NHS
Health Research Authority

FULL TITLE:

Evaluation of models of care to provide national access to anti-obesity medication in England

SHORT TITLE:

NEWA (National Evaluation of Weight-medication Access)

Version 1.3 – 7th January 2026

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This protocol has regard for the HRA guidance and order of content

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AMENDMENT HISTORY

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made

STUDY SUMMARY

Study Title	Evaluation of models of care to provide national access to ant-obesity medication in England
Internal ref. no. (or short title)	National Evaluation of Weight-medication Access (NEWA)
Study Design	A mixed methods study involving quantitative, qualitative and health economic approaches. Descriptive and cross-sectional study (objective 1) Interrupted time series study (objective 2) Repeated measures cohort study (objectives 2-4) Qualitative study (objectives 5-6)
Study Sample/Participants	Patients eligible to receive NHS Tirzepatide (Mounjaro) treatment for weight loss (objective 1) Patients receiving NHS Tirzepatide (Mounjaro) treatment for weight loss (objectives 2-6) ICB service providers and commissioners (objectives 4-6)
Planned Study Period	June 2025 to January 2028
Research Question/Aim(s)	We aim to evaluate the feasibility, acceptability, safety, clinical effectiveness, and cost-effectiveness of new weight management service models to provide Tirzepatide, across socio-demographic groups. This will inform future implementation and evaluation of service models to improve equity in access to anti-obesity medication.

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	FINANCIAL AND NON FINANCIALSUPPORT GIVEN
National Institute for Health and Care Research	**£1,669,778.02**

ROLE OF STUDY SPONSOR AND FUNDER

The University of Bristol will act as sponsor for this study and is committed to ensuring that research is conducted according to appropriate ethical, legal and professional frameworks, obligations and standards. The University of Bristol is also committed to meeting the commitments of Universities UK's Concordat to Support Research Integrity, 2025. Neither the sponsor (University of Bristol) nor the funder (NIHR) has any influence over study design, conduct, data analysis and interpretation, manuscript writing, or dissemination of results.

ROLES AND RESPONSIBILITIES OF STUDY COMMITTEES & GROUPS

Study Management Group: This group comprises all work package leads and researchers as well as the three PPIE leads. Its main remit is to monitor and plan ongoing research activities, to maintain connections between the wider team who are geographically distributed as well as working on separate work packages.

PPIE group: This group comprises ten members in total, three of whom act as both PPIE group leads and members of the Study Management Group. The purpose of the group is to provide lay and lived experience perspectives on all aspects of the project. See section 7.4 below for more detail.

Stakeholder group: This group is convened by the NIHR and comprises the NEWA co-Chief Investigators (KC and JP), along with representatives from the NIHR, DHSC and NHSE. The purpose of this group is to provide a connection between those enacting the Tirzepatide rollout (NHSE) and those evaluating it (NEWA), facilitated by NIHR. NHSE can inform the NEWA team about relevant aspects of the Tirzepatide rollout, and the evaluation team will provide feedback about findings to NHSE. However, NHSE will not advise on study design or research methods.

Study Steering Committee: This group will oversee all research activities and ensure adherence to standards. Group members include the study co-Chief Investigators and independent members (including an independent chair) who are independent from both the investigators and the study sponsors.

Data Monitoring and Ethics Committee: This group will safeguard the interests of study participants, ensure appropriate research governance approvals and adherence, and oversee data quality and ethical collection and handling of data. The members are independent from both the investigators and the study sponsors.

KEY WORDS: Tirzepatide, Obesity, Weight management, Evaluation

LIST OF ABBREVIATIONS

BMI	Body Mass Index
DHSC	Department of Health and Social Care
EHR	Electronic Health Records
GIP	Gastric Inhibitory Peptide
GLP1-RA	Glucagon-like peptide 1 receptor agonists
GP	General Practitioner
HRQoL	Health-Related Quality of Life
ICB	Integrated Care Board
ITS	Interrupted Time Series
ITT	Intention-to-treat
NEWA	National Evaluation of Weight-medication Access
NHSE	National Health Service England
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
PLWO	People Living with Obesity
PP	Per protocol
QALY	Quality adjusted life year
REC	Research Ethics Committee
SWMS	Specialist Weight Management Services
T3SWMS	Tier 3 Specialist Weight Management Service
WM	Weight management

STUDY PROTOCOL

Evaluation of models of care to provide national access to anti-obesity medication in England

1 BACKGROUND

Obesity (Body Mass Index (BMI) ≥30 kg/m^2), is a complex disease affecting nearly a third of adults in England, with serious health, societal, and economic consequences (Baker, 2023; Finer, 2015; DHSC, 2020; Frontier Economics, 2022). Widespread prevention and treatment strategies are urgently needed. Clinical trials have demonstrated that new medications like Semaglutide (Wegovy) and Tirzepatide (Mounjaro) are a major breakthrough, far outperforming older medications and aiding substantial weight loss when combined with behavioural interventions (Coutinho & Halpern, 2024; Wilding et al., 2021; Jastreboff et al., 2022).

Glucagon-like peptide 1 receptor agonists (GLP1-RA) are a new family of medications for weight loss. Some members of the class have activity at additional receptors such as the Gastric Inhibitory Peptide (GIP). Semaglutide, a GLP1-RA was approved by NICE in 2023 - as an adjunct to behavioural support for people with at least one weight-related comorbidity and BMI ≥35.0 kg/m^2 or 30.0-34.9 kg/m^2 and meeting criteria for referral to Tier 3 Specialist weight management services (T3SWMS) (with lower thresholds for higher risk ethnic groups) (NICE [TA875], 2023; NICE [CG189], 2023). Together with behavioural support, Semaglutide yields ~12% more weight loss than placebo (Wilding et al., 2021). Subsequently, Tirzepatide, a dual GLP1/GIP (Glucose-dependent insulinotropic polypeptide) receptor agonist was approved by NICE in 2024 (NICE [TA1026]). Tirzepatide appeared to elicit 17-18% more weight loss than placebo, suggesting it might be even more effective than Semaglutide (Jastreboff et al., 2022). Subsequently, a large-scale observational study confirmed this, observing that Tirzepatide elicited 6.9% greater weight loss than Semaglutide at 12 months, with no difference in side effects (Rodriguez et al., 2024). Based on efficacy for weight loss, therefore, Tirzepatide is now set to become the preferred medication for weight loss in the UK.

As NICE advised that Semaglutide should be prescribed only by T3SWMS (NICE [TA875], 2023; NICE [HTE14], 2023), this has significantly restricted access to this medication. Recognising the demand and need for wider access, NICE guidance for Tirzepatide has opened prescribing, in conjunction with behavioural support, to primary care (NICE [TA1026], 2024). However, the most appropriate service delivery models to optimise access to Tirzepatide and similar medications are not currently defined. To improve access to new medications, NHSE proposes four new implementation models (described in more detail below) and there is therefore a need to establish feasibility, (cost-) effectiveness, and scalability of these service models.

While short-term effectiveness and cost-effectiveness of individual obesity treatment modalities, such as Tirzepatide, are supported by trials, research on real-world health service delivery and optimal treatment combinations (e.g. medications and behavioural therapies) is lacking (Wilding et al., 2021; NICE [TA875], 2023; Hartmann-Boyce et al., 2014). Limited evidence from behavioural weight management (WM) trials suggests ‘more advantaged’ participants exhibit higher engagement and adherence (Birch et al., 2022; Ahern et al., 2016). Research is therefore needed to support equitable access to new treatments across socio-demographic groups.

GLP1-RA prescribing and monitoring are complex with emerging side effect profiles (Chao et al., 2022). It is crucial to assess the safety and feasibility of non-hospital-based service models for conducting complex assessments, prescribing, and monitoring new medications, and providing necessary training and support. Evaluating the integration of these new models with existing T3SWMS is essential.

Models of care

Based on the NHSE interim commissioning guidance (NHSE, 2025) approximately 220,000 patients in three priority cohorts will be treated over the initial three-year implementation period (starting June 2025). Priority cohort 1: BMI ≥40 kg/m^2 and ≥4 'qualifying' co-morbidities (months 1-12); cohort 2: BMI 35.0-39.9 kg/m^2 and ≥4 'qualifying' co-morbidities (months 13-21); and cohort 3: BMI ≥40 and 3 'qualifying' co-morbidities kg/m^2 (months 22-36). In all cases the BMI threshold is reduced by 2.5 kg/m^2 for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean ethnic backgrounds. Patients will be treated within one of four implementation models:

1. Community / Local based delivery model
2. General Practice delivery model
3. Specialist weight management services provision of community outreach delivery model
4. Specialist weight management services Community & General Practice shared-care model.

Each ICB will choose the model they wish to adopt. Within each model, ICBs can choose to provide wraparound care through local provision or through a centrally funded NHSE provision.

New service models can broaden access to improved obesity treatments, reducing economic and health burdens. Research is essential to effectively implement these models. Given the socioeconomic disparities in obesity prevalence, particularly among disadvantaged groups, understanding the acceptability, feasibility, and effectiveness of interventions across groups is crucial (Loring & Robertson, 2014; NICE, 2023). This evaluation will consider the feasibility, acceptability, safety, costs and outcomes of these new models, their integration with existing services, and the flexible delivery of multidisciplinary behavioural support in various healthcare settings. Identifying effective support models for different populations is a key focus.

2 RATIONALE AND AIMS

2.1 Research question/aim(s)

We aim to evaluate the feasibility, acceptability, safety, clinical effectiveness, and cost-effectiveness of new weight management service models to provide Tirzepatide, across socio-demographic groups. This will inform future implementation and evaluation of service models to improve equity in access to anti-obesity medication.

2.2 Objectives

1. Identify the socio-demographic factors associated with rates of referral, uptake and completion of service models

2. Evaluate the short-term clinical effectiveness, cost-effectiveness, and safety of different service models, including socio-demographic differences

3. Model the long-term health outcomes and costs of the different service models

4. Explore the potential cost-effectiveness of implementation initiatives to increase service uptake and adherence

5. Investigate the feasibility and safety of new service models including staff and training needs, impact on primary care, and implications for the wider WM system

6. Assess the acceptability and user experience of different service models, including behavioural support components, within different demographic groups

3 STUDY DESIGN

3.1 Design overview

This mixed methods study will incorporate quantitative and health economics components to assess service utilisation, clinical effectiveness and cost-effectiveness (see 3.1.1), and qualitative components to evaluate feasibility, acceptability and user and provider experience of service models (3.1.2). The ordering of these sub-sub-sections, and the order of research components within each, will be maintained throughout later sections in the protocol for clarity.

The project involves an initial information gathering and mapping stage that will collate details of the models of care being implemented at each ICB. This will feed into the research components described below. However, as this initial stage is based on stakeholder engagement and publicly available data, it is beyond the scope of HRA/NHS ethics. This has already been approved by the University of Bristol Faculty of Health Sciences research ethics committee (Appendix 1) and more details are provided in main study protocol (see Appendix 2, sections related to work package 1).

Table 1 below summarises the data sources and data collection methods as well as the target participant groups for all research activities relevant to HRA/NHS ethics.

3.1.1 Service utilisation, clinical effectiveness, and cost-effectiveness

Quantitative and health economics aspects of the evaluation will use pseudonymised electronic health records (EHR), a questionnaire completed by patients receiving Tirzepatide treatment, and resource use interviews undertaken with commissioners.

Electronic health records:
Pseudonymised linked primary and secondary care EHR data from the clinical practice research datalink (CPRD) will be used for five research components:

1. The assessment of service utilisation will examine Tirzepatide treatment uptake and adherence-related factors (see list of factors in section 3.4.1) among those eligible to receive treatment according to NICE guidelines (NICE [TA1026], 2024). Uptake and adherence related outcomes will be summarised using descriptive statistics and choropleth heat maps, including examining differences across socio demographic factors (age, sex, ethnicity, deprivation, etc.). We will also treat each factor as an outcome in a cross-sectional analysis employing multivariable regression to assess their associations with socio-demographic factors. The analyses will identify potential inequalities in uptake/adherence between social groups.
2. A longitudinal cohort design within a target trial framework will be used to compare the short-term effectiveness between each of the models of care, assuming models can be assigned to discrete categories. This will involve assessing the mean change in body weight (one of the primary study outcomes) among patients receiving treatment at six- and 12-month time intervals after treatment commencement compared to baseline. In light of the emerging evidence of heterogeneity of models of care between, if it is not possible to group these into discrete categories, an alternative approach will be to define a set of model attributes so that each model of care is represented by a series of binary covariates in the analysis (one for each attribute type) rather than a single categorical variable.
3. An overall assessment of clinical effectiveness will apply a natural experimental design to electronic health records of patients who receive Tirzepatide. A population-level analysis will use an interrupted time series design to assess changes in monthly population averaged body weight spanning a period before and after Tirzepatide rollout (June 2025). A patient-specific analysis will assess changes in body weight before and after commencement of Tirzepatide treatment with commencement date being specific to each patient.

4. The estimates of effectiveness from the natural experimental analyses will be compared with a counterfactual scenario (assuming no intervention effect), and the difference between observed and counterfactual time series will form the basis for calculating the overall cost-effectiveness of models of care.
5. Resource use data (e.g. GP visits for assessment & monitoring; prescriptions; hospitalisations) will be extracted from electronic patient records (from CPRD – Hospital Episode Statistics (HES) linked data). National unit costs will be used to value NHS resource use (PSSRU, 2022).

Patient questionnaire:
A questionnaire will be carried out within a repeated cross-sectional design and the data collected will be used to assess short-term clinical- and cost-effectiveness The questionnaire sections will encompass demographic information, height and weight, measures of health-related quality of life (HRQoL), along with questions about capability, labour market participation service experience (see Appendix 3).

1. An evaluation of short-term effectiveness based on repeated questionnaire responses (analogous to point 2 above for EHRs), will assess the change in HRQoL at six and 12 months compared to baseline between the different models of care. This will be analysed using both intention-to-treat and per-protocol approaches.
2. Cost-effectiveness will use HRQoL, capability, labour market participation, to determine the cost per quality adjusted life year (QALY) among patients receiving Tirzepatide treatment.

With patient consent, questionnaire responses will be linked with primary and secondary care EHRs within the CPRD system to allow relevant additional variables (deprivation, comorbidities, prior anti-obesity medication prescriptions, etc.) to be included in analyses of questionnaire data, and reduce the number of questions asked in the questionnaire thereby reducing participant burden. This will allow for appropriate confounder adjustment in analyses as well as examination of inequalities in outcomes. Linked data will also be an important part of estimating resource use related to the tirzepatide roll-out.

Resource use surveys/interviews (NHS commissioners and health professionals):
To estimate the resource requirements on capacity from non-specialist setting (e.g. primary care) and capacity requirements for specialist weight management services (SWMS), we will also conduct a resource-use survey or interview with commissioners (ICBs) and, if necessary, service providers (including GP, local T3SWMS, or digital providers as appropriate). This will explore the structure of the commissioning contracts with local NHS services and digital or other private providers. The service provider survey will explore service delivery and spillover costs of the new services for medication delivery and wraparound care. These survey results will inform health economic estimates of the resource impact of delivering Tirzepatide treatment (i.e. capacity requirements of specialist and non-specialist services). See Appendices 4A, 4B and 4C for the patient information sheet, consent form and topic guide.

3.1.2 Feasibility and acceptability of new service models

Four ICBs, each representing a service model type, will be purposefully selected as case study sites. A key feature of our proposal is a ‘researcher in residence’ approach at our case study ICB sites together with PPIE community researchers to support recruitment of underrepresented groups to the research. We will seek NHS honorary contracts for our qualitative researchers (LH, CF) to facilitate this approach, enabling our researchers to be fully embedded within case study sites and build essential relationships with clinical teams, commissioners, and local communities. PPIE community researchers will be local to each case study site (ICB) area and will also be part of our study specific PPIE group which will be set up during this time.

To address objectives 5-7, we will use a qualitative case study design to address key operational and behavioural parameters that shape the effective functioning of the new service models from the perspective of people living with obesity (PLWO) taking part in the models, and professionals delivering or managing services. This will involve:

1. Initial and follow-up semi-structured interviews with PLWO, using an optional photovoice approach
2. Photovoice workshops with PLWO
3. Initial and follow-up semi-structured interviews with service delivery professionals
4. Lightning reports with service delivery professionals.

Assessment of the feasibility and acceptability of the pilot models for both service users and providers will draw on two frameworks, namely the inner setting construct of the consolidated framework for implementation research (CFIR) and the theoretical framework of acceptability (TFA). Identity-based motivation and COM-B (Capability, Opportunity, Motivation – Behaviour) frameworks will be used to understand the impact of the pilot models on patients' health beliefs and behaviours. A particular focus here is on the notion of intra-individual change since commencing medication; this may include behavioural and lifestyle change and accompanying cognitions, and social change.

Data collected will be instrumental in informing an emerging logic model, in terms of the mechanisms by which the respective models tested in this study function. It aims to establish the feasibility and acceptability of the models and understand their impact on behaviour change.

Table 1. Data sources/collection methods and participant groups

	Patients eligible to receive treatment	Patients receiving treatment	Service providers/ commissioners
Quantitative and Health Economics			
EHRs			
Patient questionnaire			
Resource use survey/interview			
Qualitative			
Initial and follow-up semi-structured interviews			
+ optional photovoice			
Photovoice focus groups			
Lightning reports			

3.2 Data collection

3.2.1 Service utilisation, clinical effectiveness, and cost-effectiveness

Questionnaire: Patients receiving Tirzepatide treatment will be invited to participate in a series of questionnaires, the first of which will occur as close to the beginning of treatment commencement as possible (within 6 weeks) and will be considered the baseline measurement. Thereafter that cohort of patients will be invited to complete the questionnaire again at six-monthly time intervals up to, but no more than, 18 months after baseline for cohort I and up to 6 months after baseline for cohort II. The initial invitation will come via GP practices, facilitated by the CPRD Interventional Service, with follow up invitations sent by the research team.

Resource use surveys: Professionals will be given the option of completing the surveys via a structured telephone/video call with the researcher or electronically via REDCap (with any follow-up questions to clarify particular details via email or telephone). Surveys with professionals will take place once the service model has been running for at least 6-12 months to allow for any 'bedding in' that may occur in the early set-up phases.

3.2.2 Feasibility and acceptability of new service models

Data will be collected by the 'researchers in residence' (LH, CF). These are university employed and supervised researchers placed within the system that they are evaluating or researching, either virtually or via co-location. PPIE community researchers may also conduct or co-conduct interviews and/or workshops (with appropriate training) to facilitate participation from underrepresented groups. Topic guides will be developed and piloted with support from PPIE members who will also support with training of participants for photovoice. All interviews and workshops will be conducted either by telephone, online (e.g. or Microsoft Teams/Zoom) or in-person depending on participant preferences/availability. All interviews will be recorded either using the encrypted audio recording function on Microsoft Teams or an encrypted recording device.

Data collection with PLWO**:**

1. **Semi-structured interviews** will be conducted at an initial and follow-up time point (approx. 6 months apart) by the researchers in residence or a PPIE community researcher with approximately 48-50 PLWO to explore the acceptability and feasibility of the models. Participants will have the option to use photos during their interviews (see "2. photovoice approach" below). Interviews will last approximately 45-90 mins, and participants will have the option to complete the interview either over the phone, online (e.g., Teams or Zoom), or in-person. The interviews will explore the following topics
    a. **Initial interview:** explores experiences of accessing weight management medication (see Appendices 5A, 5B.i, 5B.ii, 5C.i, 5E.i, 5E.ii and 9 for more detail):
    b. **Follow up interview:** explores any changes experienced since beginning weight management medication prescription (see Appendices 5A, 5B.i, 5B.ii, 5C.ii)
2. **Optional photovoice approach for interviews**: Participants will have the option to use photographs to help facilitate the interview. Prior to the interview, those participants who opt to use photographs will have a conversation (phone/teams/in-person as per their preference) with the researcher (approximately 45 minutes) who will explain the photovoice method and provide information on the parameters and procedures for taking photographs. Participants will take photographs depicting their experience and will be asked to reflect on their photographs during interviews incorporating SHOWeD questions ('root-cause questioning') as prompts (see also Appendices 5B.iii and 5D)
3. **Workshop**: Interview participants will be invited to take part in a workshop (one per case study site), to collectively discuss emerging themes, and consented photographs. The workshops will take place either in person within the local case study site area or online depending on the preferences of the group. They will be facilitated by the researcher in residence and PPIE community researcher. The photos and themes will be presented at a community exhibition as part of our dissemination plan (see Appendices 5A and 5B.i).

Data collection with service delivery professionals**:**

Semi-structured interviews will also be conducted with 24-26 professionals delivering or managing the service models by the researchers in residence (LH & CF), to explore feasibility and safety of new service models including staff and training needs, how implementation of the model impacts staff workloads and delivery of patient care and implications for the wider WM system; Appendix 6C.i further outlines the topics these interviews will cover. We anticipate carrying out interviews with professionals approximately 6 -12 months after the Tirzepatide implementation start date in primary care (June 2025) to allow time for experience with new service models. Interviews will last approximately 60 minutes. Participants will have the option of undertaking the interview either over the phone, online, or in-person. See also Appendices 6A, 6B, 6C.ii and 6D.

To capture ongoing challenges and adaptations during the implementation process we will conduct monthly phone/Teams calls (of approximately 15 minutes in duration) with a small number of key staff involved in the delivery of the models across the four ICBs. These calls will either be undertaken 1:1 with individuals or within a group call depending on preference and availability of the professionals. The calls will follow the lightning report method; a three-step structured question format, based around the CFIR framework. Questions focus on what is working, what needs to change, and any insights participants may have. Notes collected from these calls will be recorded on a structured form (Appendix 6C.iii) from which qualitative summaries will be created for each reporting timeframe. These summaries **(lightning reports)** will outline implementation activities, barriers and facilitators, how they were addressed and any learnings. These data will be triangulated with data generated from the interviews.

Follow-up semi structured interviews (approximately 45 minutes each) with 24-26 key staff (6-8 from each case study ICB) will be carried out 12-18 months into delivery to explore key themes emerging from the lightning reports. These will be conducted by the researchers in residence (LH &CF). Field notes will also be kept by the researchers in residence to provide important information on any adaptations to services over the course of the project to aid with analysis (Appendix 6C.ii).

3.3 Study Setting

This study focuses on the implementation of Tirzepatide prescribing for weight loss in NHS primary care settings in England.

3.3.1 Service utilisation, clinical effectiveness, and cost-effectiveness

Electronic health records: CPRD data recording Tirzepatide treatment and prescribing, namely primary and secondary care records, will be derived from EMIS records from over 700 contributing practices in England (Wolf et al. 2019)

Questionnaire: This will involve participating GP practices in the CPRD interventional research service who will invite patients receiving Tirzepatide treatment for weight loss to participate. These practices will be geographically distributed throughout England. Questionnaire completion by patients will be through an online survey platform (REDCap), but will also available for completion on paper.

Resource use surveys: ICBs and, if necessary, service providers (including GP, local T3SWMS, or digital providers as appropriate) from non-specialists and specialist services (SWMS).

3.3.2 Feasibility, acceptability and impact of new service models

Based on the mapping work undertaken in the initial stage of the project, we will select four case study sites (ICBs), representing each of the four service models, for an in-depth evaluation of feasibility and acceptability, including key factors related to behaviour change in different socio-demographic groups. The sites will be purposefully selected for geographical and socio-demographic diversity and any key service-level components identified in the mapping stage. As soon as we know which sites we have

recruited, site specific information will be gathered by meeting with key staff within each site and any specific requirements needed.

3.4 Outcomes

3.4.1 Service utilisation, clinical effectiveness, and cost-effectiveness

The outcomes for service utilisation to be used in descriptive analyses and multivariable regression are defined as the number of eligible PLWO identified in electronic health records who:

- Are started on a National Health Service obesity medication pathway (based on SNOMED code)
- Decline the National Health Service obesity medication pathway (based on SNOMED code)
- Receive a first prescription
- Go beyond introductory dose (2.5 mg)
- Achieve sustained higher doses (e.g. 3+ months at 10 mg or 15 mg)
- Stop the medication (prescriptions stopped) before three months and six months
- Achieve/do not achieve a 5% weight loss at six months
- Experience an adverse reaction to the medication (based on SNOMED codes)
- Are referred to wraparound support pathway (based on SNOMED code)
- Take up/engage with wraparound support pathway

Assessment of short-term clinical effectiveness will use two co-primary outcomes: patient weight from EHRs and HRQoL from questionnaires.

The natural experimental assessment of population- and patient-level clinical effectiveness will use the time-specific average weight of patients receiving treatment over the study period.

Cost-effectiveness analysis will use three co-primary outcomes: patient weight from EHRs and HRQoL from questionnaires, and cost per quality adjusted life year (from EHR and questionnaires).

3.4.2 Feasibility, acceptability and impact of new service models

The qualitative components of the project will capture process outcomes related to implementation (including any contextual factors that may act as a facilitator or barrier) and how the models operate across different demographic groups to impact patient outcomes.

4 SAMPLE AND RECRUITMENT

4.1 Eligibility Criteria

Treatment eligibility: The eligible population to receive Tirzepatide for weight loss according to the NICE Technology Appraisal includes adults with a BMI ≥35kg/m2 (≥32.5kg/m2 for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean backgrounds) AND at least one weight-related co-morbidity (NICE [TA1026], 2024). This is estimated at 3.4 million people and due to capacity constraints, NHS England has initially defined three priority cohorts of adults (aged ≥18) who are eligible to receive treatment with Tirzepatide according to the following criteria and time frame (NICE [TA1026], 2024):

Table 2. Tirzepatide treatment eligibility criteria for initial priority cohorts

Cohort	Eligible from	BMI	Comorbidities
I	June 2025	≥40*	At least 4 out of: hypertension, dyslipidemia, obstructive sleep apnoea, cardiovascular disease, type II diabetes.
II	June 2026	≥35*	At least 4 from the above list
III	March 2027	≥40*	At least 3 from the above list

*A lower BMI threshold to be used (usually reduced by 2.5 kg/m2) for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean ethnic backgrounds

4.1.1 Service utilisation, clinical effectiveness, and cost-effectiveness

Electronic health records: All patients who have been registered with their GP practice for at least a year, have complete information on age, sex and deprivation, and meet the eligibility criteria for receiving treatment will be included in all analyses of service utilisation. The assessment of short-term effectiveness will additionally use the inclusion criterion that patients 'received treatment', defined by receiving at least three months of prescriptions.

Questionnaire: Any patient who has commenced treatment is eligible to take part in the questionnaire and will be invited to do so within six weeks of commencing treatment.

Resource use surveys: All ICBs will be eligible to take part in the resource use surveys. Within ICBs commissioners and providers (e.g. health professionals) and any other relevant informants will be eligible to take part.

4.1.2 Feasibility and acceptability of new service models

Any patient who satisfies the criteria to receive treatment and has commenced treatment is eligible to take part in interviews and/or workshops, and extra support will be provided to enable participation. We will include both those who completed at least three months of treatment with Tirzepatide and those who ceased medication within three months of starting. For the former group (treated for at least 3 months), we will aim to include participants with a range of treatment durations. Eligible patients may include individuals with physical or learning disabilities or other disabilities that impact mental capacity; as well as individuals who do not have English as their first language. This will require a flexible approach to support participation and guided by individual needs; examples include interpreter and translation support, carer support, and provision of adapted documents. See 4.4.2 consent for further detail of how informed consent will be facilitated.

Professionals will include those directly delivering the pilot services, those coordinating or managing services and those referring into the services. This may include healthcare professionals from primary care, local SWMS, or other providers and commissioners depending on model adopted and local set-up at each case study site.

4.2 Sampling and sample size

4.2.1 Service utilisation, clinical effectiveness, and cost-effectiveness

Electronic Health Records: we will initially consider all primary and secondary care records spanning the period starting two years before implementation of Tirzepatide prescribing up until the end of the study period, i.e. June 2023 to January 2028. We will require all records relating to patients who meet the NICE eligibility criteria, regardless of whether they take up Tirzepatide treatment.

We anticipate 220,000 eligible patients from all three priority cohorts across England, and about 30,000 in cohort I. Based on population coverage of CPRD estimated at 24%, this would give approximately 53,000 eligible patients in the EHR data, and over 7,000 in cohort I.

Questionnaire: The data provider (CPRD) will facilitate GP practices identifying patients who have recently begun Tirzepatide treatment and inviting all such patients to participate in the questionnaire via email or text message. GP practices will be selected with the aim of representing all models of care, as well as the nine English regions, a range of deprivation levels and both urban and rural localities. We will compare socio-demographics of questionnaire respondents (at baseline, 6, and 12 months, and, where available, 18 months) to the wider population (using service utilisation data), to identify any sociodemographic groups with lower questionnaire response rates. This will inform the need for targeted sampling with particular groups who are less well-represented. Targeted sampling strategies for identified groups will be developed in conjunction with our PPIE community researchers and PPIE group.

For HRQoL, baseline mean BODY-Q score was assumed to be 50 (out of a possible 100) with standard deviation of 10 (Dalaei et al., 2024) and correlation between repeated measures set at 0.7. Assuming an average score increase of 10 over a 12-month period, setting the equivalence limits at +/- 3 and allowing an underlying difference of up to 2 between service models, the required sample size per model is 320, hence 1280 in total for the four models. We anticipate a questionnaire uptake/completion rate of 30%. Applying this discounting rate to the sample size estimates above, we would need to recruit a total of 4267 patients for each of the priority cohorts.

Resource use surveys: We will conduct these surveys with a purposive sample of ICBs, representing all service models and will draw on our key contacts set up during the stakeholder engagement phase.

We anticipate sampling 2-3 ICBs per model (8-12 ICBs total). Within each ICB we anticipate conducting surveys with approximately four professionals depending on the service model type (e.g. one key commissioner, one General Practitioner, one local provider representative, one specialist T3SWMS), but we will tailor this to local circumstances.

4.2.2 Feasibility acceptability of new service models

We will sample two main PLWO groups at each case study site (representing each model): 1) Those who continue treatment for three months or more and 2) Those who stop treatment before three months. Within these two groups we will apply an equity lens to our sampling using the PROGRESS (Riley et al, 2019) framework to ensure that individuals from a range of socio-demographic groups are included, particularly groups experiencing more obesity-related inequalities. Recruitment of

participants into the study will coincide with priority cohort 1 and the first 6 months of cohort 2. Therefore, we will sample people at different timepoints to ensure both cohorts are included in the qualitative work. All who take part in the interviews will be invited to take part in a workshop to discuss emerging themes.

Key professionals to invite for interview will be identified through stakeholder contacts established in the initial mapping stage and by our researchers in residence based at case study sites. Interviews will be conducted at least six months after implementation to explore any adaptations that may have occurred during the early set-up phases. From this sample of professionals, we will invite key members of staff to the monthly phone/Teams calls as part of the lightning reports.

We anticipate conducting interviews with approximately 48-50 PLWO (approximately 12 per case study site) who will be interviewed twice during the study. We estimate approximately 6-8 PLWO per case study site (e.g. 24 to 32 of the 48-50 interviewees) will take part in the workshop. We anticipate conducting initial and follow-up interviews with approximately 24-26 professionals (approximately six per case study site). Sampling, however, will be undertaken iteratively, with the final sample size dependent on achieving sufficient conceptual depth across interview groups. Four to six weekly check-ins (lightening reports) will be conducted with approximately 16-24 (4-6 per site) key ICB staff involved in the roll-out of the prescribing models, who may have also participated in an interview.

4.3 Recruitment

4.3.1 Service utilisation, clinical effectiveness, and cost-effectiveness

Questionnaire: GP practices who are signed up to the interventional research service of CPRD will be asked by CPRD whether they wish to participate as a recruiting site for this study. The CPRD interventional research team will conduct a search of eligible patients receiving Tirzepatide for weight loss (based on SNOMED codes and prescriptions) at the participating GP practices. Those practices will then login to the CPRD portal to review eligibility of the identified patients. Patients that are confirmed as eligible will be sent an invitation from their GP via email or text message inviting them to take part in the questionnaire and providing a unique URL linking to the online questionnaire in REDCap. Those who decide to complete the questionnaire will have the option of being entered into a prize draw to win a £50 shopping voucher.

Resource use surveys: Professionals will be contacted and invited to take part in the resource use survey via our list of ICB contacts who have expressed interest in being contacted about the evaluation (see Appendix 1, p.11) for expression of interest form approved by University of Bristol faculty level ethics as service evaluation), and the research team's professional networks.

4.3.2 Feasibility and acceptability of new service models

Qualitative interviews and workshops with PLWO

PLWO to invite for interviews will be identified in two ways:

1) From the questionnaire of PLWO – individuals completing the questionnaire and who are located within ICBs acting as case study sites will be able to indicate their interest in taking part in a qualitative interview

Those who have indicated they are happy to be contacted about an interview will be invited to take part in a qualitative interview by the research team, using their preferred method of contact (as indicated on the questionnaire). They will be sent an invitation letter and the PIL, either via email, post or text message, depending on preference.

2) Researchers in residence will work with health professionals/service providers and community contacts including PPIE community researchers at case study ICBs to identify PLWO prescribed Tirzepatide with particular characteristics (based on the PROGRESS framework) to invite to interview. Health professionals/service providers and/or community contacts/community researchers would provide the study information (invitation letter and PIL) to identified individuals. Interested individuals would then get in touch with the research team directly.

All participants who take part in an interview will be invited to participate in a workshop.

Individuals will have the opportunity to discuss over the telephone/email/video-call any queries and/or concerns they have about the interviews with the researcher. Researchers will contact participants who are interested in taking part in an interview, having reviewed the study information sheet, to arrange a time for the interview at a mutually convenient time. At this stage, participants who want to use photographs in their interview will be invited to attend an additional pre-meeting to provide further information on taking and sharing photographs with the researcher.

Participants will be offered a £25 gift voucher at the end of the interviews (and an additional £25 for those that elect to take photographs and take part in a pre-meeting) and a £50 voucher for the workshop as a thank you for their time. The study will also cover participants' travel and family care costs if applicable.

Interviews and monthly check-ins (Lightning reports) with professionals

This will include those directly delivering the pilot services, those coordinating or managing services and those referring into the services. This may include healthcare professionals from primary care, local SWMS, or other local providers depending on model adopted and local set-up at each case study site. Key professionals to invite for interview and for the brief monthly check-ins (Lightning reports) will be identified through stakeholder contacts established in the initial stakeholder engagement (see Appendix 1 for University ethics) of the project and by our researchers in residence based at case study sites. Professionals will be sent an invitation letter and PIL from the research team. If they are interested in taking part, they will then get in touch with the researcher who will arrange an interview and set up the monthly check-ins at a mutually convenient time. Individuals will have the opportunity to discuss over the telephone/email/video-call any queries and/or concerns they have about the interview/check-ins with the researcher. Interviews, either online or in-person, will be conducted at least six months after implementation start date (June 23rd, 2025) to explore any adaptations that may have occurred during the early set-up phases. Participants will be offered a £25 gift voucher at the end of the interviews. Following the interviews, we will invite key members of staff to monthly check-ins to capture on-going learning via phone/Teams calls. Six-eight key professionals at each ICB will be identified (based on implementation challenges) for a follow up interview 12-18 months into delivery to explore key themes emerging from the initial interview and monthly check-ins (lightning reports).

4.4 Informed consent

4.4.1 Service utilisation, clinical effectiveness, and cost-effectiveness

Electronic Health Records: we will only be using pseudonymised patient records and will have a range of measures in place to minimise risk of re-identification (see section 7.6) including CPRD's established data storage, access and transfer requirements. Hence, informed consent from individual patients will not be required.

Questionnaire: Information on the study in general and what is involved in participation, including the right to withdraw, will be included in the landing page of the online questionnaire. This will also include a field where participants can indicate their consent for the study to use the questionnaire responses

for research purposes, as well as options to consent to linking questionnaire responses to EHRs and to express interest in participating in interviews. See Appendix 3 for information sheet and consent questions included at the beginning of the questionnaire.

Patients can still take part in the questionnaire if they decline to link their questionnaire responses to their EHRs. Those who decline will have more socio-demographic questions in their questionnaire to enable adequate information to be collected for analyses of inequalities.

Resource use survey: Information on the study and what is involved in participation will be provided before taking part in the survey via a patient information sheet (Appendix 4A). Consent will either be taken by the researcher at the start of the survey discussion (for the telephone/video call option) or through an online consent form linked to the landing page for the survey for those completing the survey online. Information will be treated with an appropriate level of confidentiality and handled in accordance with the Data Protection Act 2018. This information will be made available only to those within the study team who need access in order to fulfil the evaluation.

4.4.2 Feasibility acceptability of new service models

Informed consent will be sought from all participants (PLWO and professionals) taking part in an interview or workshop (including 'lightning reports'). All participants will be provided with an information sheet with the study details (Appendices 5A and 6A) as well as the co-chief investigators' contact details should they wish to seek further information about the study and the use of data collected or to withdraw from the study, and details of the ethics committee should they wish to raise a complaint. Participants will be provided with a copy of the consent form at least 48 hours before the interview to allow them to review this and ask any questions ahead of the interview. (see Appendices 5B.i, 5B.ii 5B.iii and 6B for consent forms). Participants will be offered either to a) return the consent form in advance of the research activity; or b) verbal consent will be taken by researchers and participants' agreement audio recorded using encrypted dictaphones or Microsoft Teams before the interview commences. Consent forms will be completed by the researcher, with a copy provided to participants after the interview. Where participants are interviewed on more than one occasion, verbal reconsent will be taken at each subsequent contact to confirm ongoing willingness to participate. Where an individual is receiving tirzepatide but does not have capacity to consent to an interview, a carer for that individual (who does have capacity to consent) will be invited to an interview to share their experiences of caring for the individual in relation to tirzepatide.

In order to include a diverse range of individuals, participants will be provided with information about the research in video format in addition to written information sheets. Translation and interpreter support will be provided where necessary during recruitment, consent, and interview participation. For participants who are not able to provide informed consent independently, such as some individuals with intellectual disability, proxy consent will be sought from a legally acceptable representative (e.g., parent, guardian, or nominated person). In addition, the participant's assent will be actively sought using easy-read materials and verbal explanations tailored to their communication needs. Participation will only proceed if the individual provides clear assent, and they will be reminded of their right to decline or withdraw at any time without consequence. As per the mental capacity act 2005, individuals will be presumed to have capacity unless proven otherwise. Carers may participate in interviews to support the individual to share their experiences of taking weight management medication, where the patient has capacity to consent but wishes to have a carer present to help them share their views.

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PLWO photograph use and guidance: We will follow ethics guidance as set out by Wang and Redwood-Jones (2001); Wang is a co-developer of photovoice. We will clarify to participants that they should only capture images where photography is normally allowed (i.e., not where there are signs

indicating photography is prohibited) and where they feel safe. We will instruct them to inform any individual(s) whom they wish to photograph about the purpose of the study and how the photographs will be used (e.g., publications, photo exhibitions). We will advise participants not to take images of individuals who are not in their immediate family, or in a crowd shot. Participants will be advised not to take photographs which may reveal identifying information of those under age 16. Participants will be asked to provide written consent (i.e., sign a photograph release form for their photographs to be used in the dissemination of study findings).

Consent relating to the capture and use of photographs: We will have additional consent forms for subsequent use of the photographs for display and publication (to be signed by participants to grant the research study rights for the reproduction of photographs for research and educational purposes). After participants have taken all their photographs, they can choose which ones can be included in the research study/exhibition (Appendix 5D).

Participants will be given the option to be identified or not as the authors of their captions and photographs. If not, a pseudonym or ‘anonymous’ will be used. Photographs containing identifiable images of ‘third parties’ will not be used in the photo exhibition or any study outputs.

Workshops: It will be highlighted at the start of the workshop that, due to the nature of workshops, confidentiality between participants cannot be guaranteed, so they should consider what information they share and only share things they would not mind other people knowing. All participants will be encouraged to keep confidential what they hear during the workshops, with this being covered and agreed by participants and researchers in the workshop ground rules.

5 DATA ANALYSIS

5.1 Service utilisation, clinical effectiveness, and cost-effectiveness

Service utilisation evaluation based on electronic health records

We will examine these uptake and adherence-related factors in relation to socio-demographics using descriptive statistics and choropleth heat maps. We will also treat each as an outcome in multivariable regression to assess their association with socio-demographic factors. The analyses will identify potential inequalities in uptake and adherence between social groups. These findings will also be compared across service models and ICB locations using Geographical Information System maps as per Lenguerrand et al. (2023). This analysis will be undertaken approximately three months after implementation start to assess uptake and adherence in the initial stage of implementation and then at six-monthly intervals thereafter.

Short-term clinical effectiveness evaluation based on electronic health records and patient questionnaires

We will conduct intention-to-treat (ITT) and per-protocol analysis (PPA) for the primary outcomes (HRQoL and body weight). Analyses will be conducted separately for priority cohorts 1 and 2. For priority cohort 1, analysis of HRQoL based on questionnaire data will occur once all patients have had 12 months of follow-up, and will use data from baseline, six and 12 months. Interim analyses will be conducted approximately midway through the study period. Analysis of data up to 18 months will be undertaken for patients in priority cohort 1 who complete the questionnaire at the 18-month time point and do so within the study time frame (see Table 3). For priority cohort 2, analysis of HRQoL data will occur once all patients have had six months of follow-up. Analysis of change in weight based on routine data will also use 12 months (priority cohort 1) and six months (priority cohort 2) as the endpoints, although weight measurements during that period will be recorded at irregular intervals.

ITT: We will use multivariable repeated measures linear regression models to estimate absolute change in the outcomes and to compare the amount of change over time between models of care, adjusted for baseline and other covariates (age, sex, ethnicity, disability status, deprivation, rurality). A random intercepts approach will be used to account for correlation of the outcome within patients, and potentially within GPs and ICBs. Random intercepts will also allow for more robust estimation in the presence of missing questionnaire data at particular time points for individuals. For these comparisons, the model of care with the largest change from baseline will be treated as the reference and the other three models will be compared in a pairwise fashion. From the regression coefficients comparing slopes between models of care, we will assess equivalence (rather than difference) using a two one-sided test (TOST) approach. Equivalence limits are +/- 3 points for HRQoL and +/- 5kg for weight.

We will use repeated measures Poisson regression models of adverse events and losses to follow-up to examine changes in those outcomes over time and between service models. We will adjust for baseline measurements: patient characteristics (e.g. age, sex, ethnicity, disability status, deprivation, rurality), patient comorbidities, and weight at baseline, as well as date of referral to account for potential changes/improvements in service provision over time. We will use inverse-probability for treatment weights (IPTW) to adjust for factors associated with loss to follow-up. We will use multinomial logistic regression to determine the denominator for IPTW, by modelling the adherence to the treatment assignment as a function of the baseline characteristics.

PPA: For the per protocol analysis, we will conduct multivariable repeated measures regression models, as stated above, but censor individuals if and when they deviate from their assigned treatment strategy. We will do this by replicating patients (“cloning”) and censoring them at point of

non-adherence. We will apply IPTW and inverse-probability of censoring weighting (IPCW) to adjust for factors associated with adherence and loss to follow-up.

To account for possible delays between pathway start and treatment start, we will conduct a sensitivity analysis emulating a nested trial design, allowing patients to only be included in the dataset on the day of their first prescription. All analyses will include interactions between treatment arms and time to allow differential estimates of mean change in outcomes between arms.

Interrupted time series (ITS): As a secondary assessment of short-term effectiveness, we will use an ITS approach to evaluate the overall impact of Tirzepatide treatment on mean body weight measured over time among eligible patients using data from CPRD. The eligible population will be based on the priority cohorts defined in the commissioning guidance, e.g. for the first cohort only those with BMI ≥40 kg/m2 and four or more comorbidities will be included. This is a quasi-experimental design (40-42), where the 'intervention' is the date the GP practice introduced the service delivery model. Each GP practice acts as their own control (McLaughlin et al., 2023), to compare trends in mean body weight before and after initiation of the service delivery model. Segmented linear regression models will estimate the trend in outcome prior to the intervention, and after the intervention, and test for changes pre- and post-intervention in a) the overall (absolute level) of outcome, and b) the slope of the trend in level of outcome. We will assess changes in mean bodyweight over a period encompassing 12 months before and 12 months after the implementation date of June 23rd, 2025. As an alternative to this population level assessment of the rollout, we will also consider an analysis of the patient-level treatment effect using generalised linear mixed models and encompassing the patient-specific treatment start date and patient-level covariates.

Analyses will be applied to each model of care and each cohort. Individual estimates for each model of care within a given cohort will then be combined using meta-analysis methods to generate an overall estimate of the impact of the rollout on mean bodyweight in the eligible population. Analyses will be stratified according to measures of inequality (e.g. age, sex, IMD deprivation, ethnicity). Th post intervention predicted estimates and the counterfactual time series (assuming no intervention effect) will then be used to calculate overall cost effectiveness.

Cost-effectiveness analyses based on questionnaire and resource use surveys

We will conduct a within-study cost-effectiveness analysis focusing on the NICE reference case of NHS cost-per-QALY for the different service models and Real World Evidence framework (PSSRU, 2022).

The cost of delivering different service models will be assessed using a bottom-up, micro-costing approach following best practice (Manca et al., 2005). Data will be collected from electronic patient records (CPRD and HES), questionnaires with PLWO to estimate labour market participation, and the resource-use surveys of service providers and commissioners. National unit cost databases will be used to value resource use (Steijger et al., 2022). Cost analysis will distinguish between initial set up costs and ongoing service delivery costs.

The primary health measure for the economic analysis will be QALYs derived from the EQ-5D-5L (Fabron et al., 2023). Utility scores will be estimated using NICE recommended algorithms at the time of analysis. Baseline utility scores and interpolation will be used to estimate QALYs for each patient (McLaughlin et al., 2025). Secondary outcomes will be selected domains of the BODY-Q (Harris et al., 2019), and the ICECAP-A (Al-Janabi et al., 2021). By including these more in-depth measures of weight-related quality of life and general capability well-being, we aim to identify any differential effects of service models not picked up by the EQ5D-5L.

Costs and QALYs beyond 12 months will be discounted at a baseline rate of 3.5% following NICE guidelines. Appropriate regression models with IPTW (described above) will be used to compare costs

and health outcomes between service models. We will calculate the incremental cost per QALY for each service model and the Incremental Net Monetary Benefit (INMB) for willingness-to-pay thresholds of £20,000 and £30,000 per QALY. We will use bootstrapping to address uncertainties in cost-effectiveness. Cost-Effectiveness Acceptability Curves (CEAC) will be used to illustrate the probability of each service model being most cost-effective at different thresholds of decision-makers' willingness to pay per QALY gained.

Sensitivity analyses will explore the NHS perspective versus wider NHS & patient perspective. We will use distributional cost-effectiveness analysis (DCEA) (Thomas et al., 2022) to explore whether the efficiency of the service models differs by key population strata (e.g. deprivation, ethnicity) and the potential impact of introducing equity considerations on our findings.

We will study the economic viability of strategies for further implementation. We will use a framework that combines evidence of service effectiveness and service implementation (Sekhon et al., 2017). If service uptake or effectiveness is suboptimal in specific sub-populations (e.g., ethnic minorities, high deprivation), we will explore the economic viability of additional investment for implementation initiatives (e.g., quality improvement initiatives or outreach services) based on the cost-effectiveness results.

We will use the School for Public Health Research Diabetes Prevention (SPHR-DM) model (Breeze et al., 2015) to assess long-term cost effectiveness. This model has the advantage of including labour market participation and informal care costs. Inputs for the model will be based on study results (e.g., weight loss up to 18 months). The model will be used to estimate the lifetime costs and QALYs of service models. We will use scenario analysis to explore key assumptions (e.g. the extent to which weight loss is sustained beyond 18 months) based on the literature.

5.2 Feasibility and acceptability of new service models

For the interviews, thematic analysis will be undertaken for each interview group (PLWO and professionals). We will use the Framework approach to index, sort, review, and display data for both cross-case and within-case analyses. Data collection and analysis will occur concurrently, allowing us to explore initial themes in subsequent interviews and cross-reference findings between PLWO and professionals. The data driven codes across all transcripts will be grouped into natural clusters and labelled accordingly to create an analytical framework from which further analysis of the codes and categories will be carried out to generate themes. These emerging themes will also be explored and refined during the workshops.

Quantitative questionnaire data on patient satisfaction and engagement with the service models and qualitative summaries of implementation at each reporting timeframe (Lightning reports) will be triangulated with data generated from the interviews and workshops. Analysis will be conducted by the 'researchers in residence' (CF&LH, supported by JL and MT) and, interested community researchers and PPIE members (training will be provided).

6 DATA MANAGEMENT

6.1 Data management and access plan

A detailed plan governing data management and access is required by the NIHR, a copy of which can be found in Appendix 7. This covers data collection and re-use, quality control, storage and backup, and sharing and transfer between participating institutions.

6.2 Archiving and long-term storage

Anonymised qualitative data will be transferred from the University of Exeter to the University of Bristol at the end of the study via the University of Bristol Fluff service (Facility for the Upload of Large Files service). At the end of the study period, pseudonymised questionnaire data stored on REDCap servers will be deleted after being downloaded to the University of Bristol SafeHaven. All data will then be securely archived in the University of Bristol Research Data Storage Facility (RDSF). Data will only be accessible by named members of the research team. All paper records of personal details will be securely shredded and electronic records of personal data will be deleted once the research is complete. In accordance with the University of Bristol's '*Guidance on the Retention of Research Records and Data For studies involving human participants, their tissue and/or human data*', anonymised, analysed data – e.g. NVIVO database and summaries of data – will be retained for a minimum of ten years. It will then be destroyed in accordance with the University of Bristol's Records Management and Retention Policy (IGP-03, https://www.bristol.ac.uk/secretary/records/).

With participants' consent we will deposit anonymised interview and workshop transcripts (and Photovoice photos) in the publicly accessible Research Data Repository (data.bris) at the University of Bristol where it will be made available to other researchers under a Restricted Access arrangement. All requests for access to the anonymised data will be assessed by the University of Bristol data access team to check they are authentic research requests. An aggregated version of the questionnaire response data will be made available as open access since the data in that format will be entirely anonymised with no possibility of reidentification. Resource use data collected through surveys/interviews with commissioners will not be made available to other researchers as this may be commercially sensitive information.

6.3 End of the study

The current funding extends until 31st January 2028, and all data collection activities are to completed on or before that date. We will notify the REC committee of the end of the study within 90 days of this date, and will provide a final report to the REC within 12 months of the date. If the study ends prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination.

7 ETHICAL AND REGULATORY CONSIDERATIONS

7.1 Assessment and management of risk

The protections and limits of confidentiality will be clearly highlighted to participants both verbally before data collection and through information sheets during the process of informed consent, with conditions for the need to breach confidentiality being highlighted (i.e., prevention of significant harm, safeguarding issues).

A distress protocol has been developed for both interviews and workshops (see the interview procedure document in Appendix 8, section 5). Should a participant become distressed, the interview will be paused. In the case of the workshop the participant will be supported to step out of the group; two researchers will facilitate workshops to allow one researcher to provide support while the workshop continues. Initially, the interviewer will listen to the participant and offer support in situ, to determine whether further action is necessary. Should the interviewer remain concerned, they will offer information about local help services, offer to contact a support person on behalf of the interviewee, or offer to make initial contact with clinical services (primary or secondary) on behalf of the individual and with their consent. In the event a participant does not consent researchers to contact their clinical team, the interviewer will discuss with medical doctors (JP, + others) and clinical psychologists (JM) within the study team. Details of support resources will be outlined in the participant information leaflet, as well as alerting the participant that their clinical team may be contacted if researchers are concerned for their wellbeing.

If a participant becomes distressed during the interview, the session will be paused and the participant will be offered support, including the option to take a break, stop the interview, or continue at their own pace. They will be reminded of their right to withdraw at any time without consequence. If appropriate, information about relevant support services will be provided. All interviewers will be trained to recognise and respond appropriately to signs of distress, including receiving training in trauma-informed care. In the event that there are concerns around the health or well-being of participants then these would be discussed with the participants and potentially discussed with the participant's general practitioner. It will be made clear in the Participant Information Sheet that, should a participant disclose information to a researcher during an interview that indicates a risk or harm to themselves or others, it may be necessary to breach confidentiality. The need for this breach would be discussed with the participant beforehand and the incident would be reported to the appropriate safeguarding contact for the given participant.

In workshop settings, if a participant becomes distressed, the facilitator will discreetly check in with them and offer the option to step outside or withdraw from the group without drawing undue attention. Participants will be reminded at the start of the session that they can take a break or leave at any time. Where appropriate, the facilitator or a support person will follow up with the individual privately, and information about support services will be provided. The facilitator will also monitor group dynamics to ensure a respectful and safe environment for all participants.
Lone working: interviews conducted off site may involve lone working, including by community researchers. As per institutional lone working policies, researchers will be asked to check in with a nominated team member upon arrival at a venue, and upon leaving. The nominated team member should be made aware of the expected duration of the visit, location of the visit, and contact details of the person(s) being visited. Where a researcher cannot be contacted, the nominated team member will attempt to contact the participant, general practice, or institution being visited. If contact can still not be established, local emergency services will be contacted. We will also follow local institutional lone working policies.

7.2 Research Ethics Committee (REC), Amendments & Reporting

Before the start of the study, a favourable opinion will be sought from an NHS REC for the study protocol, information sheets, consent forms, questionnaire, survey and other relevant documents before any data is transferred or any potential participants contacted.

Substantial amendments that require review by NHS REC will not be implemented until that review is in place and other mechanisms are in place to implement at site.

All correspondence with the REC will be retained.

The Chief Investigator takes on the responsibility to produce the annual reports as required and all progress reporting will be in line with REC requirements.

7.3 Peer review

This study is funded through the NIHR HSDR programme and thus underwent peer review as part of the funding process. Subsequently the main study protocol has been reviewed and approved for scientific content by the NIHR. This protocol has also been reviewed by an independent statistician: the chair of the study's Data Management and Ethics Committee.

7.4 Patient & Public Involvement

We are using a PPIE co-lead mentorship model, based on our collective experience that a limited number of individuals undertake obesity PPIE leadership roles nationwide. We currently have three PPIE co-leads who were also co-applicants on the funding bid, and with the recruitment of a further seven PPIE contributors, we aim to cultivate a more diverse group of individuals with the confidence and skills for PPIE lead roles, fostering future PPIE capacity and diversity in obesity research.

The PPIE group members represent a range of backgrounds, with many members having had prior experience as public/patient contributors to health research. They also bring a range of experiences of living with obesity, interacting with weight management services and/or receiving weight-management medication. The three PPIE co-leads are co-applicants on the funding bid and have contributed to the study design and main NIHR-approved protocol.

PPIE co-leads, contributors, and their activities as a group will be supported by an experienced PPIE coordinator. All PPIE members will be reimbursed for their time, travel, and remote working costs following NIHR guidance.

PPIE activities will be agreed with the group, but as a minimum includes planning recruitment strategies and materials, co-designing questionnaires and surveys, participating in data collection and analysis, and contributing to research summaries and creative dissemination outputs. Our three PPIE co-leads attend regular study management group meetings. Information sheets, consent forms and the questionnaire as part of this IRAS application have all received PPIE input. However, more intensive workshopping of patient facing materials by the PPIE team is planned, and any later modifications to questionnaires, information sheets, consent forms and so on will be submitted as a subsequent amendment.

7.5 Data protection and patient confidentiality

General considerations: For the purposes of this research, the Chief Investigator is the data custodian. All information collected during the course of the study will be kept strictly confidential and handled in accordance with the principles of the Data Protection Act 2018 and the data protection policies of the University of Bristol, the University of Plymouth and the University of Exeter. Participant data will be stored securely in locked filing cabinets within security card access university buildings (for paper

records) and on password-protected, encrypted servers (for electronic records) accessible only to authorised members of the research team.

For all reporting of quantitative results beyond the study team, we will follow the ONS guidance on Safe Outputs (a component of the 'five safes') in order to minimise any risk of disclosure. This will involve applying appropriate disclosure controls such as suppressing small counts, perturbing counts to avoid back calculation of small counts, and cross checking between various study outputs to minimise secondary disclosure through combinations of results.

Electronic Health Records: Data will be made available to researchers only in pseudonymised form and only for the patient records relevant to the evaluation. This will involve working within the established data protection and research governance policies of the data provider. As per the conditions of the University of Bristol's multi-study CPRD licence, all datasets are kept in a dedicated secure password protected University of Bristol Safehaven folder (\\ads.bris.ac.uk\filestore\HealthSci SafeHaven\CPRD Projects UOB). Each approved study has access-controlled subfolders. Only researchers or students named in the ISAC/ERAP are given access to the specific project sub-folder they are working on. Access is controlled by use of user accounts and file access control lists. If the University of Bristol does not renew the multi-study licence during the research period, continued data access will be through CPRD's trusted research environment (CPRD Safe). All data processing and analysis will occur within that secure remote environment and only non-disclosive outputs will be exported to the University of Bristol's servers.

Questionnaire: As part of the CPRD interventional research service, existing data sharing agreements are in place between CPRD and approximately 300 GP practices. These agreements cover the identification of eligible questionnaire participants by CPRD and then patient record review and patient contact by practices. Invitations sent by GPs will be through whichever means is standard for that practice (e.g. SMS, email, etc.).

Digital questionnaire responses will be captured by the REDCap secure online platform at the University of Bristol. Password protected access to responses is via an encrypted SSL website only accessible by registered members of the study team. Response data will be downloaded directly to the University of Bristol SafeHaven on a monthly basis and stored in pseudonymised form. Identifiable personal information collected via questionnaire to enable follow up questionnaires will be stored on a separate University of Bristol REDCap server to the main response data. This will be downloaded to the University of Bristol SafeHaven on a monthly basis and then deleted from REDCap servers.

Questionnaires completed on paper will be converted to digital scans using a dedicated study scanner at the University of Bristol and the response data entered into the data file of digital responses extracted from REDCap, all of which will be stored in the University of Bristol SafeHaven. Once recorded in the data file and saved as a scan, the original paper copy will be destroyed according to the University of Bristol's confidential waste disposal procedure.

Data linkage between questionnaire responses and electronic health records will be carried out by CPRD and only for those participants who have consented to the linkage. Participants will indicate consent for their questionnaire responses to be linked to EHRs by using a dedicated field on the questionnaire to enter an ID number provided with the initial invitation text message or email. Pseudonymised questionnaire responses will be transferred to CPRD via the MOVEit secure managed file transfer platform. Encrypted, pseudonymised, linked datasets will then be transferred from the CPRD to the University of Bristol via the same means, where they will be stored in the SafeHaven.

At the end of the study period (January 2028) all personal information will be deleted, and all pseudonymised questionnaire response data will be saved in study-specific folders on the UoB network and deleted from REDCap servers.

Resource use surveys: Information on contracts with digital/private providers will be treated as 'commercial in confidence' in all analyses and reporting. All data will be stored on University of Bristol servers.

Interview, photovoice, workshop, workshop and lightning report participants:

Participants' data from qualitative components will be held in secure storage at the University of Exeter. Measures will be taken to ensure that all qualitative data, including photographs, are processed securely, accurately and in accordance with data protection principles. Audio data from qualitative interviews will be recorded using an encrypted digital audio recorder or an encrypted Microsoft Teams meeting recording (if online). Data will initially be stored on Microsoft SharePoint on the University of Exeter's secure server using the participant's unique study number. Two-factor authentication, to log-in to SharePoint sites, is standard practice at the University of Exeter. Audio recordings and transcribed data will only be accessible to the designated research team. Transcription of audio recordings of interviews will only be carried out by members of the research team or professional services with confidentiality agreements in place. Following transcription, members of the research team will edit the transcript to anonymise the participant and remove all identifying elements prior to analysis. Where consent is taken verbally via a recorded audio or video call, the portion of the recording containing the consent will be separate from the main interview recording and stored in a separate folder. The link to the participant's identity will be contained in electronic format and stored in a separated file in the dedicated University of Exeter SharePoint site. Further checks to ensure that participants' identities are pseudonymised will take place prior to any publication of research data in the public sphere and prior to submission of any research reports.

The photovoice participants will have the option to use their own mobile phone or camera to take photos, or use a device provided by the research team. Participants will securely transfer their photos to the research team using the Qualtrics platform hosted by the University of Exeter. They can then delete the photo from their own device if desired and will be asked to delete any photos from devices provided by the study. Photographs will be stored on secure SharePoint site at the University of Exeter. Only researchers analysing the data will be able to access the photographs.

7.6 Indemnity

The University of Bristol has arranged Public Liability insurance to cover the legal liability of the University as Research Sponsor in the eventuality of harm to a research participant arising from management of the research by the University. This does not in any way affect an NHS Trust's responsibility for any clinical negligence on the part of its staff (including the Trust's responsibility for University of Bristol employees acting in connection with their NHS honorary appointments).

7.7 Quality event and breach reporting

In the event of any deviation from the approved study protocol in such a way as to contravene the Conditions and Principles of Good Clinical Practice (i.e. quality events), we will notify Research Governance at the University of Bristol as soon as possible after your becoming aware of it. We will then, as Sponsor Representatives, determine whether any further reporting is required, or if it is sufficient to document the Breach along with all Corrective and Preventative actions taken in response to it. The university of Bristol procedure for quality events is detailed here: https://www.bristol.ac.uk/media-library/sites/red/documents/research-governance/RG SOP 8 - Quality events.pdf

8 DISSEMINATION POLICY

8.1 Dissemination policy

Our dissemination strategy, developed in collaboration with our PPIE co-applicants, PolicyBristol and NIHR ARC West's communications team, will be finalized in partnership with our full study PPIE group, NHSE, and key stakeholders. We will work closely with NHSE, using an Action Research approach to share interim findings that could enhance user uptake and experience or significantly support service delivery, particularly in primary care, throughout the project's duration. This approach, alongside NHSE's MDS, offers the opportunity for earlier implementation and evaluation of service improvements by NHSE and providers.

We anticipate that our outputs will include:

- Workshops at interim and project completion stages to engage stakeholders
- Regular briefing emails to NHSE
- A preliminary logic model articulating the functioning of the three service models tested, from commissioning and service set-up through to patient outcomes. This would be further developed within a future full evaluation.
- Interim and final evaluation reports for NHSE, incorporating key insights focusing on improving service reach, processes, and patient experience across different socio-demographic groups. An important focus will be the experience of primary care teams and implications for wider roll-out.
- Identification of training and resources needed for primary care professionals and commissioners to support future roll-out, including identification of potential online platforms to host this. This will be led by our expert GP co-investigators HP and CH who have extensive experience of managing patients living with obesity in primary care including working in T3SWMS in primary care, supported by our PPIE team (for the patient perspective) and clinical co-applicants KCo, JM, JP, and RB. This also benefits from our experience of developing online learning packages for health professionals on behavioural WM in the PROGROUP study (MT, JL, JP, RB).
- At least three open-access peer-reviewed journal publications
- Presentations at clinical and policy conferences, co-presented with PPIE members.
- Four photovoice exhibitions and knowledge exchange workshops, located in our case study communities. These will be run by our PPIE members. Local stakeholders including study participants, commissioners, health professionals, politicians and the voluntary sector will be invited.
- A plain English summary and short video summaries co-developed with our PPIE team and NIHR ARC West communications team.

The main study protocol will be registered with ISRCTN as required by the funder (https://www.isrctn.com). Analysis code from quantitative and health economics analyses will be made publicly available on GitHub.

Summaries of research findings will be provided to research participants who indicated their interest in receiving that information either during interview or questionnaire completion.

8.2 Authorship eligibility guidelines and any intended use of professional writers

We will use the ICMJE guidelines on authorship (ICMJE, 2025) to determine who is included as an author on the various published outputs described in section 8.1.

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10 APPENDICES

10.1 List of Supporting documentation

Appendix 1. Faculty REC approval letter for stakeholder engagement (work package 1), with protocol and expression of interest form circulated to stakeholders (ICBs)

Appendix 2. Main study protocol (NIHR approved)

Appendix 3. Participant questionnaire

Appendix 4A. Professional interview/survey for resource use: participant information sheet
Appendix 4B. Professional interview/survey for resource use: consent form and topic guide
Appendix 4C. Professional interview/survey for resource use: interview topic guide

Appendix 5A. Patient interviews (including photovoice) and workshops: information sheet
Appendix 5B.i Patient interviews and workshops: consent form
Appendix 5B.ii Patient interviews and workshops: Carer consent form
Appendix 5B.iii Patient interviews and workshops: photo release consent form
Appendix 5C.i Patient initial interview: topic guide
Appendix 5D. Patient interviews and workshops: instructions for taking photos
Appendix 5E.i Patient invitation letter from health professionals
Appendix 5E.ii Patient invitation letter following questionnaire participation

Appendix 6A. Professional interviews: information sheet
Appendix 6B Professional interviews: consent form
Appendix 6C.i Professional initial interview: topic guide
Appendix 6C.ii Professional follow-up interview: topic guide
Appendix 6C.iii Professional interviews: Lightning report template
Appendix 6D Professional interviews: invitation letter

Appendix 7. Data management plan

Appendix 8. Interview and workshop procedure (including distress protocol)

Appendix 9. Carer interviews: information sheet

10.2 Study diagrams and flowcharts

STUDY FLOW DIAGRAM