Appendix 1. Secondary Outcomes

Unless stated otherwise, the secondary outcomes listed below will be assessed at 52 and 104 weeks.

Anthropometric Outcomes

- Weight (kg), from which these secondary outcomes will be derived (also at 16 and 32 weeks):
  - Absolute change in weight (kg) from baseline
  - Relative change in weight (%) from baseline
  - Proportion of participants reaching weight loss of ≥5%, ≥10% and ≥15%
  - 104 weeks only: Proportion of participants maintaining weight loss of ≥15% among those who lost ≥15% at 52 weeks
- Height (cm), from which this secondary outcome will be derived:
  - Change in BMI (kg/m^2) from baseline
- Waist circumference (cm)

Obesity-related co-morbidities and their treatments (General)

- King's College Obesity Staging System assessment (a system to assess multiple co-morbidities related to obesity and their severity, see Appendix 1)
- Quality of life (EQ5D)
- Impact of Weight on Quality of Life-Lite (IWQOL-Lite)
- Patient Health Questionnaire-9 (PHQ9)

Obesity-related co-morbidities and their treatments (Prediabetes/Diabetes)

- HbA1C
- Proportion of participants with normoglycaemia (defined as HbA1C <42.0 mmol/mol without glucose lowering medications)
- Proportion of participants with prediabetes (defined as HbA1C 42.0-47.9 mmol/mol without glucose lowering medications)
- Proportion of participants with diabetes (defined as HbA1C ≥48 mmol/mol or on glucose lowering medications)
- Dose, class of medication, and number of agents for diabetes
- Monitoring of microvascular complications for patients with diabetes [Albumin-Creatinine Ratio (ACR)]

Obesity-related co-morbidities and their treatments (Hypertension)

- Blood pressure
- Proportion of participants with hypertension (defined as patients on antihypertensive medications or systolic blood pressure>140mmHg)
- Dose, class of medication, and number of agents for hypertension

Obesity-related co-morbidities and their treatments (Obstructive Sleep Apnoea)

- Epworth score for all participants to determine levels of daytime sleepiness

- Stop Bang questionnaire for all participants to identify undetected OSA - it will be administered by research team or taken from medical notes
- Proportion of participants on CPAP
- CPAP pressures for patients on variable pressures CPAP
- Apnoea Hypopnea Index (AHI) for participants with sleep apnoea who cannot tolerate CPAP or for participants on fixed pressures CPAP
- Oxygen desaturation index for participants with sleep apnoea who cannot tolerate CPAP or for participants on fixed pressures CPAP

Obesity-related co-morbidities and their treatments (Dyslipidaemia)

- Lipids
- Dose, class of medication, and number of agents for dyslipidaemia

Number of participants referred for other obesity intervention

- Number of participants referred to Tier 4 for bariatric surgery over the 104 weeks study period

Direct healthcare cost

- Frequency and cost of contact with General Practitioner (GP) (type and duration of contact will be recorded to enable use of Tariff prices from http://www.pssru.ac.uk/project-pages/unit-costs/2016/index.php?file=full to calculate accurate costings – accessed 21/07/2017)
- Frequency and cost of contact with Healthcare Professionals (HCP) (type and duration of contact will be recorded to enable use of Tariff prices from http://www.pssru.ac.uk/project-pages/unit-costs/2016/index.php?file=full to calculate accurate costings)
- Frequency of admissions, length of stay and cost of admissions to the hospital
- Frequency and cost of outpatient appointments with the hospital
- Prescription medication costs
- Health Service and Resources Use Questionnaire (HSRUQ)

Budget impact of Specialist Weight Management Service

- Cost of the proposed LIRA 3mg (as per protocol - e.g. actual dose taken = number of days taking study drug x daily cost of drug, or cost of total amount of study drug used)
- Cost of visits to clinician for assessment and medication prescription during Specialist Weight Management Service programme
- Cost of visits to dietician during Specialist Weight Management Service programme
- Cost of visits to psychologist during Specialist Weight Management Service programme
- Cost of physical activity physiologist/physiotherapist during Specialist Weight Management Service programme (if applicable)

- Cost of Multidisciplinary Team (MDT) discussion in Specialist Weight Management Service
- Cost of blood tests in Specialist Weight Management Service
- Cost of consumables and goods
- Cost of referral into Tier 4

Estimated cost-effectiveness of treatment over 2 years

- Length of treatment with LIRA 3mg
- Daily dose of LIRA 3mg (based on actual doses taken)

Safety/adverse events

- Gastrointestinal symptoms (nausea, vomiting)
- Overall hypoglycaemia rate
- Overall AE/SAE rate
- Rates of severe hypoglycaemia
- Heart rate
- Blood pressure

Treatment satisfaction

- Treatment Satisfaction Questionnaire for Medication (TSQM)

Compliance of patient with the treatment and patient related outcomes

- The number of participants who did or did not attend at least 70% of the scheduled appointments with the Specialist Weight Management Service (completers)
- The number of participants who had to stop treatment with LIRA 3mg because of adverse effects
- The adherence of participants with the LIRA 3mg (monitored through specific questionnaire and return of used pens)
- The number of participants who stopped LIRA 3mg at 16 weeks after randomisation
- The number of participants who stopped LIRA 3mg at 32 weeks after randomisation
- The number of participants who stopped LIRA 3mg at 52 weeks after randomisation
- The number of participants who completed 52 weeks of the Specialist Weight Management Service programme despite stopping LIRA 3mg at 16 weeks
- The number of participants who completed the 52 weeks of the Specialist Weigth Management Service programme despite stopping LIRA 3mg at 32 weeks
- The number of participants in the treatment group who had to stop treatment with LIRA 3mg because of side effects
- The number of participants started on anti-obesity drugs

Physical activity assessment

- International physical activity questionnaire (IPAQ- Long Form)