group should be acknowledged in the manuscript, normally by authorship stating the research workers "on behalf of the SCOTS group".

The access to the cohort study for bona-fide external researchers will be mediated through the soon to open 'safe haven' facility at Glasgow University, providing secure and confidential access to linked NHS data resources (directed by one of the applicants, Professor JN, funded through the recent Scottish Academic Health Sciences Collaboration)

4. Project timetable and milestones

The Project timetable and milestones are outlined in figure 1 and summarised below:

Jan 2012	IT and questionnaire design in conjunction with surgeons and patient groups
Jan 2013	Apply for ethical and management approval
Jul 2013	Staggered introduction of recruitment across sites
Jan 2014	Recruitment begins at all sites
Jan 2019	Recruitment ends
Jul 2026	Follow-up ends

Outcomes timetable:

Jan 2015	Methods paper: Outlining the methods used in the study including the IT based nutritional blood monitoring and the dataset being collected.
Jan 2020	1 year postoperative complications including mortality.
Jan 2021	2 year diabetes, quality of life, and nutritional outcomes including, glycaemic and cardiovascular risk factor control.
Jan 2024	7.5 year (mean follow-up) outcomes including mortality, CVD events, incident diabetes, diabetes outcomes, quality of life, surgical complications, fractures, nutritional deficiencies.
Jul 2026	10 year (mean follow-up) outcomes including mortality, CVD events, incident diabetes, diabetes outcomes, quality of life, surgical complications, fractures, nutritional deficiencies.

Outcome	Method of collection	Timing of collection												Comparator
		Pre-op	1/12	6/12	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y	
Demographics															
Age/Sex	Surgical team	√													
Clinical															
Date of operation	Surgical team	√													
Type of operation		√													
Weight	Surgical team/ GP	√		√	√	√	√	√	√	√	√	√	√	√	Baseline BMI
Height	Surgical team	√													
Nutritional bloods	GP results	√		√	√	√	√	√	√	√	√	√	√	√	Reference intervals/ baseline results
Medications	Patient questionnaire	√		√	√		√		√		√			√	
HR Quality of life															
SF36	Patient questionnaire	√	√	√	√		√		√		√			√	Baseline results
EQ-5D		√	√	√	√		√		√		√			√	Baseline results
Employment		√		√	√		√		√		√			√	Baseline results
Clinical events															
Mortality - all cause CVD mortality Cancer mortality CVD events total CVD events fatal CVD events non-fatal CHD events total CHD events fatal CHD events non-fatal Malignancy - all Malignancy by type Malignancy fatal Malignancy non-fatal Fractures - by type	NHS information services division (ISD) data linkage	Continuous routine data collection by NHS Scotland													BMI, age, sex, smoking, deprivation matched control group
Length of stay	Patient questionnaire (phone)		√												

Outcome	Method of collection	Timing of collection												Comparator
		Pre-op	1/12	6/12	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y	
Surgical complications															
Surgical site infection	Patient questionnaire (phone)		√												
Gastric-related symptoms			√												
Bodily pain			√												
Acute post-op pain			√												
Chronic pain	Patient questionnaire	√		√	√		√		√		√			√	Baseline results
Related readmission	Data linkage with ISD	Continuous routine data collection by NHS Scotland													
Physchological															
HADS 14 items		√		√	√	√	√		√		√			√	Baseline results
Expectation of surgery		√													Baseline results
Diabetes outcomes															
Lipids Blood pressure HbA1c Cardiovascular medications Diabetes medications Retinopathy Foot complications	Data linkage with Sci-DC national diabetes registry	Continuous routine data collection by NHS Scotland													Matched control group from Sci-DC (BMI, age, sex, smoking, duration diabetes, baseline treatment, HbA1c, DepCat)
Development of diabetes	Sci-DC/HbA1c monitoring	Continuous routine data collection by NHS Scotland													Matched control group

Table 1. Outcome matrix including method and frequency of collection and available cohorts for comparison.

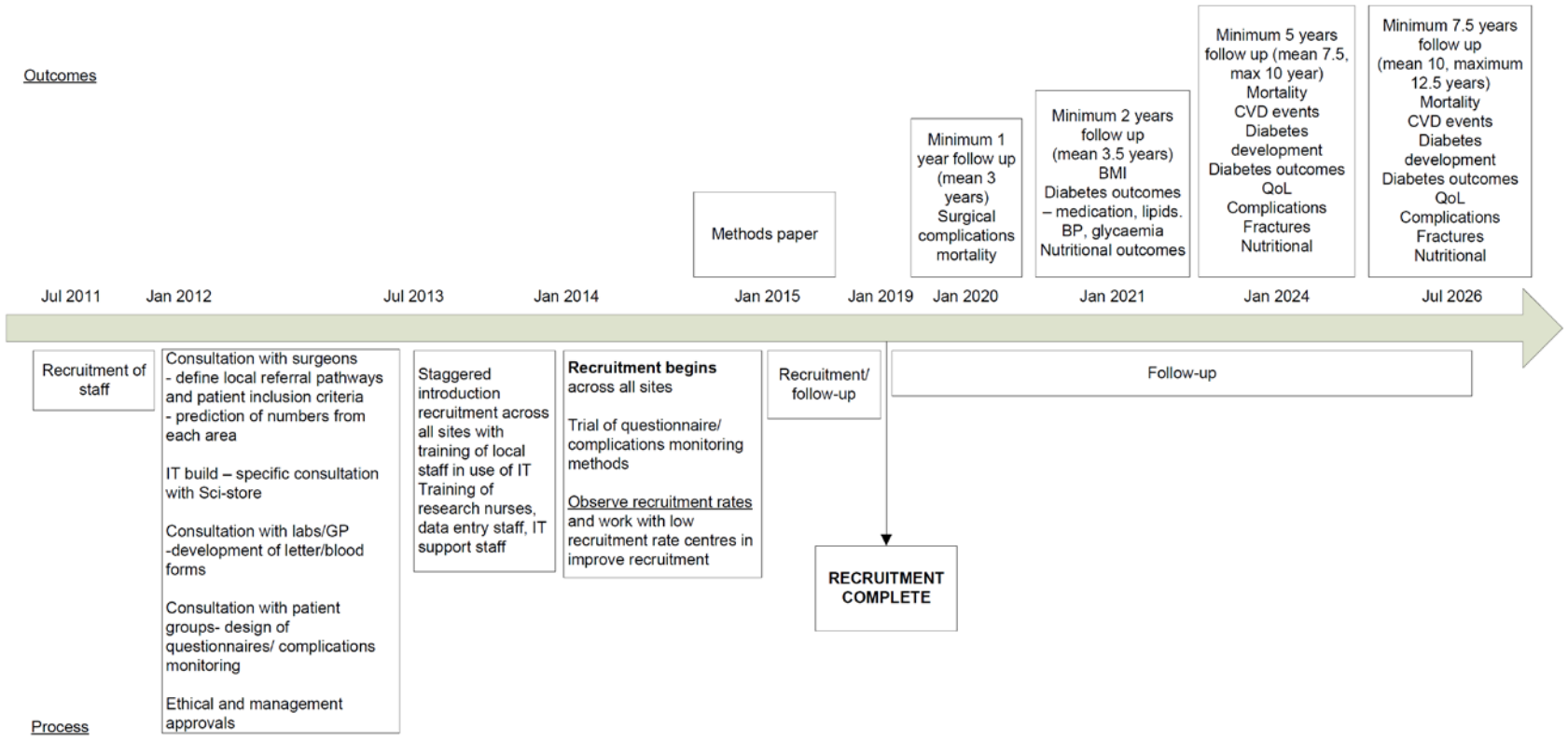


Figure 1. Project timetable and milestones

5. Expertise

JL *(Specialist interest in management of complicated obesity, obesity epidemiology and micronutrient assessment, and co-author of SIGN obesity guidance on bariatric surgery)*
Principal investigator, chair of trial management group, member of trial steering committee recruitment, study design, lead for project management, staff training, data collection, analysis and publication.

RL (*Expert in diabetes epidemiology and diabetes in pregnancy*) Chair of the SDRN epidemiology group. DR Lindsay is involved in a number of projects using the SCI-dc national diabetes dataset and is well placed to facilitate the long term follow up of the cohort for diabetes outcomes.

ML *(Expertise on obesity and its management; co-author /advisor for many clinical guidelines on Obesity, Diet composition and Diabetes, including SIGN, Diabetes UK, New Zealand, Malta, CDC, WHO; 25 years clinical trials experience)* will provide guidance on the application of results to clinical practice alongside providing expertise in conducting the study.

JB (*Principal Research Fellow/Reader*), expertise in surgical epidemiology, management of clinical/surgical cohort studies & measurement of surgical outcomes (awarded MRC Fellowship to investigate surgical adverse events). Research interests include chronic post-surgical pain, surgical/healthcare-associated infection & psychological predictors of recovery. Contribution to study: epidemiological design & outcome measurement.

DB *(Experienced Bariatric Surgeon and Chair of the Scottish Bariatric Surgeons' Group)* will lead coordination and liason with bariatric surgeons and provide expertise on changing techniques and new procedures, as well as providing data from his own NHS and private patients.

NS (*Expert in CVD, diabetes and obesity trials and epidemiology*) chaired the treatment subgroup of SIGN obesity guideline and is a member of SDRN epidemiology group. He also chaired the programme committee for Diabetes UK annual meeting 2010 and is on the European Association for Study of Diabetes programme committee for 2011. Professor Sattar helped with study design and is well placed to input on several aspects of study. He will be member of study management committee.

AB is an experienced health economist that leads a growing Health Economics and Health Technology Assessment team at University of Glasgow. He has extensive experience of developing health economic models from patient-level data. With Dr Robert Lindsay, he is leading a programme of work around burden of diabetes in Scotland as part of the Scottish Health Informatics Programme. Professor Briggs will take responsibility for leading the health economic aspects of the SCOTS proposal and work to ensure that SCOTS provides an outstanding resource to support future health economic analyses.

JM *(Specialist interest in patient support and information in bariatric surgery and experienced tissue viability nurse)* will help Dr Bruce develop the patient questionnaires, working with service user groups. She shall also supervise the complications questionnaire data collection and liaise with bariatric surgical nurses and allied health professionals during the set up of the study and throughout to maximise interest, recruitment and completion.

JN is an experienced clinical trialist and medical statistician with over 20 years experience of the design, conduct, analysis and reporting of major medical projects, including landmark clinical trials. He will lead the input of the Robertson Centre for Biostatistics, which has a reputation for in particular the creation and maintenance of large, international registries for various cardiovascular diseases.

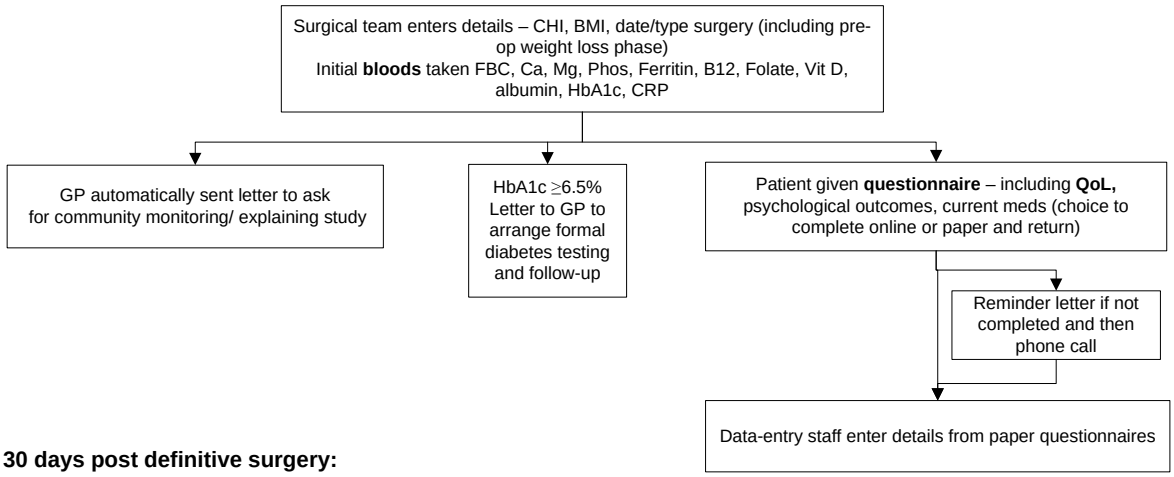
6. Service users

As far as possible we will uphold the principles embodied by NIHR INVOLVE in relation to user involvement in research, to provide training and support, negotiated roles, time and equitable access for service users involved in this study. We will be involving service users in the design of the study, in particular to advise on the burden to patients and on material and resources that will be given to potential patients. Mrs AS is chair of the West of Scotland bariatric surgery patient support group and has had bariatric surgery herself and will lead the service user involvement, with input from other members of the group. We will also include a service user, LM (a patient who has had bariatric surgery) on our Steering Group.

Figure 2

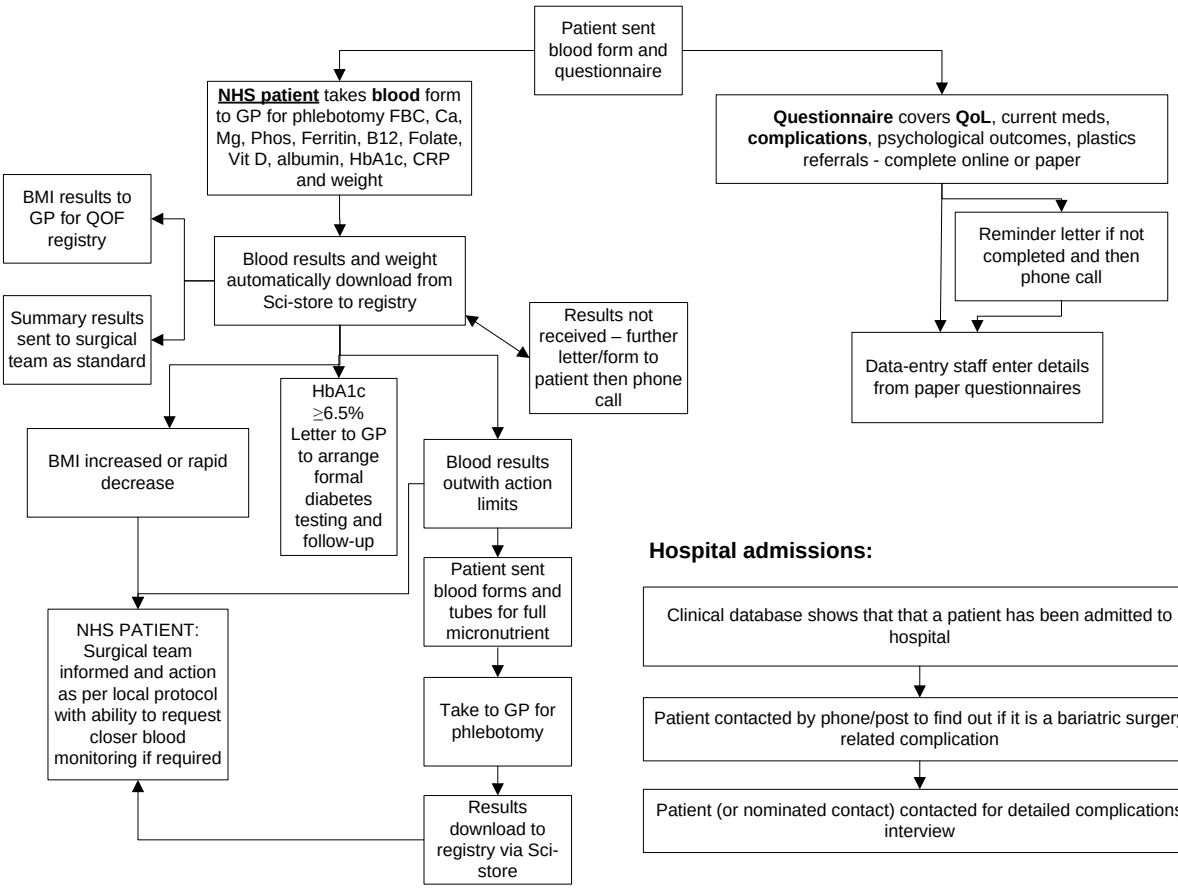
SCOTS: SurgiCal Obesity Treatment Study

Baseline – Prior to operative weight loss (including pre liver-prep diet or balloon phase):



30 days post definitive surgery:

6/12 post definitive surgery and annually thereafter:



Hospital admissions:

9.

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