The Plan-it study.

The acceptability and feasibility of a planned pre-pregnancy weight loss intervention

v1.1 03.04.19

Sponsor:	N/A
Sponsor ref:	N/A
Funder:	National Institute for Health Research (NIHR) Health Technology Assessment (HTA)
Funder ref:	17/130/05
REC ref:	N/A CU Ethics
IRAS number:	N/A
Review registrations	
Q-Pulse Document Template Number:	TPL/003/2

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the relevant trial regulations, GCP guidelines, and CTR's SOPs.

I confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

Director:		
Name	**Signature**	**Date**
Chief Investigator:		
Name	**Signature**	**Date**

General Information This protocol describes the Plan-It Study, and provides information about the procedures for entering participants into the study. The protocol should not be used as a guide, or as an aide-memoire for the treatment of other participants. Every care has been taken in drafting this protocol; however, corrections or amendments may be necessary. These will be circulated to the known Investigators in the study. Problems relating to the study should be referred, in the first instance, to CTR

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Study Co-ordination:

The Plan-it study is being coordinated by the Centre for Trials Research (CTR), Cardiff University, a Clinical Research Collaboration (UKCRC) registered trials unit.

This protocol has been developed by the Plan-it Study Management Group (SMG).

For **all queries** please contact the Plan-It Study team through the main study email address. Any clinical queries will be directed through the Study Manager to either the Chief Investigator or a Co-Investigator

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Glossary of abbreviations

BMI	Body Mass Index
CF	Consent Form
CI	Chief Investigator
CPRD	Clinical Practice Research Datalink
CRF	Case Report Form
CTR	Centre for Trials Research
CTU	Clinical Trials Unit
CU	Cardiff University
GCP	Good Clinical Practice
GP	General Practitioner
HES	Hospital Episodes Statistics
HTA	Health Technology Assessment
IC	Informed consent
ICH	International Conference on Harmonization
ISRCTN	International Standard Randomised Controlled Trial Number
IS	Information Systems
IUD	Intrauterine Device
LARC	Long-acting reversible contraceptive
NIHR	National Institute for Health Research
PI	Principal Investigator
PIAG	Participant Information Advisory Group
PIC	Participant Identification Centre
PIS	Participant Information Sheet
PHW	Public Health Wales
QC	Quality control
REC	Research Ethics Committee
RGF	Research Governance Framework for Health and Social Care
SAG	Stakeholder Advisory Group
SHC	Sexual Health Clinics
SHCD	Sexual Health Clinic data
SMF	Study Master File
SMG	Study Management Group
SSC	Study Steering Committee
WP	Workpackage

1 Amendment History

The following amendments and/or administrative changes have been made to this protocol since the implementation of the first approved version.

Amendment No.	Protocol version no.	Date issued	Summary of changes made since previous version
N/A			

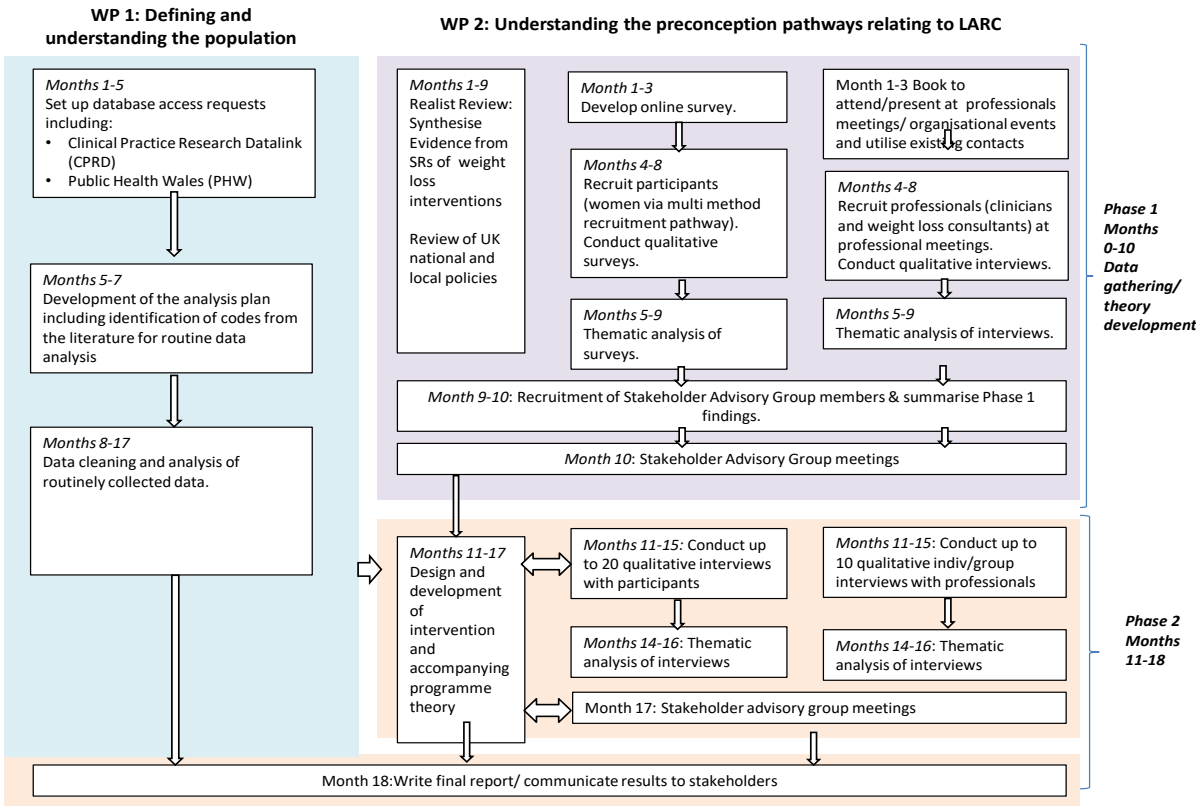
2 Synopsis

Short title	The Plan-it study. The acceptability and feasibility of a planned pre-pregnancy weight loss intervention.
Acronym	Plan-it
Internal ref. no.	
Development phase	Phase 1
Funder and ref.	Health Technology Assessment 17/130/05
Study design	Feasibility/ acceptability study
Study participants	Women in both phase 1 and 2 : i) of reproductive age (16-48 years old) ii) who have experience of using LARC, iii) who think/know either that their current weight would put them in the overweight/obese category or their weight when they were planning a pregnancy would have put them in the overweight/obese category. Clinicians: i) with the Faculty of Sexual and Reproductive Health letter of competence Weight loss intervention practitioners: group leaders of widely used community based weight loss programmes
Planned sample/data collection	Phase 1: • 200-500 responses to online survey by women • Professional responses thorough attendance at maximum 8 professional meetings Phase 2: • Up to 20 interviews with women and 10 clinician/practitioner interviews
Inclusion criteria	***Workpackage 1: Routine Data*** CPRD: Women of reproductive age (16-48 years old) who have LARC use/removal Read Code during 01JAN2009-31DEC2018. SHCD: Women of reproductive age (16-48 years old) who have LARC use/removal Read Code during 01JAN2012-31DEC2018 ***Workpackage 2: Phase 1 and 2*** Online surveys and participant interviews: i) women of reproductive age (16-48 years old) ii) have experience of using LARC iii) who think/know either that their current weight would put them in the overweight/obese category or their weight when they were planning a pregnancy would have put them in the overweight/obese category . Clinician interviews: i) clinicians who remove LARC as part of their clinical role

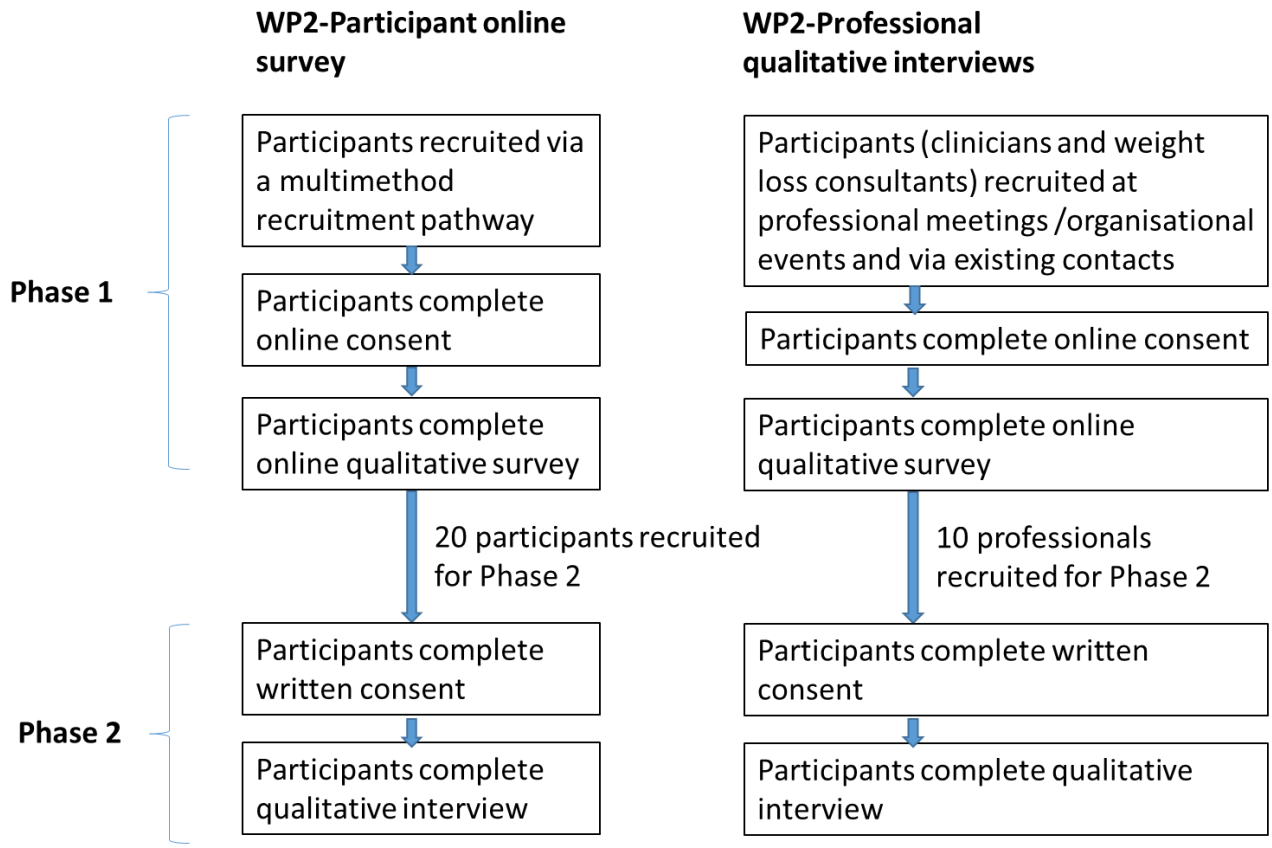
	Weight loss intervention professional interviews: i) professionals who are involved in the management or delivery of weight loss intervention (private or NHS) programmes
Exclusion criteria	***Workpackage 1*** Records that do not meet the inclusion criteria/not present in CPRD data. ***Workpackage 2*** Online surveys and participant interviews: i) Insufficient written English to participate in online surveys and consent to participate in the study. Clinician interviews: i) None Weight loss intervention professional interviews: ii) Insufficient written English to participate in online surveys and consent to participate in the study.
Planned study period	1/5/19-31/10/20
Objectives	The study objectives are to identify 1. The annual number of women in the UK of reproductive age who request LARC removal and subsequently have a pregnancy. 2. Means of identifying women at study sites who are overweight/obese and plan to have LARC removal for the purpose of planning a pregnancy and identify opportunities to intervene. 3. Suitable and acceptable interventions that could be incorporated into a pre-pregnancy weight loss intervention with a theory-based programme model. 4. Willingness of clinicians to raise weight loss in consultations with eligible women and recruit them to the intervention. 5. Views of eligible women as to the feasibility of the intervention and acceptability of future research. 6. Future potential intervention and study designs based on feasibility and acceptability to stakeholders.
Primary outcomes	Rates of women in the UK who request LARC removal and subsequently have a pregnancy through routine data. Identification of opportunities to intervene in preconception pathway. Assessment of the barriers and facilitating factors for incorporating a weight loss intervention in the preconception period from the perspective of all stakeholders Identification of suitable weight loss interventions that are acceptable to the stakeholders. Assessment of the views of eligible women and potential recruiting clinicians as to the feasibility of the intervention and acceptability of future research.
Tertiary/Exploratory outcomes	None

3 Study summary & schema

3.1 Study schema



3.2 Participant flow diagram



3.3 Study lay summary

Approximately 50% of women of childbearing age in England are overweight or obese (Public Health England, 2015). With the known health risks this presents in pregnancy to mother and child, services need interventions to support women planning a pregnancy with weight loss. Current weight loss interventions in pregnancy do not make enough difference and so attention has turned to interventions before the woman becomes pregnant (pre-pregnancy). This is not a group that services could specifically identify, with the exception of women using long-acting reversible contraception (LARC) such as the intrauterine device ("coil") or sub-dermal implants, who need them removed by a GP or Sexual Health Practitioner (clinician) before they can become pregnant. However it may be difficult to ask women to delay the removal in order to lose weight, as it is likely that they have decided about removal and the possibility of pregnancy already. The aim of this study is to discover if it is possible to do a research study that asks women who are overweight/obese to

delay LARC removal and take part in a pre-pregnancy weight loss intervention. We want to find out i) how many women request a LARC removal each year and if it is possible to identify from clinic data if they are overweight/obese, ii) what type of weight loss intervention might suit them, iii) if the clinicians who remove LARCs are prepared to refer patients to weight loss interventions, iv) how best to design a study to tell us whether such an intervention will work. Some of the possible problems have been identified in other studies e.g women do not feel they have time to attend weight loss sessions, clinicians lack confidence in discussing weight when it is not the reason for the consultation. Also women attending for LARC removal may already be committed to becoming pregnant and hesitant to delay trying for a baby. We want to understand this combination of elements to ensure we design a study that is acceptable and feasible or explain why this study cannot currently be done.

The Plan-it study focuses on finding out the views of women and clinicians about this type of intervention and also if we can identify the population from information collected by NHS clinicians (routine data). We will find out if we can use routine data to identify the number of LARC removals and if those women are overweight/obese. We will run online surveys through social media e.g Facebook, weight loss forums etc asking women who have used LARCs and are overweight/obese what they think would be the reasons to take part or not in such an intervention, whether they think it can be done and if so how they could imagine it working. We will ask clinicians and people who run weight loss interventions the same type of questions and also their views about asking women to take part in a study. We will look at the types of weight loss interventions that might work and also any guidelines that might affect clinicians' practice. We will put this information together and work with groups of women and professionals (our stakeholder advisory groups, SAGs) to translate this into possible interventions and study designs. We will ask women and professionals in individual/group interviews, for their views of our suggestions and then we will draft a proposal that will be finalised by discussion with the SAGs. The final study design, or reasons for no study, will be written up as the final report, published, put on the study website and presented at conferences

4 Background

Women who are obese (those with a body mass index (BMI) of 30 or over) are at a greater risk of experiencing complications during the antenatal, intrapartum and postpartum periods; such

complications include gestational diabetes, shoulder dystocia and venous thrombosis. The risk of adverse effects on the child is also increased; there is a known greater risk of child obesity (Marchi et al, 2015) and evidence continues to emerge from longitudinal cohort studies which demonstrates further health-related risks such as the increased risk to females born to overweight or obese mothers, of having polycystic ovary syndrome later in life (Valgeirsdottir, 2018). Despite many studies of weight management interventions in pregnancy, systematic reviews have demonstrated limited effectiveness; interventions in the antenatal period are associated with modest reductions in gestational weight gain and improvements in diet, but do not demonstrate improvements in maternal outcomes (Flynn et al, 2016; Muktabhant et al 2015). The recently published Preconception Health series in the Lancet, argues the need for increased focus on preconception health, with particular attention drawn to diet and nutrition (Stephenson et al, 2018). The development of effective pre-pregnancy weight loss interventions for overweight/obese women may provide an important step in reducing health risk to mother and child, but there are challenges to be overcome. As in pregnancy (Phelan, 2010), the preconception period may also be considered a "teachable moment" where efforts may be made to positively influence women's diet and health behaviours. However, women's enhanced motivation to be healthy may not translate into action due to perceived barriers such as time, relevance and care-provider attitudes (Harden et al, 2017).

Much of the research in pre-conception weight loss has been with very specific populations such as gastric by-pass patients (Adams et al, 2105), or has been small-scale (Harden et al, 2017), hence the lack of findings from two Cochrane reviews (Opray et al 2015; Furber et al 2013). The "pre-conception" population is largely invisible in health-service terms, with no clear time point of intervention apart from within the small proportion of women who attend surgeries for preconception advice. Therefore, women who use long-acting reversible contraception (LARCs) and who require removal of the device to become pregnant represent an opportunity for intervention. However, at this point in their reproductive decision-making, it may be difficult to ask women to delay conception through continued use of LARC and engage in weight loss programmes, raising pragmatic and ethical issues for future trial design. A small feasibility study of an intensive weight management programme offered to women with a BMI of 30 or more attending for LARC removal (Brackenridge et al, 2018) demonstrated that some women were willing to consider delaying LARC removal for six months in order to participate. It is not clear how many women were approached in total, but of the 34 women expressing an interest nine declined, in large part due to the nature of

the intervention (milk-based meal replacement), and six completed the 24-week intervention. This small evidence base demonstrates that there may be an interest in weight loss and a willingness to delay LARC removal in relevant populations, but it has not yet been established what the nature of an acceptable intervention would be.

Rapidly rising rates of women of childbearing age who are overweight/obese, significant health risks for mother and child associated with maternal overweight/obesity (compounded by the link with socioeconomic deprivation) (Public Health England, 2015) and lack of progress in developing successful interventions, underline the importance of exploratory research to develop novel approaches to tackle this issue. The complexities associated with this research require a mixed methods approach incorporating use of routine data, qualitative data collection and analysis, and a central role for stakeholders. The target population are not visible to services and span all sociodemographic groups so any study needs to identify the population and capture a wide range of community views. As people prepare to become a parent, it presents an opportunity to influence behaviour, building on spontaneous changes in behaviour and attitudes (Foresight report, Butland et al, 2007). Given the evidence that although pregnancy boosts women's motivation to improve health (Jackson et al, 2011) this does not translate into weight loss for women who are overweight/obese, we need to understand the barriers to engaging with weight management before and/or during pregnancy, and include these while developing an overall theory of how we expect any intervention to work.

Practitioners also experience barriers to raising weight management in pregnancy including lack of skills, time, sensitivity of topic and confidence in the available interventions. (Stotland et al, 2011, Blackburn et al, 2015). These barriers need to be explored if practitioners are to direct women to pre-conception weight management. Weight loss requires significant behaviour change at any life-stage: Asking women to postpone a life-choice to become pregnant and also engage in weight loss raises many challenges including finding an appropriate study design. This will require an iterative process between the MRC development and feasibility phases (Craig et al, 2008) and identifying an acceptable model of consent and randomisation (Wendler, 2018).

4.1 Rationale for current study

Despite many studies of weight loss interventions in pregnancy, systematic reviews have demonstrated limited effectiveness. The recently published Preconception Health series in the Lancet argues the need to target the preconception period for weight loss intervention. However, there are several perceived challenges to incorporating a weight loss intervention into preconception care. In order to identify ways of ameliorating the difficulties and develop an acceptable intervention deliverable by the NHS, we need to better understand the LARC pathway from an individual and population perspective and its interface with weight management. This includes women's decision making, engagement and experience of LARC services, management of weight around pregnancy, clinicians' routine LARC practice and consultation patterns regarding LARC use and removal. We will do this by utilising datasets, collected routinely across the four UK nations, to compare the population across the different health care settings, as well as over time, taking into account factors such as the impact of different GP incentives on activity and recording (Arrowsmith et al, 2014, QOF 2017/18). In addition, stakeholder views of the study design, particularly the methodological issues associated with the timing of informed consent and the weight loss intervention, will be collected. All this information will be critical to consider when developing a future intervention and associated feasibility trial.

5 Study objectives

The aim of the Plan-it study is to establish if it is acceptable and feasible to conduct a study that asks women who are overweight/ obese to delay removal of LARC to participate in a targeted pre-pregnancy weight loss intervention.

The study objectives are to identify:

1. The annual number of women of reproductive age in the UK who request LARC removal and subsequently have a pregnancy.
2. Means of identifying women at study sites who are overweight/obese and plan to have LARC removal for the purpose of planning a pregnancy and identify opportunities to intervene.

3. Suitable and acceptable interventions that can be incorporated into a pre-pregnancy weight loss intervention with a theory-based programme model.
4. Willingness of clinicians to raise weight loss in consultations with eligible women and recruit them to the intervention.
5. Views of eligible women as to the acceptability and feasibility of the intervention and of future research.
6. Future potential intervention and study designs based on feasibility and acceptability to stakeholders.

5.1 Outcomes measure(s)

i. Rates of women in the UK who request LARC removal and subsequently have a pregnancy (using routine data).
ii. Identification of opportunities to intervene in preconception pathway.
iii. Assessment of the barriers and facilitating factors for incorporating a weight loss intervention in the preconception period from the perspective of all stakeholders
iv. Identification of suitable weight loss interventions that are acceptable to the stakeholders.
v. Assessment of the views of eligible women and potential recruiting clinicians as to the feasibility of the intervention and acceptability of future research.

6 Study design and setting

To meet the research aims and objectives this study needs to ascertain the availability of adequate routine data to identify the population and potential study sites and also the acceptability and feasibility of a theory-driven intervention and study design for stakeholders. The study will take a concurrent mixed methods approach incorporating use of routine NHS data and qualitative data collection and analysis. There will be two work packages (WPs): WP1 will address objectives 1 and 2 and will establish the feasibility of defining and understanding the population through routine data. WP2 will address objectives 3, 4 and 5. Engagement with LARC users, clinicians who remove LARCs and practitioners who deliver weight loss interventions through qualitative data collection will provide an understanding of the preconception pathway relating to LARC and the acceptability to

women and practitioners of incorporating a pre-pregnancy weight loss intervention. Potentially suitable weigh loss interventions will be identified and information on the theories underpinning them will be extracted.

At the end of Phase 1 the information will be synthesized to describe the core components of a future intervention, together with the contextual factors likely to be important influences on outcomes and study designs. This will be refined through work with both service user and professional Stakeholder Advisory Groups (SAGs). The outputs from Phase 1 will be explored in Phase 2 with targeted qualitative work addressing acceptability and feasibility of the proposed interventions and study designs to women in the target population and to the clinicians in services who could be recruiting them.

The findings from the two work packages will be brought together in the final report of the study, addressing objective 6, which will delineate the key design elements of a future trial or, depending on stakeholder response, identify the barriers that currently prevent such a trial taking place.

Work Package 1: Understanding the population through routine data

This WP will use routine data from Sexual Health Clinics and General Practices (GPs) relating to women attending for LARC removal.

The tasks are to set up access to anonymised data from multiple health settings in order to:

1. understand the pattern of LARC use to identify opportunities to intervene;
2. report the annual number of women in the UK requesting removal of LARC without replacing it with an alternative prescribed contraception;
3. identify women requesting LARC removal who subsequently become pregnant who would be eligible to recruit to a weight loss intervention study
4. identify events in GP and hospital records to explore time from LARC removal to conception or appointments relating to difficulties conceiving (if possible).

We will access the following anonymised data:

1. Clinical Practice Research Datalink (CPRD) which provides UK-wide individual level anonymised patient GP data. Data covers over 20% of general practices in the UK and is representative of practices by country, rurality and deprivation quintiles, (Herrett et al,

2015). The anonymised primary care patient data can be individually linked to secondary care and other health-based datasets. One of these is the Hospital Episode Statistics (HES) which includes inpatient, outpatient data A&E data.

2. Public Health Wales which holds individual level patient data from all Sexual Health Clinics in Wales (from 2012). An anonymised extract will be provided to include information such as Age, LARC removal and, where available, reason for LARC removal and BMI.

We will also access or request aggregate SHCD from Scotland (via National Sexual Health System) and England (via NHS Digital) to compare rates with the Welsh SHCD. As this is a feasibility study it would not be cost-effective to request individual level data from Sexual Health Clinics from, for example, England via NHS Digital, however we will request aggregate data to enable comparisons and draw conclusions on a national level. NHS Digital (Data Controller of SHCD in England) produce annual reports based on the SHCD from across England and make the aggregate data openly available. We will request the equivalent data from Scotland via the electronic Data Research and Innovation Service (Gatekeeper of health data in Scotland) or directly from the NHS National Services Scotland (Data controller).

A data access request to CPRD will be reviewed by the Independent Scientific Advisory Committee (ISAC) prior to it being made available to the project team. Sexual Health Clinic data (SHCD) will be agreed by Public Health Wales who are the Data Controller for these data. The aggregate data for England and Scotland will not require a formal data access request (for England the data are already available via NHS Digital https://digital.nhs.uk/data-and-information/publications/statistical/sexual-and-reproductive-health-services).

For all anonymised individual-level datasets we will aim to identify the target population of women of reproductive age, who attended for LARC fitting and removal over a ten-year period (2009 – 2018) for CPRD and seven-year period (2012-2018) for SHCD (due to availability of data). We will explore the completeness of Body Mass Index (BMI) data and if it is possible to identify those with a BMI of 25 and over. Fitting and removal of LARCs, and where possible, reason for LARC removal, will be reported over time, by country, by attendance type and we will compare the case-mix of women attending their GP with those who visit a sexual health clinic for LARC removal.

Analysing these datasets will identify variation in numbers, pattern and duration of use of LARCs in the different health settings, geographical areas (rural/urban) and demographic groups. It will be

possible to consider what opportunities (e.g., consultation types, frequency of consultations) are available to intervene in the different service delivery designs across the UK. The routine data analysis will determine the most appropriate LARC removal settings, the annual numbers of potential participants available to recruit and an indicative time-frame for recruitment.

Using CPRD data, it will be possible to map the time from LARC removal to conception (the estimated start date of pregnancy and the first antenatal clinic visit), birth, then further contraception pattern. It will not be possible to definitively know from the routine data if a LARC was removed with the intention to start a family and therefore by following up patients, this will provide more insight with regards to their assumed motivation for LARC removal. We will examine the time between LARC removal and conception to see if a natural cut off exists. Using this cut off and in lieu of any events after LARC removal that would indicate that it was NOT for the purpose of planning a pregnancy (such as starting another form of contraception) it will be assumed that if a participant becomes pregnant in a certain period of follow-up allowed by the datasets, that LARC removal was for the purpose of planning a pregnancy. We will attempt to define women as those that LARC removal was (a) definitely for purposes of conception (e.g. conception within 3 months of removal and a contrary event), (b) probably for purposes of conception (conception after 3 months of removal and no contrary event), (c) probably not for purposes of conception (no conception within follow-up period and a contrary event such as further contraception), (d) inconclusive (no conception within follow-up period and no contrary event). This will inform the numbers of potential participants available to take part in a future trial which could be extrapolated across to the SHCD. As overweight / obese women may have difficulty conceiving this may be an underestimation of the target figure and a limitation to the study design.

Cardiff University will be the Data Processor for all data.

Work Package 2: Understanding context and stakeholder views

The tasks in WP2 will meet objectives 3-5 and be conducted in two phases; Phase 1 comprises

i) Scoping work to identify suitable weight loss and weight-related health behaviour interventions and the theories that underpin them

ii) Developing an understanding of typical pre-conception pathways related to LARC/LARC removal from the perspectives of service users and service providers.

WP2 Phase 1: Scoping suitable interventions and underlying theories

During the first phase of WP2 we will start to develop theories about how and when health behaviour interventions in the pre-conception phase may function. This process will be guided by the principles of scientific realism (Pawson & Tilley, 1997).

We will examine studies identified in recent systematic reviews of weight loss interventions prior to and during pregnancy and relevant behaviour change interventions including those identified by the HTA as being of significant relevance to understanding how and when preconception weight loss interventions might successfully be applied (e.g. Flynn, 2016, Forsum, 2013; International Weight Management in Pregnancy collaboration, 2017).

We will incorporate identified health gains or risks to health associated with the intervention into the review, paying particular attention to factors which potentially could improve or compromise health in the context of preparation for conception. We will examine the studies included in these reviews together with other relevant reviews (e.g. Better Beginnings - Health in Pregnancy, 2017) and companion papers (e.g. qualitative studies, process evaluations).

We will draw on the processes of theory generation used in realist synthesis (Pawson, 2006), but will limit the scope of our review to the known papers, as we intend to use the literature to build and develop early theories for later refinement (rather than to conduct a full realist synthesis which might also aim to test these theories). Furthermore, we will focus our theory development on the barriers and facilitators to engagement in pre-conception health behaviour change interventions and research.

We anticipate developing a range of programme theories, drawing on existing mid-range theories as appropriate, relating to various aspects including attitudes to randomisation and consent processes, approaches to intervention recruitment, and the characteristics of interventions themselves. We will aim to describe contextual influences on reasoning process during each of these stages (at the levels of the women participating, clinicians, the healthcare system and wider society).

The outcome of this task will be a set of context-mechanism-outcome configurations which will be taken forward to our Stakeholder Advisory Groups as the basis of an early overall programme theory, to be further developed within Phase 2.

WP2 Phase 1: Understanding the preconception pathways relating to LARC

A range of qualitative methods, including documentary analysis, an on-line survey and stakeholder interviews, will be used to generate a detailed understanding of typical pre-conception pathways related to LARC/LARC removal from the perspectives of both service users and service providers.

The specific aims of WP2 in Phase 1 will be to generate an understanding of: the LARC removal service contexts, typical family planning pathway(s), how LARC are managed by women and their clinicians, the inter-relationship between discussions about weight/ obesity and family planning, what additional health-related content would be appropriate to include (e.g. information on folic acid, availability of smoking cessation services), and feasible opportunities to intervene.

There are three components to this work:

1) Analysis of policy documents.

We will review UK national policies and guidelines and a number of local policies (based on availability and saturation of core concepts) to understand:

i) How services are expected to approach discussions of weight loss with women who are overweight/obese (e.g. Fertility services BMI thresholds for treatment, NICE public health guideline 27 weight management before during and after pregnancy);
ii) How LARC treatment pathways currently operate;
iii) Guidance on health behaviours prior to conception;
iv) The practical/ethical challenges to successful service delivery in current service structures including equity of access to interventions.

2) Online qualitative survey of women

Qualitative surveys using open-text questions (Clarke and Braun, 2013) will be utilised to understand:

i) How, where and when women currently access pre-pregnancy weight loss interventions;

ii) Women's preferences relating to the experience of being offered pre-pregnancy weight loss interventions;

iii) Where and with whom women discuss issues relating to pregnancy, obesity and weight loss.

Qualitative surveying has been identified as an appropriate method for addressing sensitive subjects in research (Opperman et al, 2014). An online qualitative survey of women of reproductive age who self-identify as being or having been overweight/obese in the past will be advertised through a range of relevant social media platforms (this approach that has proven successful within our research on family planning (STARFamilyStudy; Phillips et al, 2018). A minimum of 200 and a maximum of 500 responses will be collected, depending on the depth of responses and volume of data provided. Once 200 responses have been collected the qualitative research team will decide whether provide sufficient 'information power' to answer our research questions (Malterud et al, 2015), or whether further data should be collected. Data collection will cease when sufficient 'information power' has been generated.

3) Professional engagement (Clinicians and weight loss consultants)

We will attend up to eight relevant professional meetings in order to identify and consult with clinicians who are registered with a letter of competence in intrauterine devices and/or subdermal implants with the Faculty of Sexual and Reproductive Health (FSRH). We will adopt a similar strategy for consulting with group leaders of widely used community based weight loss programmes such as Slimming World and Weight Watchers at organisational events or via individual interview through existing contacts.

Interview guides for clinicians will focus on any pre-pregnancy care provision, the discussion of weight and pre-conception health both generally and in the specific context of LARC removal, challenges to service delivery, equity of access to interventions and their views on the potential for an intervention postponing LARC removal as part of pre-conception weight loss plan. Interviews with consultants for weight loss programmes will address questions of feasibility and their views on the provision of weight loss programmes in the pre-conception phase.

For the events attended individual fieldwork strategies will be adapted to fit the particular context of the event: for example an 'interview pod' may be utilised, being positioned next to an exhibition stand promoting the study and providing space for brief interviews to be conducted with delegates during the professional meetings or organisational events. Alternative strategies include pre-arranged group discussions added to local event agendas and/or a brief on-line survey for event delegates (facilitated through the availability of iPads and online links which enable delegates' own internet-enabled devices access). Where practitioners prefer to participate in interview outside the context of these events, appointments will be made to conduct telephone or in-person interviews in times and locations which do not impact on clinical hours/spaces.

Stakeholder Advisory Groups

At the end of Phase 1 the information gathered will be synthesized to generate potential intervention components and study designs which will be refined through work with two Stakeholder Advisory Groups (SAGs). The service user SAG will comprise of up to 10 women. The service provider SAG will comprise of up to 10 practitioners recruited through the exploratory work in Phase 1 when each participant will have been asked if they were happy to be contacted about the further work of the study. The practitioner SAG will be run as part of a Continuing Professional Development event in order that practitioners can be incentivised to attend but without disruption to clinical activity. Both SAGs will be informed of the current knowledge and guidelines on effective programmes and good practice principles in working on pre-conception weight loss. Both SAGs will work with the research team to generate potential intervention and study designs which are in keeping with the findings of Phase *1* and consider the issue of equity of access to the intervention. They will also consider the key questions to ask participants in Phase 2. The two SAGs will meet again at the end of Phase 2.

Phase 2: Acceptability and feasibility of proposed intervention & study design

During Phase 2 outputs from Phase 1 will be used to address the questions of acceptability and feasibility of a potential weight loss intervention and study design. During phase 1, recruited participants (women and practitioners) will be asked whether they consent to contact for a follow-

up phase 2 interview. Phase 2 interview schedules will be informed by the feedback from the Stakeholder Advisory Groups and the interviews will further test and refine the theories developed in Phase 1. Up to 20 participant interviews and 10 professional interviews will be conducted.

Clinicians who remove LARCs and practitioners delivering community weight loss interventions will be asked to explore their views about the type of intervention, the potential study designs and, for clinicians, their willingness to recruit women to such a study. This will be conducted via individual or group interviews with up to ten clinicians and practitioners. Clinician interviews will be conducted either at professional meetings (e.g. Faculty of Sexual and Reproductive Health, British Association for Sexual Health and HIV, Welsh Sexual Health meetings or, if the clinicians prefer, appointments will be made to conduct telephone or in-person interviews in times and locations which do not impact on clinical hours/spaces.

Individual interviews, by phone or face to face, with up to 20 women who would fit the eligibility criteria of a future intervention study, will explore their views of the acceptability and feasibility of the potential weight loss intervention and study design. Participants will be provided with £10 high street vouchers as a thank you for taking part in the interview.

Following completion of this work, the service user and practitioner SAGs will meet with the research team to discuss findings. At the end of Phase 2 the final report will describe the key design elements of a potential future study or the reasons why such a trial is currently not feasible to deliver.

Theoretical/conceptual framework

The work in WP2 will be guided by the principles of Pawson and Tilley's scientific realism (Pawson & Tilley, 1997). This approach was designed for the evaluation of complex social interventions based on realist understanding of causation which recognises that social interventions lead to outcomes by triggering a reaction within individuals. The way in which individuals respond to interventions is understood to relate both to characteristics of the interventions themselves, and also characteristics of the context into which the intervention is delivered. Realist research focusses on the development of explanatory theories which describe how all of these factors interact using context-mechanism-outcome configurations We will use a range of different sources of data as part of an iterative process of theory development and refinement, recognising that different stakeholders may illuminate different important theories. The resultant programme theory can be used to guide

decisions about which interventions are most likely to succeed in which settings. It could also guide a theory driven evaluation of any future feasibility study.

6.1 Risk assessment

A Study Risk Assessment has been completed to identify the potential hazards associated with the study and to assess the likelihood of those hazards occurring and resulting in harm. This risk assessment has been completed in accordance with the MRC/DH/MHRA Joint project guidance document 'Risk-adapted approaches to the management of Clinical Trials of Investigational Medicinal Products' and includes:

- The known and potential risks and benefits to human subjects
- How high the risk is compared to normal standard practice
- How the risk will be minimised/managed

This study has been categorised as a low risk study where the level of risk is no higher than the risk of standard medical care. A copy of the study risk assessment may be requested from the Study Manager. The study risk assessment is used to determine the intensity and focus of monitoring activity.

7 Site and Investigator selection

N/A

8 Participant selection

Participants are eligible for the study if they meet all inclusion criteria and no exclusion criteria apply.

8.1 Inclusion/ exclusion criteria

Workpackage 1: Routine Data

Participants will be included in routine datasets if they meet the following inclusion criteria and none of the exclusion criteria apply.

Inclusion Criteria:

CPRD: Women of reproductive age (16-48 years old) who have a LARC use/removal Read Code during 01JAN2009-31DEC2018.

SHCD: Women of reproductive age (16-48 years old) who have a LARC use/removal Read Code during 01JAN2012-31DEC2018

Exclusion Criteria:

Records that do not meet the inclusion criteria/not present in CPRD data.

Workpackage 2: Phase 1 online surveys

Participants will be eligible to be included in the online surveys if they self-identify as meeting the following inclusion criteria and none of the exclusion criteria.

Inclusion Criteria:

iv) women of reproductive age (16-48 years old)
v) have experience of using LARC
vi) who think/know either that their current weight would put them in the overweight/obese category or their weight when they were planning a pregnancy would have put them in the overweight/obese category .

Exclusion criteria:

iii) sufficient written English to participate in online surveys and consent to participate in the study.

Workpackage 2: Clinician participant interviews

Participants will be included in clinician participant interviews if they meet the following inclusion criteria.

Inclusion Criteria:

i) clinicians who remove LARC as part of their clinical role

Workpackage 2: Weight loss intervention professional participant interviews

Participants will be included in participant interviews if they meet the following inclusion criteria and none of the exclusion criteria apply.

Inclusion Criteria:

i) professionals who are involved in the management or delivery of weight loss intervention (private or NHS) programmes

Exclusion criteria:

ii) sufficient oral English to participate in qualitative interviews and provide consent to participate in the study.

Workpackage 2: Phase 2 Qualitative participant interviews

Participants who were recruited to Phase 1 online surveys may be recruited to take part in qualitative interviews. They must meet the following inclusion criteria and none of the exclusion criteria.

Inclusion Criteria:

i) women of reproductive age (16-48 years old)

ii) have experience of using LARC

iii) who think/know either that their current weight would put them in the overweight/obese category or their weight when they were planning a pregnancy would have put them in the overweight/obese category .

Exclusion criteria:

i) sufficient oral English to participate in qualitative interviews and consent to participate in the study.

Workpackage 2: Phase 2 Qualitative clinician interviews

Clinicians must meet the following inclusion criteria and none of the exclusion criteria.

Inclusion Criteria:

i) clinicians who remove LARC as part of their clinical role

Exclusion criteria:

i. None

Workpackage 2: Phase 2 Qualitative professional interviews

Professionals must meet the following inclusion criteria and none of the exclusion criteria.

Inclusion Criteria:

i) Weight loss intervention practitioners or managers of weight loss interventions

Exclusion criteria:

ii) sufficient oral English to participate in qualitative interviews and provide consent to participate in the study.

9 Recruitment, Screening and registration

9.1 Participant identification

All participants for WP2 will be recruited by publicity through adverts, posters, websites and leaflets.

Workpackage 2: Online surveys

Our online qualitative survey of women will recruit a purposive sample of women who self-identify as being/having been overweight/ obese and have experience of LARC. We have identified relevant social spaces in online locations from which to advertise the study, including the Maternity Voices network; weight loss forums e.g. A Big Girl's Journey To Lean; Mumsnet; Netmums; Facebook; Twitter, YouTube and Bigbirthers. An advert will also be distributed via Healthwise Wales (a national registry, healthwisewales.gov.wales). The range of online spaces targeted will be purposively broad in order to maximise involvement across a range of demographic backgrounds.

Workpackage 2: Clinician participant interviews

For the clinician interviews, we will undertake interviews with suitably trained professionals attending relevant training and events. Such meetings will include local auditing and training/CPD events, as well as national events such as the regular 'Contraceptive Matters' sessions, and the FSRH Annual Scientific Meeting.

Workpackage 2: Weight loss intervention professional participant interviews

For professionals delivering weight loss interventions, we will use our existing networks to identify group leaders or managers of widely used community based weight loss programmes, such as Slimming World and Weight Watchers, to take part in interviews.

Our qualitative research in Phase 2 will involve interviews with women who would fit the criteria to take part in a future trial, and clinicians and weight loss practitioners who would deliver the future intervention. Participants will be recruited from those who provided consent in Phase 1 to undertake a further interview about intervention design.

9.2 Screening logs

N/A

9.3 Recruitment rates

Workpackage 2-Phase 1

A total of at least 200 responses will be obtained via online surveys with women.

Professionals will be recruited from up to 8 professional meetings over a 5 month period.

9.4 Informed consent

Workpackage 1: Routine data

We will be accessing anonymised data and therefore consent is not required to access the routine data.

Workpackage 2: Online surveys

Participants will be asked to confirm eligibility in the online survey; inclusion and exclusion criteria will be clearly specified in the publicity materials and consent procedure. The participants' electronic informed consent will be obtained online, which will follow the Participant Information Sheet (PIS) and detail all necessary information. The participant will be told to take as much time as required to consider the information before taking art in the study.

Workpackage 2: Clinician participant interviews

A member of the study team will explain the study in detail and will provide the clinician with the PIS and will give sufficient time to consider the information. The participants will be asked to sign a consent form. One copy of signed informed consent forms will be given to the participant but the original copy will be kept in the investigator site file. Participants have the right to refuse to participate in the study without giving a reason.

Workpackage 2: Weight loss intervention professional participant interviews

A member of the study team will explain the study in detail and will provide the professional with the PIS and will give sufficient time to consider the information. The professionals will be asked to sign a consent form. One copy of signed informed consent forms will be given to the participant but the original copy will be kept in the investigator site file. Participants have the right to refuse to participate in the study without giving a reason.

9.5 Registration and Randomisation

N/A for this study design

10 Withdrawal & lost to follow-up

10.1 Withdrawal

WP1: It is not possible to identify individuals therefore it will not be possible to remove records once an extract has been produced. Data are to be aggregated

WP2: Participants have the right to withdraw consent for participation in the study at any time. The participant's care will not be affected at any time by declining to participate or withdrawing from the study.

Participants will withdraw from the study by contacting a member of the study team. Contact details will be provided in study information. The withdrawal of participant consent shall not affect the study activities already carried out and the use of data collected prior to participant withdrawal. The use of the data collected prior to withdrawal of consent is based on informed consent before its withdrawal.

In all instances participants who consent and subsequently withdraw should be requested to complete a withdrawal form or the withdrawal form should be completed on the participant's behalf by the researcher/clinician based on information provided by the participant. A copy of the withdrawal form should be sent to the study manager by email. Any queries relating to potential withdrawal of a participant should be forwarded the study manager.

10.2 Lost to follow up

No follow-up is conducted for study participants.

11 Study Intervention

N/A

12 Study procedures

Workpackage 2: Phase 1 online surveys

Participants will be screened and consented using the online survey. If participants are eligible and have consented electronically, they will be able to complete the online survey. They will be asked to provide contact details for future contact. There will be no follow-up assessments.

Workpackage 2: Phase 1 Professional interviews (clinicians and weight loss consultants)

Participants will be screened and consented face-to-face. If participants are eligible and have consented, they will be asked to complete a short qualitative interview. They will be asked to provide contact details for future contact. There will be no follow-up assessments.

Workpackage 2: Phase 2 Participants and professional interviews (clinicians and weight loss consultants)

Participants and professionals who have previously consented to be contacted will be contacted via email or telephone and asked to take part in a further qualitative interview. Participants will be screened and consented face-to-face or over the telephone. If participants are eligible and have consented, they will be asked to complete a short qualitative interview. There will be no follow-up assessments.

13 Safety reporting

N/A. No safety data is being collected in this study.

14 Statistical considerations

14.1 Randomisation

N/A. There will be no randomisation of data in this study.

15 Analysis

15.1 *WP1: Routine data*

To identify the target population through routine data we will restrict all datasets to women of reproductive age, who attended for LARC fitting or removal during 01 Jan 2009 – 31 Dec 2018 (SHCD will be available from 01 Jan 2012).

For the data requested from the Sexual Health Clinics in Scotland and England we will request these data in an aggregate format at local authority level and will report rates of fitting and removal annually. We will also explore trends in rates by age group at time of fitting/removal, change of contraception method from/to LARC and if recorded BMI category and deprivation quintile. These rates will be compared to those arising from the SHCD in Wales.

For the individual anonymised data from CPRD, rates of fitting and removal of LARC will be calculated (number of LARCs fitted/removed as a proportion of all women of reproductive age); and will be reported over time (either quarterly or annually depending on numbers), by country (to compare rates across the borders); by dataset; by LARC type, and where available, by attendance type (pre-booked vs walk in consultations). We will also be able to compare the case-mix (e.g. age at removal, BMI, deprivation quintile, rural/urban, co-morbidities) of women attending their GP and how they might differ to women who visit a sexual health clinic for LARC removal (by age, ethnicity, and deprivation). We will explore the quality of recording of BMI in all datasets. Previous work in the CPRD show that completeness of BMI has increased over time (to around 77%) and was higher in females, especially in those of reproductive age (Bhaskaran et al, 2013).

Although not all patients will solely attend their GP regarding their LARC, with the large sample provided via CPRD it will be possible to follow those who do. For patients solely attending their GP for fitting or removal of their LARC, the data will allow us to explore the duration of LARC use prior to removal, the changes to contraception use over time and through linking to the Hospital Episode

Statistics (HES) Outpatient data, identify events such as antenatal clinic attendance to explore time from LARC removal to conception. We will also use a Pregnancy Register algorithm available via CPRD that will flag a pregnancy episode related to the women in the cohort (estimated start of pregnancy). Accessing these data will enable a broader understanding of the population for whom this intervention will be targeted and potentially identify those who had a LARC removed for the purpose of planning a pregnancy. It will also allow us to examine how time to conception may differ between BMI and age categories. Additionally we can use the outpatients' data as a way to validate the Pregnancy Register for the sample of practices that we will have HES data. For those where we identify a pregnancy following a LARC removal we will explore the natural distribution of the time lag between these two events to apply a rule to indicate the pregnancy and associated LARC removal was planned.

Whilst we cannot link the data between GP practices and SHCD, we will explore the recording of a LARC removal in a Sexual Health Clinic setting, in the GP notes. Previous work using an alternative primary care data source (the health improvement network - THIN) identified that 24% of LARC related records in primary care came from Sexual Health Clinic letters (Cea Soriano et al, 2015).

15.2 Workpackage 2: Understanding context and stakeholder views

The three sources of qualitative data (survey responses with women and interviews with clinicians and weight loss consultants) from in Phase 1 will be analysed using a combination of deductive and inductive thematic analysis. Deductive codes will be developed with reference to a set of key context-mechanism-outcome configurations identified via the realist theory development process described earlier, and inductive codes will be generated during analysis and within regular qualitative analysis meetings between the qualitative researchers and the appointed Research Associate. Codes will aim to identify (i) essential elements of the intervention; (ii) contextual factors and (iii) barriers and facilitators to acceptability/feasibility.

The findings from Phase 1 of WP2 will be synthesized to generate potential model(s) of intervention and study design. The model and intervention-design process will be informed by and draw upon existing formal theories as identified by the review. For example, we anticipate that the concepts from Normalisation Process Theory (May, 2013), coherence, cognitive participation, collective action, and reflexive monitoring, would be highly relevant. Two Stakeholder Advisory Groups, one comprised of up to 10 women and the other of up to 10 practitioners recruited through the

exploratory work in Phase 1, will be formed. The groups will meet twice, once in each phase. At the end of Phase 1 they will meet with the research team to consider the synthesized findings and advise on the intervention and study development.

In Phase 2 of WP2, the qualitative data from practitioners and service users will be analysed thematically, using deductive codes focused around the developing programme theory and inductive codes when new information arises.

15.3 Cost effectiveness analysis

N/A

16 Data Management

All procedures for data storage, processing and management will comply with the Centre for Trials Research Standard Operating Procedures, CPRD & Public Health Wales data sharing agreements and the General Data Protection Regulation. Data accessed for WP1 will be anonymised prior to receipt and therefore there is no risk of re-identification of patients. All electronic data will be stored on fire walled University servers. Access to files will be through password protected PCs and only accessible to named researchers. Data transfer will be secure using the data providers preferred secure transfer method.

The online survey will be hosted on a Cardiff University secure server and access password protected. A member of the research team will act as administrator.

Consent forms, contacts form and transcripts of interviews will be stored in a locked filing cabinet. Interviews will be recorded on encrypted password protected audio-recorders and voice files will remain password protected and only accessible to relevant members of the research team once transferred to secure Cardiff University servers. Recordings will be transcribed and pseudonymised in line with CTR Standard Operating Procedures. All essential documents generated by the study will be kept in the Study Master File and/or on the electronic Study Master File. Cardiff University demonstrates compliance with current information governance requirements as set out in the Department of Health Policy with an information governance toolkit score valid from 1 April 2018 of 88%.

The Data controllers are CPRD andk PHW. Cardiff University will be the Data Processor.

A Study Data Management Plan will be developed.

16.1 Data collection

WP1: Routine data

Data will be requested from CPRD and Public Health Wales on women of reproductive age who have a code related to LARC use and/or removal. The set of required codes will be developed using the data dictionaries of the datasets and from the literature and will be reviewed by the clinical co-investigators for accuracy and inclusivity of all possible codes. Cardiff University hold an Academic Risk Sharing Licence with CPRD and following ISAC approval, the data will be made available via one of the fob holders of the data analysts working within the university. Data from Public Health Wales will be transferred to Cardiff University servers upon agreement of data release. We will request aggregate Sexual Health Clinic data from Scotland (via National Sexual Health System, NHS National Services Scotland) and England (via NHS Digital).

WP2: Qualitative data collection

We will collect a qualitative data via:

i) a qualitative online survey of women using open-text questions (Clarke and Braun, 2013). Data will be collected on an online survey, developed by the Centre for Trials Research IS team and will be hosted on secure Cardiff University servers.

ii) qualitative interviews with participants, clinicians and professionals delivering weight loss interventions. All interviews will be audiorecorded on encrypted audio-recorders.

16.2 Completion of CRFs

N/A

17 Translational research or sub trial

N/A

18 Protocol/GCP non-compliance

The Principal Investigator should report any non-compliance to the study protocol or the conditions and principles of Good Clinical Practice to the CTR in writing as soon as they become aware of it.

19 End of Study definition

The end of the study is defined as the date of final data capture to meet the study endpoints. In this case end of study is defined as the final stakeholder advisory groups at the end of Phase 2.

Sponsor must notify the Cardiff University school Research Ethics Committee of the end of a clinical study within 90 days of its completion or within 15 days if the study is terminated early.

20 Archiving

The SMF and SSF containing essential documents will be archived at an approved external storage facility for a minimum of 15 years (data sharing agreements will be maintained to allow for the routine data to be archived for this duration). The CTR will archive the TMF and TSFs on behalf of the Sponsor. Essential documents pertaining to the study shall not be destroyed without permission from the Sponsor.

22 Regulatory Considerations

22.1 Ethical and governance approval

Approval will be sought for this protocol from a Cardiff University school Research Ethics Committee. Research Ethics Committee (REC). For the routine data element of the study: data access requests to CPRD and SHCD will be reviewed by the Independent Scientific Advisory Committee and Public

Health Wales respectively; as the data are anonymised, Ethical review is not required for this element of the project.

22.2 Data Protection

The CTR will act to preserve participant confidentiality and will not disclose or reproduce any information by which participants could be identified, except where specific consent is obtained. Data will be stored in a secure manner and will be registered in accordance with the General Data Protection Regulation 2018 and the UK Data Protection legislation 2018. The data processor for this study is Cardiff University.

21.3 Indemnity

Cardiff University shall indemnify the site against claims arising from the negligent acts and/or omissions of Cardiff University or its employees in connection with the study.

21.4 Study sponsorship

Due to the nature of this study, Cardiff University will not formally take on the role of Sponsor-TBC

21.5 Funding

This study is funded by National Institute for Health Research Health Technology Assessment (NIHR HTA) – Project number 17/130/05.

22 Study management

22.1 Project Management

The study will be fully co-ordinated by the UK Clinical Research Collaboration registered Centre for Trials Research, Cardiff University. The study will be managed according to the standard operating procedures of the Centre for Trials Research and contracts established between Cardiff University and the two employing health boards of the co-applicants. The lead applicant will assume overall scientific and financial responsibility for the study and the study manager will be responsible for day to day overview of the study.

22.2 Project Team (PT)

The project team will comprise Dr Sue Channon (CI), the two work package leads (Dr Fiona Lugg-Widger, Dr Heather Strange), the Qualitative Research Associate and the Study Manager. The project team will meet weekly for the duration of the study to review progress and ensure the study is delivered within time and budget and each work package lead will be responsible for the deliverables within their work package.

22.3 SMG (Study Management Group)

A Study Management Group will comprise the lead applicant, co-applicants, including work package leads and patient representative and will meet at least bi-monthly to regularly review study milestones. SMG members will be required to sign up to the remit and conditions as set out in the SMG Charter.

22.4 SSC (Study Steering Committee)

A Study Steering Committee (SSC) to include an expert in obesity in pregnancy, realist methods, complex decision-making, a lay member and a statistician will be established to provide study oversight and report to funders. The SSC will meet prior to the commencement of stakeholder data collection and then plan when it wishes to meet but as a minimum this will be at the end of Phase 1

and at the end of data collection. As the study does not intend to affect the care provided to individual participants it is not planned to have an independent Data Monitoring Committee.

SSC members will be required to sign up to the remit and conditions as set out in the SSC Charter.

23 Quality Control and Assurance

23.1 Monitoring

The study risk assessment has been used to determine the intensity and focus required monitoring of the Plan-it study. Low monitoring levels will be employed and will be fully documented in the study monitoring plan, saved in the SMF. GCP and CTR procedures will be followed.

23.2 Audits & inspections

The study may be participant to inspection and audit by Cardiff University.

24 Publication policy

All publications and presentations relating to the study will be authorised by the Study Management Group. Dissemination of the study results will include publication in a high calibre journal through open access agreement eg BMJ Open, Pilot and Feasibility Studies or BMC Obesity. Depending on the study process, there may be an opportunity to publish papers related to the routine data or a methodologically focussed paper. A plain English summary will be made available to stakeholders via the study website and links posted on the sites which hosted the original surveys. The full report will also be placed on the Centre for Trials Research website when the results are in the public domain via the results paper. The co-applicants will disseminate the results of the study through professional and lay, local, national and international meetings e.g. Society for Academic Primary Care conference, FSRH annual meeting, Society for Behavioural medicine conference.

25 Milestones

Months 0-3: Recruitment of study staff, ethics, quality assurance, set-up attendance at professional meetings, Identify codes for LARC use/removal and ISAC application submitted, request to Public Health Wales submitted

Months 4-10: Data Access and Data cleaning identify core components of potential interventions, study design, barriers and facilitators in LARC pathway for weight-loss intervention via realist review, document review, , on-line survey, attending professional network events. Stakeholder Advisory Groups.

Months 11-17: Data analysis, Establishing acceptability and feasibility through targeted interviews with women and practitioners. Second Stakeholder Advisory Groups.

Months 18: Dissemination and reporting: Final report for funders, Report and plain English summary posted on website, results communicated to stakeholders, publication plan and preparation for publication and presentation.

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27 Appendices

All participant documents will be stored in the electronic SMF.