

A website to help choose contraception: a pilot trial

PROTOCOL

Long title of the trial	Increasing uptake and adherence to long-acting reversible contraceptive (LARC) methods in young women
Short title of trial	A website to help choose contraception – a pilot trial
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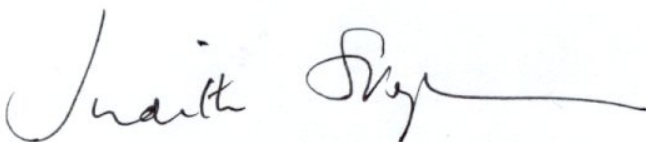
1. SIGNATURES

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles of GCP, the Sponsor's SOPs, and other regulatory requirements as amended.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publicly 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.

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Sign: 

Date: 21/12/2016

Sponsor Representative: Ms Tania West, Research Portfolio Coordinator

Sign: 

Date: 21/12/2016

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4. SUMMARY

Reducing unintended pregnancy is a national and global priority, and improving women's choice of contraception is a vital step. There are many myths, misunderstandings and concerns about contraception, and increasingly women turn to online resources for information on healthcare.

The aim of the study is to develop and test the feasibility of an online trial of a website to increase the acceptability, uptake and adherence to long-acting reversible contraceptive (LARC) methods in young women. LARC methods include the intrauterine device (IUD), intrauterine system (IUS), subdermal implant (SDI) and depo injection.

In Phase 1 of this study (completed) we developed a self-guided website that presents recommended contraceptive options in response to women's preferences. The website will be presented on a touch-screen tablet computer in clinic waiting areas or pharmacy consulting areas.

In Phase 2 (this study), we will assess feasibility of an online trial of the contraception choice website in five sites:

An NHS sexual health service (Margaret Pyke Centre, MPC)

A local general practice

A maternity service (Ashford & St Peter's Hospitals NHS Foundation Trust)

A community pharmacy (Greenlight)

An abortion service (bpas)

Phase Two will take 15 months including:

- Conducting a randomised pilot trial across the five settings
 - Conducting a qualitative process evaluation of the website, of NHS implementation issues and of research procedures
 - Analysis, reporting and dissemination of study findings
 - Preparation of outputs, including a protocol for a definitive RCT to increase uptake and adherence of LARC that is informed by both quantitative and qualitative findings
- In each setting we will recruit 80 women aged 15-30 years (40 randomised to intervention and 40 to control) and follow them up by online questionnaire at 3 and 6 months (or 2 months after delivery for post-partum women).
- *Funder-approved amendment to recruitment.* In addition to the above, we will recruit 530 more women from one site only, the Margaret Pyke Centre, via their Central (telephone) Booking System. Women requesting an appointment for

contraception will be invited to go online and enter the trial before they attend their appointment.

Data collection:

All quantitative data will be collected online. Using methodology we developed and implemented for a the Men's Safer Sex pilot trial, eligibility will be checked with a few screening questions, then eligible women will be asked for informed consent, demographic information, baseline sexual health outcomes, an email address, mobile phone number and postal address. A computer algorithm will automatically assign participants randomly to intervention or control group. All participants will be offered vouchers (by email) worth £20 on completion of follow-up at 6 months.

Funder-approved Amendment to outcomes measures: (this effectively converts the previously secondary outcomes related to contraception into primary outcomes)

The main outcome measures are

- LARC method in use at 6 months
- Satisfaction with any chosen method of contraception at 6 months

Secondary Quantitative Outcomes

- Follow-up rate at 6 months
- Recruitment rate;
- Effectiveness of contraceptive method in use at 6 months
- Pregnancy by 6 months
- Sexually transmitted infection diagnosis by 6 months
- Health service and out-of-pocket costs for contraception and other sexual health services

We will assess the feasibility of collecting the relevant **cost and outcomes** for the website and contraceptive methods provision in each setting including costs to third sector organisations and any out of pocket costs to patients. We will also calculate the cost of the development of the website and number of potential future users to estimate the cost per patient of the website.

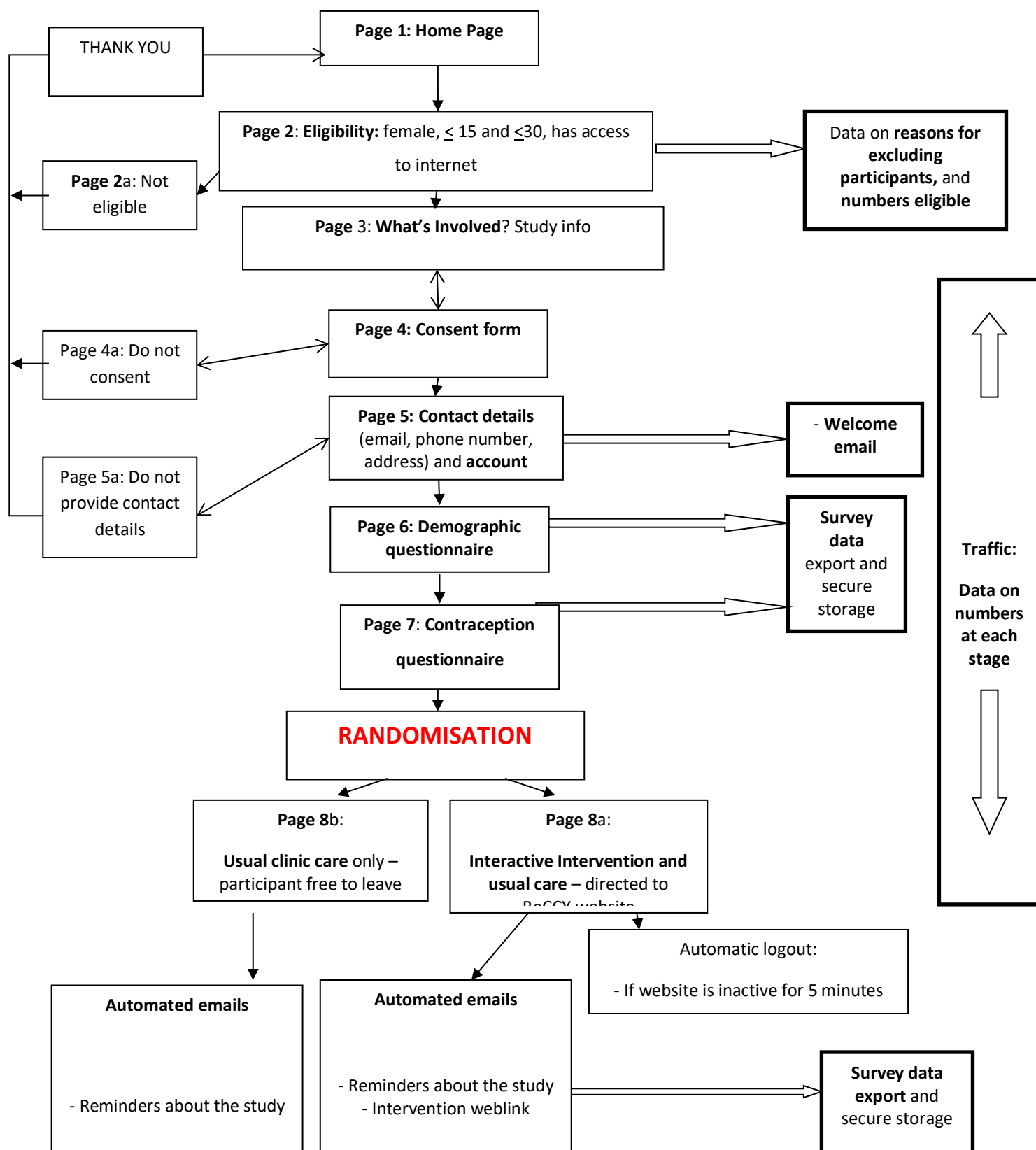
Qualitative Outcomes include

- women's views and experience of the intervention and trial procedures, specifically including socially disadvantaged young people
- provider views about trial procedures, the role of a web-based intervention for contraception, and implications for clinical services .

Assessment of trial feasibility:

Feasibility will be assessed and reported in terms of intervention acceptability and key process measures for a definitive RCT including: recruitment and follow-up rates and qualitative assessment of contextual factors, including comparative ease of implementation in different settings. Particular attention will be paid to aspects of feasibility relating to implementation in routine NHS practice and other clinical settings of a website for contraception choice that can be accessed by tablet computer and/or mobile phone.

5. TRIAL FLOW CHART



Framework of the trial software: online study information, consent, registration, data collection and randomisation

6. INTRODUCTION

Control of fertility is crucial to the health and wellbeing of women, but unintended pregnancy remains common and costly for both health services and individuals. In the UK, despite a range of freely available effective contraceptive methods, abortion rates have changed little over two decades (at around 190,000 per year for women resident in England & Wales). Despite a national teenage pregnancy strategy and recent fall in under-18 conceptions, England still has the highest rate of teenage pregnancy in Western Europe. A key report on the economics of sexual health concluded that it should be feasible to improve contraception and abortion services in ways that better meet the preferences of service users and that this could lead to a net saving of up to £1 billion over 15 years (1). In addition to the economic burden of unintended pregnancy and abortion to the NHS, and the emotional burden to individual women, unintended pregnancy plays a prominent role in persistent health inequalities in the UK and globally.

Preventing unintended pregnancy involves many steps, including timely education, awareness and socially patterned behaviours that lead women to seek, choose and use contraception consistently and correctly. Health services have a key role in supporting women to choose and use an appropriate method that best meets their needs. However, many women are still not aware of the range of different methods available to them. There are widespread myths about contraception, e.g. fears about impact on future fertility, weight gain or the significance of amenorrhoea. The pill and condoms are well known and widely used - by around half of all women on contraception - but they are not the most effective contraceptive methods.

Long-acting reversible contraceptive (LARC) methods, including intrauterine devices, depo injection and subdermal implants, offer women the most effective protection against pregnancy. Women who use oral contraceptive pills, the contraceptive patch, or vaginal ring have a 20 times higher failure rate than women who use LARC methods (2). Nearly a decade ago, NICE concluded that increasing uptake of LARC is more cost-effective in reducing unintended pregnancy than the contraceptive pill or condoms even at one year (3). At that time estimated uptake of LARC in the UK was low at 8% (2003/4 data) compared with 25% for the pill and 23% for male condoms. Since then, uptake of LARC has increased, but only slowly to 12% in the population in 2008/9 and to 30% by 2013 in women attending community contraceptive clinics (4). Even in specialist community services, younger women are less likely to use LARC (24% in those under 30 years) than older women.

There are **multiple pathways** by which women get information about contraception and choose a method. The main sources of information are the internet, family and friends, school sex and relationships education (SRE), general practitioners, community pharmacies and sexual & reproductive health services. However, not all these sources provide information on LARC and uptake of LARC is limited by the number of appropriately trained

doctors or nurses to fit them: many general practices - where 75% to 80% of contraceptive consultations occur - have little or no capacity for fitting and therefore rely on referral to specialist contraceptive services. The emergency intrauterine device (IUD) is much more effective than the emergency pill, but uptake of the emergency IUD remains low and community pharmacies - the first destination for the majority of young women seeking emergency contraception - cannot provide the emergency IUD. Recent surveys show that women's knowledge and experience of post-natal contraception is often poor (Sex and contraception after childbirth. British Pregnancy Advisory Service July 2014). Effective interventions are needed that expand women's choice of more effective methods of contraception, and improve uptake in a variety of settings.

Current **standard care pathways** for contraception vary considerably within and between different settings. Some services provide leaflets (e.g. the Family Planning Association, FPA) explaining the different methods, but the extent to which such leaflets are read, understood or help women reach an informed decision about contraceptive method is unclear. The quality of face-to-face consultation varies widely between different health care providers with different skills, competencies and experience. The evidence base for improving contraceptive uptake and adherence through better face-to-face consultations is slim and mostly disappointing (5-7); our recent Medical Research Council-funded population-based study of why women stop or switch contraceptive methods concluded that traditional consultation with a doctor or nurse in clinic has only modest influence on women's contraceptive decisions.

Health care in the UK is undergoing a **health informatics revolution**. The vast majority of young people have access to digital technology through Internet or mobile phones, which offers huge potential for health promotion. Recent data from the Office of National Statistics (ONS) indicate that 99% of 16-24 year olds have accessed the internet and 88% use it daily (8). We know that younger women are likely to turn to digital resources for information on contraception (9). For the proposed study, we will therefore explore the use of a website that provides information and decision support for contraceptive choices (10-13). The website will be available directly to users for self-guided use, and may be delivered by any digital media, including the internet, mobile telephone, and handheld computers. Access can be private and self-paced, and programmes can be tailored according to individual preferences. Digital interventions are effective at increasing knowledge of emergency contraception (14) and there is evidence of effect on sexual behaviour, (10) contraceptive choice and adherence (11-13). **However, we are not aware of any services in the UK that currently provide interactive digital interventions to support women's contraceptive decision making.** Our intervention development field-work has confirmed that women and health providers support the idea of a website for contraception choice, to be offered in clinic settings.

The proposed research is timely because it aims to provide women with better information and support to make informed choices about contraception that may have long-lasting effects on their health and wellbeing. Evaluating interventions that can be implemented within busy settings providing contraception services to improve informed choice, access, uptake and adherence to effective contraceptive methods, including LARC, which is a key priority for the prevention of unintended pregnancy in the UK.

In Phase 1 of this study a **systematic review** was undertaken to review evidence on individual level education or decision aid interventions relating to acceptability, uptake and adherence to contraception, including underpinning theories and user and provider views. In addition, we conducted a qualitative evaluation of women's views of contraception, with a focus on contraceptive myths and misconceptions on social media sources such as Youtube and various online forums.

Health professionals from each of the five study settings (GP practice, sexual health clinic, maternity ward, abortion service, and community pharmacy) were interviewed using a semi-structured interview, to gather information on their views of women's contraceptive knowledge and needs, and the perceived challenges to supporting and understanding contraceptive decision-making, to hear their experiences of existing websites (if any) and their preferences for future websites as well as to understand how a website can complement, enhance or replace and/or fit with established services. In addition, an **expert workshop** was facilitated in order to gain insight on intervention content from a wider range of professionals, including experts in e-health, psychology, decision aids and human-computer interaction.

Women aged 15 to 30 were invited to either focus groups or individual interviews to gather insight into their contraceptive beliefs, experiences, when, where, why and how they access information on contraceptives, and how they make personal choices and decisions around contraception.

Findings from the social media evaluation, qualitative interviews with health professionals as well as focus groups and interviews with women from each of the five study sites were in line with each other, so sampling stopped once data saturation had been reached.

Our **main findings** were that:

- Women don't fully understand contraceptive side-effects
- There tends to be an underestimation of contraceptive benefits and an overestimation of contraceptive side-effects
- The 'unnaturalness' of hormones is by far the most common concern
- Infertility, irregular bleeding, no periods, and cancer are side-effects women are also particularly worried about

- Partners' views are important to women
- Many women think it is unhealthy to skip periods
- Many women think their bodies need a break from contraception
- Women like seeing honest videos of other women talking about their experiences of contraception
- Women don't like seeing too much text on a website and would prefer to have options for more information if they wish to know more

The intervention website

We have integrated the findings from the systematic review, women's views on social media, the expert workshop, and interviews with women and health professionals, to develop a trial-ready self-guided website that presents a number of contraceptive options in response to input of women's preferences and concerns. The website will be ready for launch in January 2017.

7. AIM AND OBJECTIVES

The aim of the study is to develop and test the feasibility of an online trial of a website to increase the acceptability, uptake and adherence to long-acting reversible contraceptive (LARC) methods in young women. LARC methods include the intrauterine device (IUD), intrauterine system (IUS), subdermal implant (SDI) and depo injection.

The objectives are:

Phase 1 (completed)

1. To systematically review evidence on individual level education or decision aid interventions relating to acceptability, uptake and adherence to LARC, including underpinning theories and user and provider views.
2. To obtain the views of contraceptive service users and providers in six settings (general practice, sexual & reproductive health services, abortion services, maternity services and community pharmacies) relating to access, acceptability, uptake and adherence to LARC
3. To apply the information from objectives 1 and 2 to identify the key design issues and content for an interactive digital intervention (website) and an appropriate comparator
4. To co-develop the website with young women (through focus groups and interviews) and healthcare professionals (through an expert workshop)

Phase 2

5. To conduct a randomised pilot trial of the website in five different service settings (general practice, sexual & reproductive health service, abortion service, maternity service and community pharmacy).
6. To conduct a qualitative process evaluation with women and clinic staff, to assess the acceptability of the trial procedures, women's views of the intervention itself and implementation considerations.
7. To write a protocol for a definitive trial of an interactive digital intervention (website) to improve informed choice of contraception and the acceptability, uptake and adherence to LARC methods in young women.

8. OUTCOMES

Funder-approved Amendment to outcomes measures: (this effectively converts the secondary outcomes related to contraception into primary outcomes)

Primary Outcomes

- **LARC method in use at 6 months** - measured by response to study outcome questionnaire
- **Satisfaction with any chosen method of contraception at 6 months** - measured by response to study outcome questionnaire using a Likert scale 1-5. *How satisfied are you with the contraception you are using currently?*

Secondary Quantitative Outcomes

- **Follow-up rate at 6 months** after randomisation
- Recruitment rate - measured via the trial website as the time taken to recruit (up to 80) women in each site. Recruitment is assessed by completing (in full or in part) the baseline questionnaire.
- Effectiveness of contraceptive method in use at 6 months - measured by response to study outcome questionnaire and grouped as follows from least to most effective: no method; withdrawal or natural method; condoms or diaphragm; pill, patch or ring; LARC or sterilisation
- Change in method between baseline and 6 months, indicating whether any change is to a method of greater, lesser or similar effectiveness (based on grouping above)
- Pregnancy by 6 months – measured at 3 months and at 6 months by response to study outcome questionnaire
- Sexually transmitted infection diagnosis by 6 months – measured at 3 months and 6 months by response to study outcome questionnaire.

Health service and out-of-pocket costs for contraception and other sexual health services - measured at 3 months and at 6 months by response to study outcome questionnaire

Secondary Outcomes – qualitative

- Patient views and experience of the intervention and trial procedures, assessed through qualitative interviews at 2 weeks after randomisation with five women at each study site (total 25 interviews) (See Topic Guide). Questions to be explored include:
 - Are the online trial procedures acceptable to participants? E.g. the process of online registration and consent, the receipt of incentives, completing online questionnaires, contact and follow up by email and text
 - What are women's views of the intervention?
 - How might trial procedures be improved, to optimise retention in a full-scale trial?
- Provider views about impacts on the service and trial procedures, assessed through qualitative interviews with 15 key staff in total (3 per site), sampling those who have roles in facilitating the study in each setting (e.g. receptionists, practice managers, nurses, midwives, doctors and pharmacists) (see Topic Guide). Questions to be explored include:
 - Are recruitment procedures acceptable to staff?
 - How might recruitment procedures be improved, to optimise recruitment to a full-scale trial?
 - What are staff views on the feasibility and usefulness of a contraception decision website in each clinic setting?

9. SAMPLE SIZE and RECRUITMENT

The original target sample size of 80 participants in each of the five settings was based on estimating an expected follow-up rate at 6 months of 70% to within 10% precision (95% CI 60% to 80%) for each setting. This sample size also provided 80% power to detect a significant difference (at the 5% level) in the follow-up rate between two settings if the true difference is 22% (e.g. 59% vs. 81%). By pooling data across settings this sample size also provides 80% power to detect a significant difference (at the 5% level) in the follow-up rate between the intervention and standard arms if the true difference is 15% (e.g. 62.5% vs. 77.5%). The expected follow-up rate is based on a previous sexual health study that recruited and followed-up the participants online (Sex Unzipped).

Funder-approved amendment to sample size:

A further 530 participants are to be recruited from one existing site, though recruited in a different way (from the central booking system). Together with the original target size this

leads to a total of 930 participants. This new total sample size is calculated to provide power to assess the effect of the intervention on the revised primary outcome which is uptake of LARC at follow-up. Specifically, assuming a follow-up rate of 70%, this sample size provides at 82% power to detect as significant (at the 5% level) an increase from 35% (control group prevalence) to 47% in LARC use due to the intervention.

The recruitment period of 6 months is based on:

- the volume of patients attending each of the study sites, which is high i.e. hundreds or dozens of women per week in four sites - GP, SRH, maternity service and bpas- and at least 30 women per month in the pharmacy,
- the proportion of women invited to take part in the study who accept which, given the financial incentives to take part, is expected to range from 20% to 30%.

Sites

Category	Name	Details
Sexual and Reproductive Health Service	Margaret Pyke Centre	44 Wicklow Street, London WC1X 9HL
Abortion Service	British Pregnancy Advisory Service	BPAS London East. 32-36 Romford Road, Stratford, London E15 4BZ.
Community Pharmacy	Green Light Pharmacy Shepherd's Bush	228-230 Uxbridge Road, London W12 7JD
Maternity Service	Ashford & St Peter's Hospitals NHS Foundation Trust	St Peter's Hospital, Guildford Road Chetsey Surrey KT16 0PZ
General Practice	General Practice in Camden and Islington	<i>Clerkenwell Medical Practice Finsbury Health Centre, Pine Street, London, EC1R 0LP (to be confirmed)</i>

These five clinical settings were chosen because, together, they provide contraceptive care for the great majority of women in the UK. In addition, they include services that provide care for women at highest risk of unintended pregnancy (i.e. those who attend abortion services or seek emergency contraception through community pharmacies). Development of interventions that are feasible and acceptable to women and providers in these settings therefore has the greatest potential for impact.

10. TRIAL DESIGN

This pilot is an individually randomised, parallel group trial.

10.1. Inclusion and exclusion criteria

Inclusion criteria:

Women aged 15 to 30 years with a need for current or future contraception, attending one of the study sites, able to read English, with an active email account and access to the internet.

Exclusion criteria:

Women unable to provide informed consent (e.g. severe learning difficulties). Women needing a language advocate to understand English since the intervention content is intended to be accessed in private.

10.2. The Intervention

There are four main contents to the intervention. 1) General information on contraception, including information on each method as well as contraceptive benefits and side-effects and other common concerns. 2) Videos of women as well as health professionals discussing contraceptive experiences, concerns and misconceptions. 3) An interactive tool to help women chose a method of contraception which provides individually tailored results. 4) A page offering a link to NHS clinic finders as well as links to other useful resources, such as further information on sexual health, or websites offering support and advice for sexual abuse for example.

The website was based on evidence from the literature, qualitative interviews with men, and discussions with clinical and academic experts in sexual health. The development process was iterative, incorporating a high level of user involvement. The intervention is designed to be delivered initially in clinic, but also providing (and encouraging) access for the intervention group after patients have left clinic. This is to allow the intervention to be integrated into the clinic pathway, and also to take advantage of a 'teachable moment' when patients are engaged in thinking about their health, and so may be more amenable to behaviour change.¹⁵

The intervention comprises a website, displayed on a 'tablet' computer. Whilst in clinic, users allocated to the intervention group will be asked to work through a tailored package of individualised website content. After leaving clinic, the website will be available for them to re-visit and explore freely, and will be accessible on mobile phones as well as desktop computers.

Women randomised to the intervention group will be taken through a series of questions designed to identify appropriate method(s) that best suits individual preferences e.g. for a non-hormonal method, or one that does not require insertion by a health care professional, or one that is invisible, or one that can be forgotten about once inserted.

The website will give information to address women's concerns and barriers to uptake of LARC. A contraceptive choice tool will take account of women's views and preferences on the benefits and side effects of contraception and three suitable contraceptive options will be recommended with brief annotation, that can be emailed, texted to a mobile phone and used in a subsequent consultation and / or taken home.

Women randomised to the control group will be thanked for their participation and will then access standard contraceptive care only. All women in both intervention and control groups will be asked by automated email to complete the same outcome questionnaires online at 3 and 6 months (or 2 months post-partum). The control group will be offered access to the intervention website at the end of the study (after completion of 6 month follow-up).

10.3. Procedure

On arrival at each of the sites, female clinic users will be given a flyer about the trial by the reception or research staff. This will give very brief information about the study, indicating the inclusion criteria (See flyer). This information will also be available on posters within the waiting room and the clinic rooms (see poster). Flyers and posters will direct participants to the tablet computer in the waiting room, or suggest that they approach the researcher (trial manager) or research nurse, if they are available. Clinic staff will also be asked to talk to eligible patients about the research, give them a flyer with brief information (if they have not already received one), and refer them to a member of research staff or directly to the tablet device, if interested.

Where possible, recruitment will be self-directed, using a tablet computer (e.g., iPad), which will be available in the waiting room (this will be secured to prevent theft). The trial software will be set-up to allow participants to be taken through the steps of screening, consent, automatic randomisation, data collection, and intervention viewing, without assistance from the staff. The trial manager (AG) or a member of clinic research staff will be present most of the time to assist and answer questions regarding trial registration only (not concerning clinical questions). When research staff are not available, a mobile number for the trial manager (AG) will be provided for potential participants' questions. The online recruitment and consent procedures are based on those from two previous online trials conducted by members of the study team: the Sexunzipped online trial and the Men's Safer Sex online trial.^{16,17} In both of these studies, attracting participant interest was straightforward. Participants found the enrolment procedures and baseline questions onerous and time-consuming, and so we have streamlined the online trial software, and

minimised the number of questions asked at baseline and follow-up (see online trial software framework and outcome questionnaires). We will maximise follow-up rates by using three routes to contact participants (with participant permission): by email, mobile phone, and by post. Evidence suggests that online trials are an efficient method of conducting clinical trials of low-risk interventions, and such methods are acceptable to participants.¹⁸ Furthermore, online recruitment methods in trials of online interventions can improve the validity of the findings.¹⁹

The tablet device in the clinic waiting room will only allow patients to use the trial-related software and the intervention website (no other websites), and they will be led sequentially through the steps of recruitment and consent (see Figure 1). Initially, participants will be given some brief information about the trial and an invitation to participate. Then, they will be asked to complete a screening questionnaire to determine their eligibility for the trial^a. Those who are ineligible at this point will be informed of this, and thanked for their time. Those who are eligible will receive detailed information about the study^b. At this point, participants will be told that they can ask the research staff any questions regarding registering for the trial that they may have, and will be offered the mobile number of a member of research staff, in the case that none are available on site. If necessary, participants will be taken to a side room to discuss any queries regarding research participation. Participants will then be directed to a screen where they will give informed consent by agreeing to a number of statements (e.g., that we may contact them by email, mobile phone and post, that they understand what is involved, and that they agree to take part). Patients who do not consent (i.e., they do not agree to all the statements), will be informed that they cannot participate, and thanked for their time. Participants will be allowed a reasonable amount of time to decide whether they wish to consent, as they will be permitted to return to the tablet at any point during their clinic visit. However, as the intervention is designed to be integrated into the clinic journey, participants must sign up to the study before leaving the clinic.

Participants will then be asked to give their contact details (email address, telephone number, and postal address), in order to contact them for follow up assessments, to send the intervention group reminders to view the website, and to remind them that they are participating in the trial, and to send an electronic voucher to recompense participants for their time. Participants will be given the option not to give some of this information; however an email address is compulsory, to contact them for follow-up assessments. Participants who decline to give an email address will be excluded from the study.

^a This information will be completely anonymous, as participants will not be asked to give any personally identifying details. This data will only be stored for information regarding recruitment and exclusion

^b if they choose to participate, this will be sent to them via email for future reference

Demographic and baseline sexual health data will then be collected (see '*Measures*'). Participants will be given the option to withdraw from the study at any time after giving consent. All follow-up emails that participants receive will include a link to allow them to withdraw from the study, including one which will be sent to them immediately after registration.

Funder-approved amendment to recruitment

In addition to the recruitment above, we will recruit an additional 530 women from one site only, the Margaret Pyke Centre, via their Central online Booking System. Currently, when women request an appointment for contraception, they are directed to the Trust website to book their appointment. For this study, women will be informed on the Trust website that the clinic is taking part in a study to improve information about contraception, and inviting them to go online (by clicking on a hyperlink) and see if they want to take part in the study before they attend their appointment. Clicking on the hyperlink will take women to the trial website from where all procedures are the same as above.

It is routine practice at the Margaret Pyke Centre to send patients a text message to confirm their appointment. For this study, women who have booked a contraceptive appointment will be sent an additional text informing them that the clinic is taking part in a study to improve information about contraception, and inviting them to go online (by clicking on a hyperlink) and see if they want to take part in the study before they attend their appointment. Clicking on the hyperlink will take women to the trial website from where all procedures are the same as above.

Randomisation procedures

A randomisation list will be generated for the trial by a random number based algorithm in the computer software Stata. This list will be incorporated into the trial software programme before the trial begins, to allocate all participants to either the intervention or control condition. This allocation will be unalterable. Allocation will be concealed until the point of allocation, which will be immediate.

Participants allocated to the control condition will be notified that they have not been selected to view the intervention and told they will be contacted again in 3 and 6 months (or two months post-partum) to gather follow-up data. Those allocated to the intervention condition will be directed to the intervention website. Patients may stop viewing the website whenever they wish, and buttons will be included on the web pages to exit, recording whether they exiting because they want to (e.g., if they're bored), or if they are being called in to see the clinic staff. This data will be recorded, in order to give information about feasibility of website usage in practice.

For patients recruited through the MPC Central Booking Office there will be a variable interval of a few days before they attend their clinic appointment. All other registration and

intervention viewing is designed to take place in the waiting room, whilst patients are waiting to be seen by the clinic staff. This is designed to mimic how the intervention may work in practice – it can be offered to patients on arrival, so that they can complete activities in the time that they are waiting (often up to an hour).

At three and six months after their initial clinic visit, participants will receive an automated email requesting them to complete a follow-up questionnaire (see ' , including a link to the online questionnaire (see Appendix, outcome questionnaires). If they do not complete the questionnaire, they will receive 4 further email prompts, at one-week intervals, and two text messages to their mobile phone (including the web link to the online questionnaire). If participants still do not respond, the researcher will telephone these participants, reminding them about the questionnaire and offering them the opportunity to complete it over the telephone. Finally, non-responders will be sent outcome questionnaires by post (once only).

10.4. Questionnaire Measures

Demographics:

Participants will be asked to complete a demographic questionnaire at baseline, which will assess relationship status, age, employment status, and ethnicity (See Demographic questionnaire).

Contraception questionnaire:

Participants will be asked to complete a questionnaire at baseline, and at 3 and 6 month follow-up to assess what contraceptive methods, if any, they are using currently or have used before (baseline) or since enrolling in the study (at follow-up). Participants who are currently using contraception will be asked how satisfied they are with the method. At follow-up only, participants will be asked if they have had a pregnancy and, if they have, the outcome of the pregnancy (ongoing, gave birth, miscarried, terminated, or prefer not to say). All participants are asked at baseline, 3 and 6 months, whether they have been told by a doctor or other health professional that they have a sexually transmitted infection.

Service use related to contraception and sexual health:

Participants will be asked to specify where they go to get their contraception and if they pay for it themselves.

Interaction with the intervention

In order to assess engagement with the intervention (and whether this is related to outcome), we will record website usage. The software used will record the number of times

each user visits the site, the amount of time spent on the site, the pages visited, and the amount of time spent on each page.

Methods to protect against sources of bias

Participants will provide baseline data on the tablet device before randomisation. Once eligibility for the study is established, and baseline data are collected, allocation to intervention or control group will be determined from the randomisation list, and this will not be changeable by participants or researchers. Subsequent outcome data will be collected online using an emailed weblink to the online outcome questionnaire. Data will be saved on an encrypted server, and data exported will be identifiable by study ID numbers only. Most data collection procedures are therefore automatically blind to allocation to intervention or control group, since they are automated. Sealed envelope will grant access to group allocation only to those who need to know, to for data analysis.

To maximise retention, we plan to make phone calls to non-responders (conducted by the trial co-ordinator), and it could be that group allocation is revealed by participants during the phone call. Data analysis for the primary outcomes will be conducted by statisticians who are blinded to group allocation.

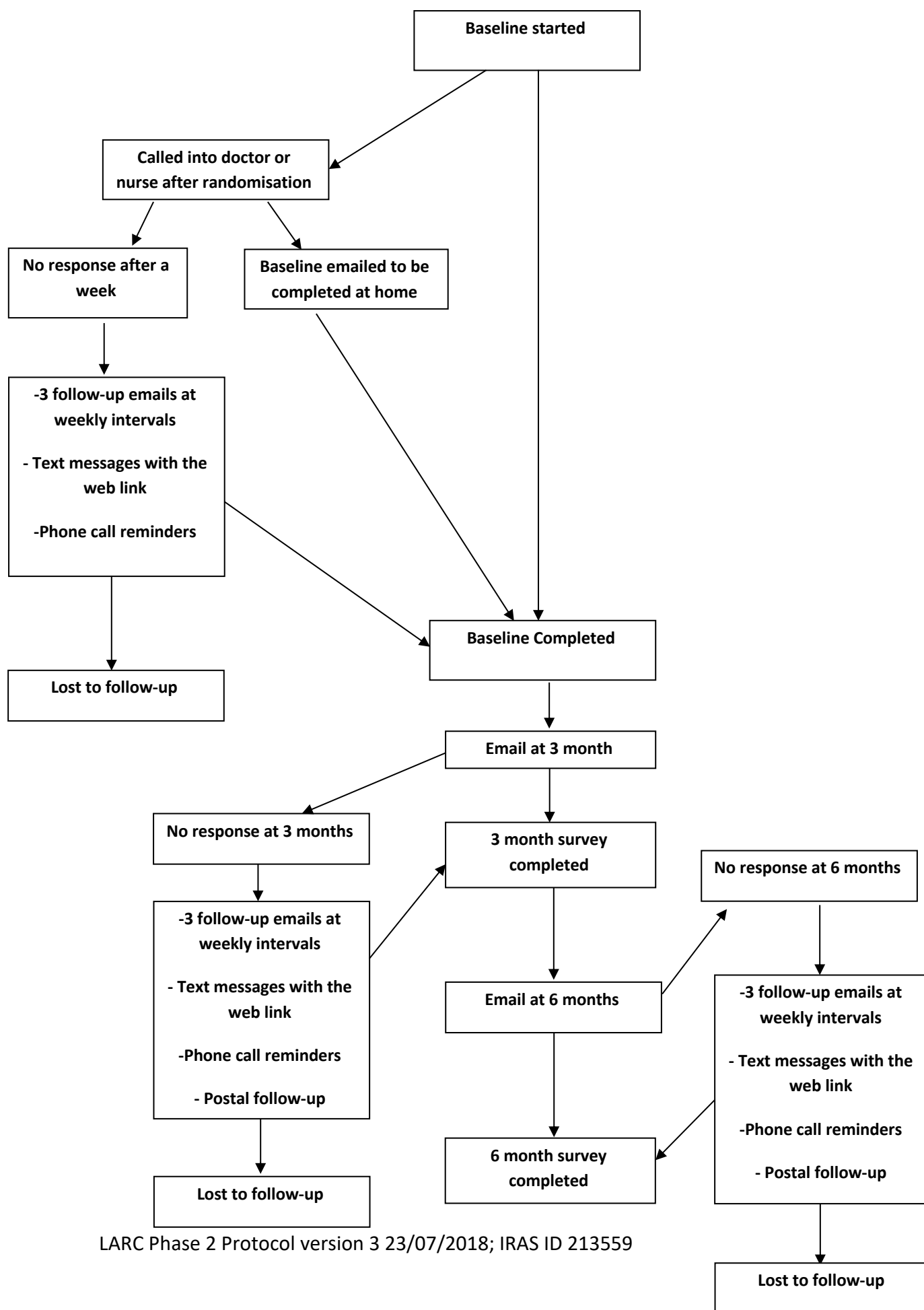
Maximising retention

Our experience in the Sexunzipped and Men's Safer Sex online RCTs indicates that follow-up by email is acceptable to participants with email accounts. The Txt2Stop smoking reduction trial obtained their excellent follow-up using multiple methods of contacting people;²⁰ similar methods will be used for the present study:

1. Automated Email, with 3 further follow-up emails at weekly intervals
2. 2 text messages – at the same time as the last two emails
3. One phone call a week after the final email
4. One final questionnaire by post

We will offer participants a £10 voucher for filling in the online questionnaire at 3 months, and a further £10 for the 6 month follow-up questionnaire. Incentives (a shopping voucher) will be sent by email.

Figure 2 Follow-up procedures



10.5. Pilot trial: Statistical analysis plan

This is a pilot RCT with original primary aim of assessing the success of recruitment and retention, engagement with the intervention, and the acceptability of trial procedures to participants and clinic staff. Power calculations were performed based on data from the Sexunzipped online trial, and were described earlier.

Following the amended recruitment plan our analysis now focuses on the effect size for key outcomes including contraception choice, and satisfaction with contraceptive method.

Statistical analysis

Primary analysis will be by modified intention-to-treat – basing analysis on those who complete at least one follow-up outcome questionnaire. For each outcome listed earlier we will present the percentage of participants if the outcome is binary (e.g. use of LARC) or ordinal (e.g. effectiveness of method, satisfaction with method) and the mean if the outcome is a score (e.g. quality of life) together with a 95% confidence interval. These percentages and means will be reported separately by intervention and standard care arm, and in the case of follow-up rate and recruitment rate by setting.

To formally assess differences between arms we will use logistic regression (for binary outcomes), ordinal logistic regression (for ordinal outcomes) or linear regression (for scores) reporting adjusted intervention effect measures with 95% confidence intervals.

The primary outcome of LARC use at 6 months will be analysed among women in need of contraception (not pregnant or currently trying to become pregnant) and the primary outcome of satisfaction with method will be analysed among women who are using a method at 6 months. The primary outcome of LARC use at 6 months will be analysed stratified by LARC use at baseline, leading to three intervention effects: the effect in baseline LARC users, the effect in baseline non-users, and the overall effect adjusted for baseline LARC use. In the event that over 90% of baseline LARC users in the control arm are using a LARC method at 6 months (or no longer need contraception) then the primary effect measure for this outcome will be the intervention effect in non-LARC users as there is limited scope for improvement due to the intervention in the baseline LARC users. If conversely fewer than 90% of baseline LARC users in the control arm are using a LARC method at 6 months then the primary effect measure will be the overall adjusted intervention effect. A further subgroup analysis will be conducted for both primary outcomes to assess, based on testing an interaction term, whether the effect of the intervention varies by setting.

Primary comparisons between arms will be based on multiple imputation where outcomes at 6 months are imputed based on outcomes at 3 months for those participants who completed the 3 month outcome questionnaire but failed to complete the questionnaire at 6 months.

Health Economics

The primary analysis will be a budget impact analysis of the website and contraception reporting the total costs to each payer (NHS (primary care versus secondary care), local government, private and out of pocket). This will be reported as total cost of contraception and pregnancy outcomes for a range of different population sizes. The analysis will conform to the ISPOR good practice guidelines for budget impact analysis.²¹

Costs will include the cost of contraception (NHS and out of pocket costs), including the cost of LARC implants, sexual health service use, sexual health related primary and acute care use and the cost of pregnancy related outcomes. Resource use collected as part of the trial will be costed based on published sources including Personal Social Services Research Unit (PSSRU) reference costs and British National Formulary. The cost of the website will include ongoing maintenance costs and how these might be incurred by organisations that wish to use the website in the future. This cost will be reported for a range of different population sizes. Any costs that each setting might incur implementing the website will also be collected and reported. In addition to the budget impact analysis of total cost for each payer, we will report descriptive statistics for each cost type. We will calculate the average total health care cost of contraception per participant for the website compared to current practice at baseline and 6 months. 95% confidence intervals for each analysis will be reported based on suitable regression models and bootstrapping.

Recent work by Public Health England has also investigated the Return on Investment of contraception. This work includes 10 year costs of unintended pregnancies. Data from this tool will be used to calculate the wider 10 year costs of the contraception choices website compared to current practice for each payer.

10.6. Ethical Issues

Potential ethical issues and safety reporting

This project aims to improve women's informed choice of contraception. We expect the trial to benefit trial participants as well as wider society.

Participants will receive detailed study information online while being led through the consent process on the trial software, including risks and benefits. Participants will have the chance to ask the researcher any further questions, to ensure that their consent is adequately informed.

As for phase I of the study, we feel that it is very important to take into account the views of women from the age of 15 in the evaluation of our website for contraceptive choice because approximately a fifth to a third of women have had sexual intercourse before the age of 16 and we want this study to help inform young women's first thoughts and choices

about contraception. A substantial proportion of women attending specialist contraceptive services in particular are aged 15.

We will assess capacity to consent to the research (as for all women that we invite), by offering written study information and by answering any queries about the research. Young women may wish to discuss this with parents or guardians, and time will be offered for any participants to discuss the study with others. However, if women under 16 wish to discuss the study with others before registering, they would need to return to the clinic site in order to register, as registration can only be done through one of our project sites. In addition, we will not *require* parental consent, since young women may be excluded from the research if parental consent was required. We have extensive experience of conducting sexual health research with women aged under 16 who are able to give informed consent about participation without a parent or guardian's consent.

To investigate the possibility that women in the study may have switched from a barrier method (that protects against STI) to a non-barrier method (which might increase the risk of acquiring an STI), we ask about diagnosed STI at baseline and follow-up.

In addition, contraception may be viewed as a sensitive or embarrassing topic by some people, although the study questions about contraception do not differ from those that are asked in routine contraceptive consultations. However, we also ask three questions to assess sexual health and quality of life: these refer to 'sexual performance', 'sexual relationship' and 'sex life'. If participants express discomfort, anxiety or distress while completing the questionnaire, this will be reported by the researcher or clinic / pharmacy staff (depending on who is present) as an adverse event in accordance with PRIMENT SOP-022. If a participant experiences an adverse event, such as feeling acutely dizzy or nauseated while using the intervention website, the researcher or clinician will assess whether this is likely to be causally related to the intervention or questionnaire and record it as an adverse event (non-causal) or an adverse reaction (causal). The duration of symptoms will also be recorded. We will be inviting comments about adverse events in free-text boxes on outcome questionnaires, and the trial manager may also become aware of problems resulting from the research via emails from participants. These sources of information will be monitored twice a week, and action taken if appropriate (see below).

All participants will be able to report any negative experiences relating to participation in the trial at any time, and they will be encouraged to report any such experiences as part of the final follow-up questionnaire. Participants who withdraw from the trial will also be invited to report any negative experiences relating to their decision. Any negative experiences will be considered adverse events in the trial.

We will discuss all concerns with at least one other member of the research team, and consider referral to social services if this is felt to be in the person's best interests (even if this is against their wishes), particularly if they are under the age of 18.

10.7. **Method: Qualitative evaluation of trial procedures**

The main aim of qualitative evaluation is to provide a patient and staff perspective on trial procedures, to inform the optimum design of a future full-scale RCT.

We will conduct qualitative interviews with 1) a sample of **trial participants**, and 2) **staff members** at each of the research sites, to assess the following:

Women's views:

- Are the online trial procedures acceptable to participants? E.g. the process of online registration and consent, the receipt of incentives, completing online questionnaires, contact and follow up by email, text and post
- What are women's views of the intervention?
- How might trial procedures be improved, to optimise retention in a full-scale trial?

Clinic staff views:

- Are recruitment procedures acceptable to staff? E.g., the process of referring patients to register electronically for the study, identifying suitable patients
- How might recruitment procedures be improved, to optimise recruitment to a full-scale trial?
- What are staff views on the feasibility and usefulness of a contraceptive choice website in each clinic setting?

Sampling Women: Once we have reached our target recruitment (400 women), we will enrol a further 40 women (eight from each site) into the trial. Participants in this study will have the same experience of the research as those in the pilot trial, except for the following:

- **Accelerated follow-up and interview:** the 40 participants in this qualitative process evaluation will be emailed a link to the follow-up online questionnaire at two weeks only, instead of at 3 and 6 months.
- **Qualitative interview:** Consent will be sought to interview 4-5 participants at each site at one month after the 2-week follow-up questionnaire or one month after giving birth for post-natal women.

Women consenting to take part in this qualitative study will be offered a £10 voucher (delivered via email) for completing the 2-week online questionnaire, and an additional £20

cash token of appreciation if they are also interviewed (which will cover any necessary travel expenses).

Sampling Clinic Staff: A sample of 15 staff members at different grades will be selected from the research sites (three per site). We will identify relevant staff to interview, i.e. those who have had most dealings with the intervention. Clinical staff are not expected to identify these individuals by themselves.

Data collection: All interviews will be audio recorded and transcribed, with participants' permission.

Data Analysis: Data will be coded thematically and analytic notes made, focusing on areas defined by the topic guide as well as emergent themes.

Invitation to interview

Following collection of two-week follow-up data, (or after failure to respond to repeated invitations to complete the follow-up questionnaire), potential participants will be sent an email inviting them to participate in an interview. A study information sheet will be attached. Those who express an interest will be contacted by telephone to give more information and arrange an interview.

Those who do not respond to the initial email will be sent an additional email one week later. Those who do not respond to the additional email will be contacted by telephone after one week. This will ensure that participants who may have changed their email address will still be given the opportunity to participate in an interview. One further attempt will be made to contact participants by telephone if there is no response.

Staff

All staff members involved in the recruitment to the trial will be invited verbally, via email, or via telephone to participate in an interview.

Inclusion/exclusion criteria

Participants

Women aged 15 to 30 years seeking contraceptive care or otherwise at risk of unintended pregnancy, attending one of the study sites for contraceptive advice or supplies, able to read English, have an active email account and access to the internet. (Same criteria as above for the pilot trial).

Staff

Sexual health clinic staff members will be eligible for interview if they were involved with the trial recruitment processes in any of the three research sites (e.g., handing leaflets to participants, identifying and inviting suitable patients, assisting in the registration and consent process).

Procedures

All interviews will be conducted by a research associate from UCL who was not involved in the trial conduct in any way.

Participants

Participant interviews will be conducted either at clinic site premises in a side room, at locations within UCL, or via telephone or Skype. A mutually convenient time and place will be arranged with each participant. On arrival at the interview, participants will be asked to re-read the information sheet (which they will have previously received via email), and asked to sign an informed consent form. Those who participate in a telephone or Skype interview will be asked to submit a signed consent form via post, fax, or email in advance of the interview. A semi-structured interview schedule will be used to guide the interview, to promote exploration of participants' experiences of being involved in the trial and their opinions of the content and usefulness of the intervention website (see Topic Guide). All interviews will be audio recorded and transcribed, with participants' permission.

Staff

Staff interviews will largely be conducted at the clinic sites in a side room; however, some may be conducted via Skype or telephone. A mutually convenient time for the interview will be arranged. Staff members will be given an information sheet prior to the interview, and will be asked to sign an informed consent form before the interview commences. A semi-structured interview schedule will be used to guide the interview, to promote exploration of staff members' experiences of being involved in the trial, and their views of the feasibility and usefulness of a sexual health website in the waiting room of a sexual health clinic (see Topic Guide). All interviews will be audio recorded and transcribed.

Materials

A semi-structured interview schedule will be used for the interviews, with different versions for participants and staff members. The interview schedule for the participant interviews will assess opinions of the trial in general, knowledge about the trial purpose (to assess remembering), opinions of the online registration and consent process, opinions of the online questionnaires, and opinions about contact by email, text message, telephone or post. Those in the intervention condition will also be asked their opinion of the intervention website. Those in the control group (who received usual clinic care) will be shown the website and asked their opinions of it.

The interview schedule for the staff member interviews will focus on opinions of the trial recruitment processes, their experience of the laptop and intervention website in the waiting room, any challenges they experienced, how the procedures might be improved to make recruitment easier and/or more successful, and their views on the content of the intervention website and its place in the patient journey through a sexual health clinic visit.

Data will be analysed as the study progresses, and findings will be incorporated into the interview schedule.

Analysis

Data will be coded thematically and analytic notes made, focusing on areas defined by the topic guide as well as emergent themes.

Ethical issues: qualitative interviews

Young women

There is a risk that participants may feel uncomfortable embarrassed or distressed when participating in qualitative interviews.

Prior to giving consent, participants will be given information about the nature of the study, and informed that they do not have to answer any questions that they do not wish to, and that they can withdraw from the study at any point. Participants will also be informed that their responses will remain entirely confidential, and will not be linked to their name at any point. The interviews will focus on the processes of participating in the trial and also on the content of the website. Interviews will be conducted sensitively, and the interviewer will maintain a non-judgemental attitude throughout. Participants will be informed that they do not have to answer all the questions if they don't want to, and that they are free to stop the interview at any time if they wish. The information sheet given to those who participate in the interview will contain contact details of organisations that can give advice and support regarding sexual health.

If participants express embarrassment, anxiety or distress during interviews, this will be reported by the researcher as an adverse event in accordance with PRIMENT SOP-022. If a participant experiences an adverse event, such as feeling acutely dizzy or nauseated while taking part in an interview, the researcher or clinician will assess whether this is likely to be causally related to the interview and record it as an adverse event (non-causal) or an adverse reaction (causal). The duration of symptoms will also be recorded.

Interviews will be facilitated sensitively, setting ground rules for mutual respect and non-judgmental stances about lifestyle or behaviour choices at the start. We will try to ensure that all participants feel free to contribute, and also ensure that participants know that they are free to stop an interview or leave a focus group at any time if they wish. The research team have many years of experience in conducting interviews and facilitating focus groups

on sexual health topics. Also, people often find taking part in interviews a very positive and helpful experience.

10.8. Data management

All data will be handled in accordance with the UK Data Protection Act 1998.

We will be using UCL's Data Safe Haven, a service providing a technical solution for storing, handling and analysing identifiable data. It has been certified to the ISO27001 information security standard and conforms to the NHS Information Governance Toolkit. Built using a walled garden approach, where the data is stored, processed and managed within the security of the system, avoiding the complexity of assured end point encryption. A file transfer mechanism enables information to be transferred into the walled garden simply and securely.

The Outcome questionnaires will not bear the participant's name or other personal identifiable data. The participant's initials and trial identification number, will be used for identification. [encrypted submission online]

Participant contact details and details of interview arrangements will be kept in a locked filing cabinet on university premises. Audio recordings and transcripts of interviews will be only identifiable by participant ID number, and will be stored on a password protected university computer, and backed-up to an encrypted pen drive. During transcription, all identifiable information will be omitted (e.g., place of work). Any quotations in publications and reports will be completely anonymised.

The delegation log will identify all those personnel with responsibilities for data collection and handling, including those who have access to the trial database.

Qualitative data analysis (see above):

All interviews will be audio recorded and transcribed, with permission. Data will be coded thematically and analytic notes made, focusing on areas defined by the topic guide as well as emergent themes. Data will be deleted from the device.

10.9. Informed consent form and information sheet

Informed consent will be obtained using a standardised Participant Information Sheet (PIS) and consent form (both integrated into the trial software), which will be approved by the ethics committee and local NHS Research and Development offices. Copies are attached.

All participants included in the trial will be asked for their consent to take part and for their contact details to be used to communicate with them (e.g., for follow-up questionnaires, and reminders to use the website. Participant responses to the questions about consent will be stored with their personally identifiable data (name, contact details), in order for a record to be kept of each individual's consent. We will ensure that all research procedures

meet the highest standards for data protection and confidentiality, storing data on an encrypted server. We will give participants the contact details for support organisations in case they are needed, and follow protocols to ensure the safety and wellbeing of participants under the age of 18 who may be at risk of harm.

10.10. Monitoring

The trial will be overseen by a Trial Management Group (TMG) that meets monthly. Their role will be to advise about all issues to do with the design and conduct of the trial.

The trial is to be conducted in association with PRIMENT clinical trials unit, which is a UK Clinical Research Collaboration registered clinical trials unit, and has experience of working on e-health trials. Representatives from PRIMENT are members of the TMG (including a statistician, a health economist, and a trialist), and they will be strongly involved in the conduct of the trial and analysis of trial data.

Our trial has been designated a 'low risk trial' by PRIMENT, in terms of the potential risks to the safety and wellbeing of women who participate in this trial, since there are low risks involved in having access to a digital intervention to improve choice of contraception. As such, the trial would normally be monitored for subject safety through robust internal process rather than scrutinised by an external data safety and monitoring board. The funding body (the Department of Health) have therefore agreed that there is no need for an active independent data-monitoring committee; rather we have appointed a 'silent' DMC that could be called upon if any unforeseen issues arise. The trial will also be monitored by an independent Trial Steering committee (TSC). The TSC will meet twice a year, and will ensure that the research is conducted to a high standard, adheres to the principles of GCP ensure that patient interests are prioritised.

Interim analyses and stopping rules

The TMG, including the trial statistician, will meet monthly at the start of the trial and then quarterly on completion of recruitment to monitor the conduct and progress of the trial. Adverse events will be presented at each TMG meeting, and the TMG will be able to invite the (otherwise 'silent') DMC to meet at any point if there are concerns. The DMC may then request a formal interim analysis of adverse events and trial outcomes by study arm on which to judge whether the trial should continue or close. There are no formal stopping rules.

10.11. Data Handling and Analysis

A database will be prepared by an external vendor, Sealed Envelope (provider of clinical trial database systems) that will include a facility for online data entry direct by participants.

All electronic data will be handled according to the Data Protection Act 1998 as well as Priment SOP for Data Handling.

Data analysis will be performed under the supervision of the trial statistician. Data analysis will be completed independently from data entry. A data analysis plan will be agreed before the database is locked.

10.12. Expertise

All members of the research team will have undergone Good Clinical Practice training. The research team (chief investigator and trial manager) have extensive experience of conducting interviews in the area of sexual health. We will ensure that the research assistant who will be employed to undertake these interviews will have adequate experience in this area. They will receive any necessary training prior to commencing the interviews, and receiving continual mentoring (by the research team) throughout this study.

11. NAMES OF COMMITTEES INVOLVED IN TRIAL

Project Advisory Group

Professor	Judith Stephenson	Margaret Pyke Professor of Sexual and Reproductive Health, Institute for Women's Health, UCL
Dr	Greta Rait	Reader, UCL
Dr	Patricia Lohr	Medical Director, British Pregnancy Advisory Service
Ms	Rachael Hunter	Principal Research Associate, UCL
Professor	Ann Blandford	UCL Interaction Centre, UCL
Dr	Andrew Copas	Reader in Medical Statistics, UCL
Dr	Julia Bailey	Senior Clinical Lecturer, Primary Care and Population Health, UCL
Professor	Sandy Oliver	Professor of Public Policy, Childhood, Families and Health, UCL
Professor	Jill Shawe	Professor of Maternal and Family Health, University of Surrey
Professor	Christopher Bonell	Professor of Public Health Sociology, London School of Hygiene and Tropical Medicine
Dr	Chris Wilkinson	Medical Director, Margaret Pyke Trust
Mr	Johnathan Poon	Pharmacist, Green Light Pharmacy
Ms	Ana Gubijev	Research Associate, Institute for Women's Health, UCL
Ms	Vas James	Research Coordinator, Institute for Women's Health, UCL

Silent Data Management Committee

Dr	Sharon Cameron	Consultant Gynaecologist, Co-Director of Clinical Effectiveness Unit
Professor	Jonathan Ross	Professor of Sexual Health and HIV
Ms	Nadine Marlin	Statistician, Pragmatic Clinical Trials Unit, Centre for Primary Care and Public Health

Steering Committee

Professor	Gene Feder	Professor of primary health care, Centre for Academic Primary Care, School of Social and Community Medicine University of Bristol
Dr	Leanne Morrison	Research Fellow, Academic Unit of Psychology, Faculty of Social, Human and Mathematical Sciences University of Southampton
Dr	Mary Barker	Associate Professor of Psychology MRC Lifecourse Epidemiology Unit University of Southampton
Professor	Cynthia Graham	Professor of Sexual and Reproductive Health, Department of Psychology University of Southampton

Trial Management Committee

Professor	Judith Stephenson	Margaret Pyke Professor of Sexual and Reproductive Health, Institute for Women's Health, UCL
Dr	Greta Rait	Reader, UCL
Dr	Rachael Hunter	Principal Research Associate – Health Economics, UCL
Dr	Andrew Copas	Reader in Medical Statistics, UCL
Dr	Julia Bailey	Senior Clinical Lecturer, Primary Care and Population Health, UCL
Ms	Shabana Khan	IT Database Developer, UCL Priment Clinical Trials Unit
Ms	Nataliya Brima	Data Manager/Research Associate (Medical Statistics) Centre for Sexual Health & HIV Research Research Department of Infection and Population Health, UCL
Ms	Natalia Lago	Senior Trial Manager, UCL Priment Clinical Trials Unit
Ms	Ana Gubijev	Research Associate, Institute for Women's Health, UCL
Ms	Vas James	Research Coordinator, Institute for Women's Health, UCL

12. DEFINITION OF END OF TRIAL

The end of the trial will be the date of the last follow-up by the last participant. The control group will have access to the website after the end of the trial for a period of 3 months, but no participant data will be collected during this time.

13. DATA OWNERSHIP

At the end of the trial, the data belongs to the Joint Research Office at University College London.

14. INDEMNITIES/INSURANCE

University College London is the research sponsor, and indemnity insurance certificates have been obtained from them.

University College London holds insurance against claims from participants for injury caused by their participation in the clinical trial. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, as this clinical trial is being carried out in an NHS organisation or an organisation contracted to the NHS, the NHS organisation or organisation contracted to the NHS continues to have a duty of care to the participant of the clinical trial. University College London does not accept liability for any breach in the NHS organisation or an organisation contracted to the NHS's duty of care, or any negligence on the part of NHS organisation employees. This applies whether the NHS organisation is an NHS Trust or otherwise.

Participants may also be able to claim compensation for injury caused by participation in this clinical trial without the need to prove negligence on the part of University College London or another party. Participants who sustain injury and wish to make a claim for compensation should do so in writing in the first instance to the Chief Investigator, who will pass the claim to the Sponsor's Insurers, via the Sponsor's office.

NHS organisation selected to participate in this clinical trial shall provide clinical negligence insurance cover for harm caused by their employees and a copy of the relevant insurance policy or summary shall be provided to University College London, upon request.

15. INTELLECTUAL PROPERTY RIGHTS/PUBLICATION POLICY

All background intellectual property rights (including licences) and know-how used in connection with the study shall remain the property of the party introducing the same and the exercise of such rights for purposes of the study shall not infringe any third party's rights.

All intellectual property rights and know-how in the protocol and in the results arising directly from the study, but excluding all improvements thereto or clinical procedures developed or used by each participating site, shall belong to UCL. Each participating site agrees that by giving approval to conduct the study at its respective site, it is also agreeing to effectively assign all such intellectual property rights ("IPR") to UCL and to disclose all such know-how to UCL.

Each participating site agrees to, at the request and expense of UCL, execute all such documents and do all acts necessary to fully vest the IPR in UCL.

Nothing in this section 9 shall be construed so as to prevent or hinder the participating site from using know-how gained during the performance of the study in the furtherance of its normal activities of providing or commissioning clinical services, teaching and research to the extent that such use does not result in the disclosure or misuse of confidential information or the infringement of an intellectual property right of UCL. This does not permit the disclosure of any of the results of the study, all of which remain confidential.

16. FUNDER

This trial is funded by a Health Technology Assessment grant from the National Institute for Health Research (13/79/09)

17. PUBLIC AND PATIENT INVOLVEMENT

Patient and Public Involvement is embedded throughout the project including: representation on the Advisory Group to help to steer the research design and conduct of the study; involvement in qualitative field work and intervention testing to ensure that the priorities of women are closely reflected; and involvement in the qualitative evaluation of research processes to elucidate the impacts – both positive and negative - on users.

The aim of actively involving service users and providers in this project is to ensure that the framing of the research, the data collection and analytical methods, and the interpretation of the emerging findings take into account the issues important to them.

Methods of involvement will be chosen and refined in discussion with the service users themselves and will be aligned with the consensus based principles of successful involvement in research. Service users will be supported to participate as full, active members of the Advisory Group, alongside service providers and researchers. This will include written briefings and discussions before and after meetings. If some of them prefer to advise from outside of the group, members of the research team and/or a service user member of the Advisory Group will meet them at their preferred location to discuss their perspectives on LARC and digital interventions, and the implications for the research. Successful involvement relies not only on supporting the service users themselves, but also in supporting the research team in adopting appropriate methods and employing active listening to make the best use of service users' insights. Some members of the research team bring considerable experience of service user involvement in research and will help less experienced colleagues prepare for, and make best use of, the involvement activities.

18. TIMELINE

Recruitment will begin in January 2017 and end in July 2017. Collection of follow up data will begin in April 2017 and end in January 2018. All analysis will be complete by end of April 2018, and final reports will be prepared as soon as possible after this.

19. STATEMENT OF COMPLIANCE

LARC Phase 2 Protocol version 3 23/07/2018; IRAS ID 213559

The trial will be conducted in compliance with the approved protocol, the UK Regulations, EU GCP and the applicable regulatory requirement(s).

20. PROJECT TIMETABLE AND MILESTONES

Project Timetable

Phase 2 Feasibility	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10	Month 11	Month 12	Month 13	Month 14	Month 15
	Jul17	Aug17	Sep17	Oct17	Nov17	Dec17	Jan18	Feb18	Mar18	Apr18	May18	Jun18	Jul18	Aug18	Sep18
Advisory Group Meeting															
Steering Committee Meeting															
Feasibility trial recruitment (80 women in each setting)															
Online follow-up at 3 months post-randomisation															
Online follow-up at 6 months post-randomisation															
Process (qualitative) evaluation															
Analysis of qualitative and quantitative data including health economics															
Dissemination of findings and final report															

21. REFERENCE LIST

1. Armstrong, N., Donaldson, C. The economics of sexual health. Family Planning Association 2005.
2. Winner B, Peipert J. F, Zhao Q, Buckel C, Madden T, Allsworth J.E, Secura G.M. Effectiveness of Long-Acting Reversible Contraception. N Engl.J.Med 2012; 366: 1998-2007
3. NICE. Long-acting reversible contraception: the effective and appropriate use of long- acting reversible contraception. Clinical Guideline 30, 2005 (<http://www.nice.org.uk/CG30>)
4. NHS Contraceptive Services: England 2012/13 Community Contraceptive Clinics
5. Lopez LM, Tolley EE, Grimes DA, Chen M, Stockton LL. Theory-based interventions for contraception. Cochrane Database Syst Rev. 2013 Aug7;8: CD007249.
6. Halpern V, Lopez LM, Grimes DA, Stockton LL, Gallo MF. Strategies to improve adherence and acceptability of hormonal methods of contraception. Cochrane Database Syst Rev. 2013 Oct 26;10:CD004317
7. Arrowsmith ME, Aicken CR, Saxena S, Majeed A. Strategies for improving the acceptability and acceptance of the copper intrauterine device. Cochrane Database Syst Rev. 2012 Mar 14;3: CD008896.
8. Office for National Statistics, internet access quarterly update Q4 2013
9. McCarthy O, Carswell K, Murray E, Free C, Stevenson F, Bailey JV. What young people want from a sexual health website: design and development of 'Sexunzipped'. J Med Internet Res 2012;14 (5):e127.
10. Bailey JV, Murray E, Rait G, Mercer CH, Morris RW, Peacock R, Cassell JA, Nazareth I. Interactive computer-based interventions for sexual health promotion. Cochrane Database of Systematic Reviews 2010
11. Garbers, S. et al. Randomized controlled trial of a computer-based module to improve contraceptive method choice. Contraception 2012;86: 383-390
12. Garbers, S.et al. Tailored health messaging improves contraceptive continuation and adherence: results from a randomized controlled trial. Contraception 2011;86: 536-542
13. Schwartz, EB. Et al. Computer-assisted provision of hormonal contraception in acute care settings. Contraception 2013;87: 242-250

14. Eleanor Bimla Schwarz, MD, MS¹, Barbara Gerbert, PhD², and Ralph Gonzales, MD, MSPH, Computer-assisted Provision of Emergency Contraception a Randomized Controlled Trial, *J Gen Intern Med* 23(6):794–9 DOI: 10.1007/s11606-008-0609-x
15. Telford R, Boote JD, Cooper CL (2004). What does it mean to involve consumers successfully in NHS Research? A consensus study. *Health Expectations*, 7, 209-220.
16. Glasier, A., Scorer, J., Bigrigg, A., (2008) Attitudes of women in Scotland to contraception: a qualitative study to explore the acceptability of long-acting methods. *JFPRH*. October 2008.
17. The Clare Bale Consultancy 2009, LARC Consumer Research Report, <http://www.askforlarc.nhs.uk>
18. Bailey JV, Webster R, Griffin M, Freemantle N, Hunter R, Rait G, Estcourt C, Anderson J, Gerressu M, Stephenson J, Michie S, Murray E. The Men's Safer Sex Trial: A feasibility randomised controlled trial of an interactive digital intervention to increase condom use in men. *Digital Health* 2016;2:1–12
19. Department of Health 2013, A Framework for sexual Health Improvement in England, www.dh.gsi.gov.uk/mandate
20. Hannes K. Chapter 4: Critical appraisal of qualitative research. In: Noyes J, Booth A, Hannes K, Harden A, Harris J, Lewin S, Lockwood C editor(s). *Supplementary Guidance for Inclusion of Qualitative Research in Cochrane Systematic Reviews of Interventions*. Version 1 (updated August 2011). Available from <http://cqrmg.cochrane.org/supplemental-handbookguidance>: Cochrane Collaboration Qualitative Methods Group, 2011.
21. Mauskopf JA, Sullivan SD, Annemans L, Caro J, Mullins CD, Nuijten M, Orlewska E, Watkins J, Trueman P. Principles of Good Practice for Budget Impact Analysis: Report of the ISPOR Task Force on Good Research Practices – Budget Impact Analysis. *Value in Health* 2007;10:336-47.

22. DEFINITIONS/ABBREVIATIONS

Acronym	Definition
CI	Chief Investigator
SOP	Standard Operating Procedure
UCL	University College London
SRE	Sex and relationships education
NICE	National Institute for Health and Care Excellence
IUD	intrauterine device (IUD or coil)
IUS	Intrauterine system
SDI	Subdermal implant
website	Interactive Digital Intervention
MRC	Medical Research Council
GCP	Good clinical practice
SRH	Sexual and Reproductive Health
BPAS	British Pregnancy Advisory Service
MPC	Margaret Pyke Centre
RCT	Randomised Control Trial
BeCCY	Best Choice Contraception for You – the website intervention
LARC	Long acting reversible contraception
FPA	Family Planning Association
GP	General Practice
NIHR	National Institute for Health Research
HTA	Health Technology Authority
IPR	Intellectual Property Rights
UCLH	University College London Hospital
PSSRU	Personal Social Services Research Unit
TMG	Trial Management Group
TSC	Trial Steering Committee
(s)DMC	(Silent) Data Management Committee