Wrapped Feasibility Trial: Protocol

Title and additional identifiers

Scientific title

An interactive digital behaviour change intervention (Wrapped) to decrease incidence of sexually transmitted infections (STIs) amongst users of STI self-sampling websites: Study protocol for a randomised controlled feasibility trial

Short title

Wrapped Feasibility Trial

Research team

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Trial registry

ISRCTN *[add reference and date once registered]*

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Background information

The problem that is being addressed

In 2017, approximately 422,000 diagnoses of Sexually Transmitted Infections (STIs) were made in England (1). Compared to those aged 25-64 years, STI diagnosis rates in 15-24 year olds are three times as high in men and five times as high in women (1). People of black ethnicity and men who have sex with men are also disproportionately affected (1). Untreated STIs can lead to serious health consequences such as pelvic inflammatory disease, ectopic pregnancy and infertility, which have a significant impact on health and quality of life (2). The estimated annual cost to the NHS of STI treatment is £620 million (3). Condoms are the only way for sexually active people to avoid STIs (4) but young people report inconsistent use (5,6).

Why this research is important

Against a backdrop of rising demand for sexual health services, sustained budget cuts mean that symptomless patients are increasingly being directed away from face-to-face services and towards online STI self-sampling websites. This change is reflected in National Chlamydia Screening Programme (NCSP) data which shows a year on year increase in internet testing (rising to 132,000 tests in 2017) against a downwards trend in overall testing over the last five years (1). The increasing accuracy and availability of self-tests for all major STIs (7), combined with the need to reduce NHS costs, presents a future in which patients may be encouraged to entirely self-manage STI screening, only being directed to Genitourinary Medicine (GUM) for more complex cases. The London Sexual Health Transformation Programme, which moved all sexual health triaging and STI testing online in 2017, is a strong indicator that provision is already moving in this direction.

Data from the NCSP indicates that self-sampling websites are effective at reaching at risk groups, with chlamydia positivity equivalent to that of other test settings (1). Furthermore, they attract equivalent numbers of males and females, and people from across the spectrum of deprivation (8). However, evidence suggests that the experience of testing via self-sampling sites does not reliably translate into future prevention efforts (8). Furthermore, whilst information on STIs and contraceptive methods is typically found on self-sampling websites, this is insufficient for behaviour change (9), and inconsistent with Public Health England guidance to provide those at elevated risk of STIs with preventative intervention (10). As such, self-sampling websites provide an important, but currently missed, opportunity to intervene with a priority group.

To reduce the incidence of future STIs amongst users, and the associated health, social and financial costs, behaviour change interventions are required. Digital interventions in particular are appealing in this context. They have the potential to be cost-effective, as once established ongoing costs can be relatively low, particularly if content is fully automated. They also offer benefits to users, enabling them to access content anonymously, repeatedly, and at convenient times. Furthermore, potential reach is high; in the United Kingdom for example, 80% of those aged over 15 years report accessing the internet daily (11).

Review of existing evidence

Scores of behavioural interventions aiming to reduce sexual risk behaviour have been developed over recent decades. Accordingly, numerous systematic reviews and meta-analyses have been

conducted to help make sense of the findings and enable conclusions to be drawn about their effectiveness. These include reviews focussing on specific populations, such as adolescents/young adults (12-15) and women (16-18), those which report on behavioural outcomes (19-22) and additionally objective STI outcomes (18,23,24), and those where interventions are delivered via face-to-face (14,21,22,25) or digital/computer-based (26-30) methods. In fact, such is the preponderance of these reviews, that there is now a systematic review of reviews (31) and a meta-review of meta-analyses (32) in this area.

What this body of work tells us is that behavioural interventions have modest favourable effects on condom use and STI incidence, including for different populations and when delivered via face-to-face or digital methods. There are a number of important qualifications to be made to this statement however. A minority of studies examining the effect of these interventions use the most defensible design, that is, a randomised controlled trial (RCT) (23,28). This is important because other types of design have a tendency to over-estimate effects. Furthermore, when RCTs are conducted they are often of poor quality. A recent meta-analysis of RCTs by Free et al (23) for example included 139 trials of which only four were judged as scoring adequately on all four quality criteria. Biological outcome measures are also rare; for example, only 15% of studies in the Free et al review (23), and 13% of studies in a meta-analysis of interactive computer-based interventions by Bailey et al (28), were found to have used this type of measure. The length of follow-up for the primary outcome is also typically limited. In the meta-analysis by Bailey et al (28) for example, five of the fifteen studies had a follow-up of less than two weeks post-intervention and the longest follow-up period was six months, achieved by only two studies. This limits conclusions that can be drawn about the long-term benefits of interventions on sexual health outcomes. In sum, despite the volume of work in this area, well designed, high quality trials are rare but urgently required to provide reliable evidence on the effect of behaviour change interventions on sexual health outcomes. This is true for all types of interventions, including those delivered via digital methods.

As well as attempting to discern the effect of behaviour change interventions on sexual health outcomes, some systematic reviews and meta-analyses aim to draw conclusions about characteristics associated with success. The two meta-reviews in this area (31,32) have synthesised these findings and both concluded that a common component of effective interventions is the inclusion of skills training, such as for condom application and facilitating condom use with sexual partners. A number of meta-analyses have also examined which behavioural determinants, if successfully changed, would have the greatest effect on condom use, and findings across these are broadly consistent. Positive attitudes towards condoms (33-35), condom availability (33), and behavioural capability and self-efficacy for communicating about (33,36,37) and using (33,35) condoms, have all been shown to have a positive effect on behaviour. This gives intervention developers a clear steer in terms of what to change.

In terms of positive attitudes towards condoms, there is strong evidence that cognitive beliefs about condoms (i.e. those which are thought-based and rational e.g. about the effectiveness of condoms in preventing STIs) are weaker predictors of behaviour than affective beliefs (i.e. those concerning emotions and feelings e.g. feelings about the pleasantness or unpleasantness of condoms) (34). This is supported by our own work which identifies that beliefs concerning the likelihood that condoms

'make sexual experiences less enjoyable' or 'reduce sexual pleasure' should be the focus of behaviour change interventions aimed at improving young adults' attitudes towards condoms (38). Changing expectations that condom use leads to reduced enjoyment/pleasure and spontaneity in particular is likely to be an effective strategy for this group. The eroticisation of condoms, using methods that encourage association with arousal, has rarely been used to target these beliefs despite evidence that it would work well (22). With regards to skills training, there is also good evidence that young people would be best served by training on talking about condoms specifically (as opposed to more general subjects such as sexual history), that is, how and when to bring the topic up, how to negotiate use and how to handle resistance (37). It is also clear that young people would benefit from support in developing skills to correctly apply and remove condoms, and to identify the best fit and feel (31,32). The frequency with which this group experience errors and problems with condoms is well documented (39) yet very few interventions have addressed this important aspect of sexual experience (40). The experience of errors and problems is also highly likely to be responsible for the variation in self-efficacy and behavioural beliefs (e.g. concerning pleasure and enjoyment) evident in the literature (34,36,38,41).

The importance of condom availability, identified by meta-analyses as a determinant of behaviour (33), has led the National Institute for Health and Care Excellence (NICE) to recommend that free condoms be provided to those most at risk via distribution schemes (42); cost can be a major barrier to use particularly for poorer people (42,43). Web-based postal schemes are a promising means of reducing inequalities but much of the evidence concerning their effectiveness is dated, of poor quality, based on non-UK populations, and does not include STI outcomes. Furthermore, whilst it has been recognised that multi-component schemes, that additionally provide content directed at skills building, are most likely to be effective, there is little understanding of what mix of components would work best (42). As a result, high quality trials of multi-component interventions are needed to determine their (cost-) effectiveness, particularly within a UK setting (42).

What we have done so far

In 2016-17, with support from MRC PHIND funding and in line with MRC guidance on the development of complex interventions (44), Wrapped was co-created by researchers, stakeholders and young people (45). This was performed using Intervention Mapping (46), a systematic and robust approach to the development of theory- and evidence-based interventions. Wrapped is a fully automated, multi-component and interactive digital intervention developed especially for users of STI self-sampling websites aged 16-24 years. It is delivered via a responsive website such that its appearance (size, orientation etc.) changes in accordance with the device being used to access it (pc, laptop, tablet, phone). It aims to reduce the incidence of future STIs through increasing correct and consistent condom use. The intention is for users of STI self-sampling websites to be signposted directly to Wrapped upon order of their self-sampling pack (via a hyperlink). Users' initial interaction is through selection of their salient barriers to condom use. These barriers reflect important behavioural determinants of condom use identified through existing meta-analyses (34-36,47), namely condom use attitudes (particularly beliefs around pleasure, enjoyment and spontaneity), condom availability, and self-efficacy for condom use and communication. Responses determine which combination of up to six different components they receive. Users therefore only receive components for which there is an expressed need, a strategy selected to optimise user engagement and cost-effectiveness. Each component has been designed to remove or reduce one or more of the

identified barriers to condom use. Wrapped is a 'sex positive' intervention. It exemplifies a holistic view of sexual health that emphasises the importance of physical health and wellbeing. The importance of 'healthy' consensual relationships where there is autonomy and an equal balance of power is emphasised and modelled in the content. All young people, regardless of gender (male, female, non-binary, transgender) or sexual identity are accommodated. See section 4 'planned intervention' for detailed information on intervention content.

Wrapped is now ready to be definitively tested using a RCT. In our usability/acceptability study, young people reported that Wrapped made them think differently about condoms and that they would use and value the content and services provided. What we don't know however is whether it is cost-effective. Conducting this trial will enable us to determine this but also to contribute important evidence to the wider field concerning the effect of behaviour change interventions on sexual health outcomes. Additionally, it will add to our understanding of behaviour change more broadly. For example, to date there has been limited success in changing condom use self-efficacy using digital interventions (28,48) and a recent meta-analysis found this whilst digital interventions were capable of increasing self-efficacy, it was unable to discern which behaviour change techniques (BCTs) were responsible for this effect. This trial would enable us to draw conclusions about the effect of included BCTs on this and other important determinants of behaviour. In order to respond to previous criticisms of trials in this area and contribute reliable evidence concerning the effect of behaviour change interventions on sexual health outcomes, it is imperative that this RCT uses procedures that minimise bias, that it has a long-term follow-up, and also that it includes an objective, biological outcome. At present however, there are too many 'unknowns' to allow us to plan for or cost this work, in particular, we do not know whether it is possible to recruit and retain sufficient participants to power a definitive trial. We therefore propose a feasibility trial.

Study Information

Aim and objectives

Research question: Is it feasible to run an RCT to test the effectiveness and cost-effectiveness of Wrapped (a fully automated, multi-component and interactive digital behaviour change intervention that aims to reduce the incidence of STIs through increasing correct and consistent condom use amongst users of STI self-sampling websites aged 16-24 years old)?

Aim: to assess whether and how it is possible to carry out a future definitive RCT to evaluate the effectiveness and cost effectiveness of Wrapped in comparison to usual care (the provision of basic information on STIs and condom use).

Primary Objectives:
To estimate for the definitive RCT:

i. the rate of recruitment of eligible participants
ii. the rate of participant follow-up for the definitive RCT primary outcome measure (cumulative incidence of chlamydia measured using biological samples) at 12 months

Secondary Objectives:

iii. Identify whether the level of deprivation of the final sample is representative of online STI self-sampling users
iv. Identify whether differential retention occurs across groups (gender, ethnicity, sexual identity, deprivation, randomised groups, chlamydia diagnosis at baseline)

v. Measure the cumulative incidence of chlamydia in the intervention and control groups (to support sample size calculation for the definitive RCT)
vi. Identify the rate of attrition at baseline, intervention and follow-up and ways of minimising this
vii. Determine the feasibility and participant acceptability of all primary and secondary outcome measures (including health economic)
viii. Identify which value proposition (statement about what trial has to offer) results in the highest rate of recruitment
ix. Identify and remove intervention 'friction points' (using web analytics data) to minimise attrition and maximise future intervention dose
x. Identify costs and resource use associated with the intervention (to inform the design of the definitive trial and the future economic evaluation)
xi. Measure contamination of intervention effect in the control group
xii. Identify possible adverse effects of the intervention e.g. participants' inadvertent disclosure that they are sexually active and/or testing for an STI if they are overseen using Wrapped by another person, initiation or increase in the consumption of pornography

Ethics approval

Preceding qualitative study

	Required?	Reference number	Date obtained
Institutional approval	Yes	LMS/SF/UH/04061	04/02/2020
IRAS	No		

Feasibility trial and embedded qualitative study

	Required?	Reference number	Date obtained
Institutional approval	Yes	*Application in progress*	
IRAS	Yes	*Application in progress*	

Ethical considerations

Fully informed consent: participants will be provided with participant information (including possible benefits and risks) and given the opportunity to ask questions

Participants' rights: participants will be able to contact the study team at any time using wrapped@herts.ac.uk. Participants will be able to withdraw from the study at any point.

Participants' safety: the intervention and control material provide support and are unlikely to have any harmful effects. Nonetheless a safeguarding page will be included on the intervention and control websites with information on organisations that can offer help and support with regards to sex and relationships. A safeguarding procedure is also in place to identify and appropriately support individuals who disclose sexual abuse/coercion during the research study (see safeguarding section below).

Research governance and project management

University of Hertfordshire. KN (mentored by KB) will lead the project, supported two post-graduate researcher assistants (PGRAs), and with oversight by the CTU. See section 10 below for details on roles of all co-applicants. UH will provide support to assist with administrative tasks, contracting and procurement, information governance protocols, risk- assessments, and to support the design and

delivery of strategies to ameliorate risk. UH is the research sponsor. UH's Data Protection Officer will oversee the development of all processes relating to the collection and processing of personal data to ensure compliance with GDPR legislation.

The Brighton and Sussex Clinical Trials Unit (BSCTU). BSCTU will provide trial management and statistical oversight. Operational Manager Nicky Perry will provide guidance on trial management, and Stephen Bremner (co-applicant and statistician) will oversee data analysis. Debbie Lambert will support and oversee data management.

Clinical Research Network (CRN) Eastern. CRN West Midlands were initially involved in the design of the project and provided AcoRD guidance and PPI advice. The lead applicant then moved institution and was accordingly supported by CRN Eastern who supported completion of the soECAT tool. CRN Eastern will continue to support the project going forward.

Study Steering Committee (SSC) and Data Monitoring and Ethics Committee (DMEC). An independent SSC and DMEC have been formed to provide oversight and ensure adherence to standards of best practice. This is comprised of the following members:

Name	Job title	Organisation	Group
Lyndsay Hughes (chair)	Senior Lecturer & Programme Director of MSc Health Psychology	KCL	SSC
Rob Bacon	Health Improvement Lead: Sexual Health	Hertfordshire County Council	SSC
Shahin Palmer	Sexual Health Facilitator - East of England	Public Health England	SSC
Dr Sarah Edwards	Consultant Physician GUM/HIV & Clinical Lead GUM Sexual Health Hertfordshire	Sexual Health Hertfordshire	SSC
Sue Burridge	Sexual Health Commissioner	Bedford Borough, Central Bedfordshire and Milton Keynes	SSC
Blake George	Business Development Manager	SH:24	SSC
Anne Philpott	Founder of the Pleasure Project	The Pleasure Project	SSC
Arushi Singh	Programme Specialist	UNESCO	SSC
Dr Barbara Barrett	Senior Lecturer and Deputy Head	King's Health Economics, King's College London	SSC
Prof Cynthia Graham	Professor in Sexual and Reproductive Health	University of Southampton	SSC
Dr Nicole Stone	Senior Research fellow	Centre for Sexual Health Research, University of Southampton	SSC
Elsie White	PPI representative	NA	SSC
Rebekah Alexander	PPI representative	NA	SSC
Dr Erica Cook (Chair)	Senior Lecturer in Health Psychology	University of Bedfordshire	DMEC

Dr Alec Miners (Deputy Chair)	Associate Professor in Health Economics	LSHTM	DMEC
Dr Yannis Pappas	Reader in Health Service Organisation and Delivery	University of Bedfordshire	DMEC

The SSC and the DMEC will meet every 6 months (5 times) throughout the study.

Study design

A two-arm parallel group randomised feasibility RCT of Wrapped plus usual care compared to usual care alone, with preceding and nested qualitative studies.

Methods, participants and settings

Preceding Qualitative study

The aim of this first qualitative study is to develop and refine a participant recruitment and retention strategy for the feasibility RCT. In collaboration with our PPI group, we will devise a provisional strategy based on evidence of approaches previously found to be associated with effective retention (49) and recruitment (50,51). This will be achieved through a day-long face-to-face creative workshop employing co-production tools such as pathway mapping, character journeys, and paper prototyping. We will use these tools to understand: the participant journey, obstacles to participation that different types of people could experience, and what additions or changes we can take to remove or alleviate these. Once we have a draft strategy, we will seek feedback on this from young people using a series of iterative focus groups with 3 groups of 16-24 year olds (5-7 per group) recruited from youth and education services across Coventry and Warwickshire (support already obtained for this from Heart of England Training college, Going Off The Rails, Youth Offending Service, and Looked After Children – see letters of support). Focus groups will take place at the recruitment site and all participants will be required to provide informed consent prior to commencement. This will be achieved using paper-based participant information sheets and consent forms. All participants will receive a £20 voucher in recognition of their time. During these focus groups, participants will be taken through a series of exercises to elicit feedback on the proposed approaches. These exercises will support the participants to add to and shape the existing ideas, and then to rank and validate them. Focus groups will be transcribed but additional data will take the form of photos (e.g. of ranked cards representing different approaches) and facilitator notes. Framework analysis (52) will be used to analyse the different types of data. This will be performed by researchers in collaboration with two PPI representatives. In partnership with our PPI group, we will then use the findings to revise the strategy prior to finalising.

Randomised Feasibility RCT

Please refer to the attached flow diagram (appendix A), based on the CONSORT extension for pilot and feasibility trials (53), for a visual representation of the study design, recruitment process, and timing of measures.

Study population and setting/context. A minimum of 230 participants will be recruited from an existing chlamydia self-sampling website (freetest.me; see letter of support) over a period of 3 months (see 'sample size and estimated recruitment rate' below for the calculation of sample size).

Freetest.me provides an online chlamydia testing service to over 100 local authority areas in England as part of the National Chlamydia Screening Programme which is free at the point of use. For the purposes of this study, users residing in one of four geographical areas will be invited to participate, namely Warwickshire, Somerset, East Sussex and Bromley (see letters of support). Inclusion criteria: young people aged 16-24 years and living in one of the above four areas. Exclusion criteria: no internet access and having sexual preferences which mean that they are unlikely to have penetrative sex (penis in vagina or anus) over the course of the study period. During our recruitment period, data will be collected by freetest.me on the number of users from each of these four areas who place an order for a self-sampling kit. This will be provided to the study team along with data on the mean deprivation score of users over that time period within each area.

Recruitment. The study invitation will be placed on the 'thank you' page viewed by freetest.me users following order of a chlamydia self-sampling kit. This invitation will convey the different value propositions determined by the PPI group. A hyperlink will take users to the study webpage for participant information and consent. We will work with our PPI group to draft the participant information and consent statements to ensure that they are clear and easy to understand. This study webpage will be located on REDCap, a secure data capture and management platform hosted on the University of Hertfordshire's (UH) server. All participants will be required to provide informed consent before joining the project. On joining the project, REDCap will create a unique ID for each participant and record their consent. We will put processes in place to minimise the risk of 1) non-genuine users of freetest.me from participating, and 2) individuals participating more than once. There are a number of potential technical solutions to this which we will explore for example, potential participants could be required to enter one of two codes from their self-sampling kit into REDCap which could then be validated by freetest.me. We would ensure that the sharing of any such data complies with GDPR. Additionally, we will put processes in place to exclude participants who, following completion of the baseline survey, are identified as responding randomly to survey items.

Survey data. REDCap will be used to monitor and manage all survey data collected as part of this study. It has been assessed by UHs Data Protection Officer (DPO) as meeting GDPR data requirement standards. Surveys will be conducted at baseline (M0), 3 months (M3), 6 months (M6) and 12 months (M12) and used to collect data on condom use attitude, behavioural capability, self-efficacy, and intentions, along with details of any partnered sexual activity and condom use that have occurred in the previous three-month period. The surveys will also be used to measure experience of partner resistance to condom use, and to collect health economic data (see 'health economics' section below for further details). The baseline survey will additionally collect participant contact details (name, email address, mobile phone number and address) to enable communication with participants regarding the completion of follow-up surveys, and basic demographics (age, gender, ethnicity, deprivation, sexual orientation). The M3 survey will also be used to collect information on participants' engagement with the intervention ('dose received – satisfaction'). We will iteratively test the surveys prior to use with our PPI group to maximise content validity, readability, clarity and comprehensiveness. Completion of the baseline survey will occur immediately after study sign up and consent. All other survey completion will be triggered by email and/or SMS. Reminders will be sent to all participants who have not completed their survey (number and frequency to be determined by the preceding qualitative study). We may also make telephone contact with participants, and/or collect a more restricted set of self-report outcome data (e.g. by a shortened survey or by phone), if evidence indicates that these strategies would be worthwhile. Those who have not completed their survey four weeks after the last contact was made will be classed as non-responders. We will however continue to send surveys to non-responders (and collect biological outcome data – see 'chlamydia tests' below) at subsequent timepoints (unless a participant asks to

be withdrawn from the study). All activity will be associated with each participant's unique ID enabling data across time points to be easily and accurately linked.

Health economics. It has been estimated that STIs cost the NHS around £620 million annually (excluding HIV), with public sector costs being much higher (3). Therefore, if Wrapped is found to be more effective than usual care in increasing correct and consistent condom use, then it is likely that important cost implications would be seen for the NHS, the public sector, and society more widely.

The principal aim of the economic component will be to determine the feasibility and acceptability of collecting cost and outcome data for an economic evaluation within a future definitive trial. The preliminary data generated on costs and outcomes will also feed into the design of the future definitive trial, for example in terms of consideration of important areas of cost and resource use. In addition, it will involve the preliminary design of a decision-analytic model to examine longer term costs and outcomes associated with the intervention.

We will use the feasibility RCT to determine health economic evaluation methods for the future definitive trial. A range of outcome measures will be included, to assess their feasibility and thus inform the design of the future economic evaluation. Processes will be established to collect data to inform a future incremental cost-effectiveness analysis (CEA) using the primary and secondary outcome measures, to give a cost per participant, cost per full engagement with Wrapped, and a cost per case of chlamydia avoided (54). We will also assess the feasibility of collecting data to inform a future cost-utility analysis in terms of cost per quality adjusted life year (QALY) gained, as well as a return on investment (ROI) analysis, and a cost- benefit analysis (CBA).

Health economic data collection and analysis. We will explore methods to measure costs from the perspective of the public sector (including the NHS, local authority and other public sector agencies as appropriate) in line with National Institute for Health and Care Excellence (NICE) recommendations for public health interventions (55) and from a societal perspective. Methods will be developed to collect resource use data prospectively to estimate the costs associated with both Wrapped and usual care. For the intervention group, the main costs to be collected include: 1) costs associated with creating, hosting, and maintaining the Wrapped website (56); 2) the costs associated with supplying condoms and other materials; 3) visits to specialist sexual health services, use of community-based sexual health services and other NHS and public sector resource use such as GP visits; 4) any costs incurred by individuals taking part in the intervention. For the control arm, costs will include the cost of the production and maintenance of sexual health information on the control website and other NHS and public sector resource use such as GP surgery attendances, visits to specialist sexual health centres etc. as well as private costs incurred by participants.

We will assess the feasibility and acceptability of collecting data on the costs incurred by participants receiving the intervention compared with usual care, as the intervention will allow participants to choose and order condoms and other materials, and access information and support online which may have implications on costs experienced by individuals and broader societal costs (57). Information on unit costs or prices will be identified. Potential sources of unit costs will include routine or published literature (e.g. PSSRU Unit costs of Health and Social Care) (58).

The feasibility study will assess the feasibility and acceptability of collecting data on health-related quality of life using the EQ5D-5L at M0, M3 and M12 (59), to allow a cost-utility analysis to be conducted in the future definitive trial, as recommended by NICE (55). We will also assess the feasibility and acceptability of collecting data to inform a return on investment (ROI) and cost benefit analysis (CBA).

If Wrapped is effective in increasing correct and consistent condom use, there may be impacts in the longer term. A decision-analytic model will be used to extrapolate costs and outcomes beyond the end of the trial and synthesise data on costs and outcomes from a range of sources (60). A comprehensive review of the literature will be undertaken to evaluate existing economic evaluations and models, and to inform the design and parameters of a future model (61).

Chlamydia tests. Chlamydia tests will be processed by freetest.me at M0, M3 and M12. All positive chlamydia tests will be treated as per the standard treatment pathway following self-sampling (all local authority areas involved in this study have agreed to absorb the cost of this – see letters of support). The chlamydia test at baseline is that triggered by participants when they order a self-sampling kit via the freetest.me website immediately prior to receiving the study invite (see 'recruitment' above). As this test will be requested and processed outside of the research study, we will ask participants to self-report their result. This request will be made 10 days after the order was made (freetest.me have advised us that samples are typically processed and results provided to users within 3-5 days of receipt thus allowing participants up to 5 days to complete and return their sample). We will do this by sending a one-item within-email or SMS survey with the following response options: negative, positive, awaiting result, and kit not returned. If a participant reports that they have not returned their kit, or if they do not respond, then we will send a repeat of this email/SMS (timing and frequency to be determined by our proceeding qualitative study). For those who test positive, we will also send a one-item within email or SMS survey asking whether the full course of prescribed antibiotics was taken (this is necessary so that we can determine at M3, whether any positive cases are a result of the same untreated infection, or a new infection). We may also make telephone contact if the evidence supports this as being an effective strategy. Those who have not provided this data four weeks after the last contact was made will be classed as non-responders. The chlamydia tests at M3 and M12 will be processed differently to that at M0, as these are managed within the study. For this purpose, freetest.me will provide the study team with a batch of self-sampling kits, each marked with a unique freetest.me kit code. As kits are sent out to each participant, the research team will record each individual participant's assigned kit code. A database will be set up specifically for this purpose within REDCap. The database will link the freetest.me kit codes with each participant's unique participant number. One week prior to posting out the kits, we will send an SMS to participants asking them to conform their postal address (i.e. that provided in baseline survey). If this has changed, they will have the option to follow a link to REDCap where they can enter a new address. The kits that participants receive at M3 and M12 will contain the usual user instructions to collect the sample and return by Freepost to freetest.me for processing. Participants who do not return their kit will be sent a limited number of email/SMS reminders (timing and frequency to be determined by our proceeding qualitative study). As before, we may also make contact by telephone. Those who have not returned their kit four weeks after the last contact was made will be classed as non-responders. Note: participants who do not provide chlamydia outcome data at either 0M or 3M will continue to be invited to complete subsequent chlamydia tests and surveys (unless they request to be withdrawn from the study). Freetest.me will set up a secure 'service area' on the freetest.me website where the test results will be recorded. A member of the research team will be given access to this and copy the data into REDCap using each individual's name and kit code. Participants who have a positive test result at 0M, 3M or 12M will receive a one-item within-email/SMS survey two weeks post-result to record whether their infection has been treated. This is to enable cumulative chlamydia incidence to be calculated. If treatment is incomplete, or the participant does not respond, we will send a limited number of emails/SMS to obtain this information. Each Local authority/trust will be informed of any positive cases (for participants residing in their area) so that they can provide appropriate treatment and follow-up.

The method for communicating this will vary by area in line with their preferred method of referral. Data sharing agreements will be set up between UH and freetest.me, and each LA/trust to ensure the secure and timely transfer of test result data.

Randomisation. Randomisation of participants to trial groups will be managed within REDCap and take place following completion of the M0 survey. Our CTU (Brighton and Sussex, UKCRC ID 66) statistician will generate the randomisation list (to be uploaded to REDCap) and will monitor randomisation on a weekly basis during active recruitment to ensure that the algorithm is being correctly applied. Randomisation will be at the individual level as we do not anticipate control group contamination (although this will be monitored to determine the suitability of this approach for the definitive trial). Stratification across groups (ethnicity, sexual identity, deprivation) will be performed to balance participants across the trial arms.

Intervention access. Participants will be individually randomised into one of two groups: usual care or Wrapped plus usual care. Those in the intervention group will be directed to the Wrapped website following randomisation via a hyperlink. Those in the usual care group will be directed to standard web-based information on STIs by hyperlink. Further details on the intervention and comparator are provided below (see 'planned intervention' and 'comparator' sections). All participants will be free to interact as much or as little with the respective materials; participants will be emailed the hyperlink to enable repeat visits. An email/SMS reminder to access the content will also be sent to all participants two weeks after first access is provided.

Analytics data. Participants' journey through the study, from sign up within REDCap, through the use of intervention/comparator materials, to the completion of all surveys, will be tracked. This will occur in the background (with each participant's explicit consent) to ensure that it is unobtrusive. Tracking of use of the intervention or control materials will be performed using an analytics package called Matomo (approved for use by UH DPO). These data will be used to gain valuable insights that will inform the definitive trial such as, which value propositions return the most participants, and whether there are any 'friction points' in the participant journey where significant drop-out occurs (e.g. at the point of consent, or within the intervention itself). These data will also be used to calculate intervention dose ('dose received') and to select participants for follow-up interviews (see 'nested qualitative study' below).

Fidelity log. UH ITS technicians will maintain the Wrapped website during the trial period. Whilst we do not anticipate any operational problems, the technicians will log any instances when the website is offline or functioning sub-optimally. Similarly, the research team will run regular tests (e.g. placing dummy orders for products, playing videos) to ensure full functionality is available. Problems identified will be raised with UH technicians who will resolve these as quickly as possible; once again these will be logged.

Nested qualitative study

During the course of the feasibility RCT we will conduct a nested qualitative study. The aims of this study will be to explore participants': i) views and experiences of the intervention, ii) experience of trial procedures and materials, and iii) perceptions of how the intervention has changed their condom use beliefs or behaviour. This qualitative data will add 'meat to the bones' of our quantitative data, providing further evidence to support or refute hypotheses drawn out from the feasibility RCT about recruitment/attrition. For example, we may have a theory about why a high proportion of participants are dropping out at consent, failing to complete a section of the survey, or losing interest at a certain point within Wrapped, but until we consult with those experiencing the whole research process then we will not fully understand this. The interviews will also be used to

better understand participant engagement with the intervention, in particular, dose received (satisfaction), and aspects of the environment which may have affected dose received (context). In line with the third aim, we will explore participants' perceptions of any changes in condom-related beliefs and behaviour, this will include attempting to gain their insight into any components that may have been responsible for this. We will also seek to gain an understanding of the influence of sexual partners on condom use decision making in light of the intervention. To further draw this out, we will attempt to interview the sexual partners of interviewees. We will initially invite approximately 30 individuals (number to be determined by data saturation) participating in the feasibility RCT to take part in the study. All participants will receive a £20 voucher in recognition of their time. We will ask participants at baseline (single question in survey) whether they are willing to take part in a semi-structured telephone/video call interview and if so, to provide suitable contact details. These contact details will be downloaded and stored separately from all other study data in a password protected folder located on the UH server, linkable only using participants' unique participant identifier. We will purposively select participants to create a varied sample representing completers and non-completers from both trial arms, those with varying levels of intervention engagement, and those which we hypothesise may have experienced specific events that have influenced drop-out. Selected individuals will be contacted and directed to a new project page on REDCap where they will be asked to provide informed consent to take part in this additional aspect of the study. Interviews will last approximately 30 minutes and will be fully transcribed prior to analysis. We will use framework analysis (52) to analyse the data.

At the end of each interview, we will discuss with participants our wish to also interview the sexual partners of those participating in the qualitative study in order to better understand any changes in condom use decision making in light of the intervention. We will then follow up the interview with an email invitation which they can choose to forward on to their partner if they wish. It will then be up to the sexual partner to make contact with us if they wish to participate. They will be given the option to email/telephone the research team if they have any questions, or simply to follow a hyperlink straight to the relevant project page on REDCap. Here they will be required to provide informed consent in order to take part in the study. All data will be collected, processed and analysed as described above for primary interviewees. Each individual who participates will be given a £20 voucher in recognition of their time.

On completion of all interviews, the research team and PPI group will review the findings from this study in combination with those from the feasibility RCT and agree final changes to the recruitment and retention strategy. This will be used to inform the protocol for the future definitive RCT.

Primary study design

Interventional

Trial setting

Internet

Trial type

Prevention

Overall trial start date

1st May 2020

Overall trial end date

31st August 2022

Condition

Sexually transmitted infection (STI)

Interventions

Planned intervention. Please see our logic model (appendix B) for Wrapped which presents the theoretical model and further information on the components. Also see our paper (45) for a detailed description of intervention content reported in line with TIDieR guidance and to view screenshots, images of intervention materials, and example videos. Wrapped consists of six different components. The set of components that each user is exposed to is determined by their responses to a set of tailoring questions that are presented the first time they access the intervention (see logic model for rules on how these are allocated). Users will receive between one and six components (note, all users receive the 'condom sample pack' as a minimum). Users also receive notifications (preference for email, text and/or system only notifications selected by user) to promote continued access to and engagement with the content. The components are as follows:

- Condom Sample Pack
  This is a box containing twelve types of condoms (different brands, sizes, textures, thicknesses), and two types of lube for users to try out. It is delivered to users in discrete packaging (image of packaging shown to users). The box includes step-by-step instructions on how to correctly apply condoms. The aims of this component are to help young people to identify their preferred type of condom/lube, to help them overcome any issues around the smell, fit & feel of condoms, and to make positive associations between condoms and pleasure by instructing users to play around with them on their own i.e. getting them out of packet, feeling them, unwrapping, smelling, tasting etc. Users will be encouraged to put the condoms on themselves, or insert in to their vagina. It will be suggested that users try out all of the different types of condom to identify their preferred type(s). Users will also be encouraged to practise putting condoms on until they can do so confidently and with ease. The box itself is designed to be a permanent store for condoms at home. The bottom of the box has the message 'running low? Get some more in'. This is a cue to remind users to replenish their supply. Users are able to select from four different designs for both the exterior and interior of the box giving a total of 16 possible combinations. It is hoped that this level of personalisation will increase users' sense of ownership and use.
- Order Condoms
  Users can register with a service that will deliver their preferred condoms to a chosen address (in discrete packaging – image of packaging shown to users). Users will be able to select and change their preferred type(s) of condom and delivery address. Condoms will be free. Delivery will be ad hoc and triggered by an online order from the user. Each user will be limited to one order per month. Each order consists of one type of condom in bundles of six or twelve. Users can also add three packets of lube to their order. A reminder email or text (as selected by user) will be sent to users when they are able to order more condoms. As well as offering this service, users will be linked to information about off-line places where they can access condoms (both online through hyperlinks to services and through written information provided with each delivery). Users will be able to post reviews of condoms/lube within the order condoms area of Wrapped thus supporting other users to make choices.

- Condom Carrier
  A product for discretely carrying condoms when out and about, delivered to users in discrete packaging (image of packaging shown to users). This is a faux-leather keyring with a discrete, hidden compartment for up to two condoms, or one condom and a sachet of lube. Behind the condom is the message 'Replace me!' to act as a cue to replace the condom after use. The case is not intended to be the sole way to carry condoms but rather to be used as one of a number options. Messaging within Wrapped when ordering this carrier, and also inside the carrier when received, encourages users to place condoms within a number of places e.g. purse/wallet, coat pockets, bags (as well as the carrier), so that users always have a condom on them whatever they take or wear out.
- Using Condoms
  This is a video providing correct step-by-step instructions on how to put a condom on (using a demonstrator). It features a number of young people all giving their tips and tricks on how to do this (correctly, with ease) so that it is enjoyable/pleasurable for self and partner and part of the flow of sex.
- Discussing Condoms
  This is a series of videos in which young people talk about ways in which they have brought up condom use with partners in the past and introduced them into sex. They talk about how this went, what worked, what didn't etc. The aim is to help users plan the best time to bring up condom use with their partner, and what to do or say if they resist.
- Real Life
  This is a series of three videos featuring three real couples aged between 18-24 years (two straight and one gay). They are made available to 18+ years only (age is taken into account during tailoring of intervention content; it is not possible to alter age within the user profile). In the videos, the couples talk candidly about sex, and in particular using condoms during sex. They talk about and demonstrate how they put condoms on; who does it, techniques, how to make their use part of sex. The shots of the couples talking are interspersed with scenes of them kissing, touching, removing clothes and having sex. The films are akin to the content of a mainstream 18 rated film. There are no explicit shots of genitals or penetration. Condoms feature in these shots and the couples are shown communicating about them (verbally/non-verbally). The aim is to show real examples of how condom use can be incorporated into sex and to help users to build positive associations with condoms.

Comparator. Usual care is the comparator. Existing STI self-sampling websites typically provide only basic information on STIs and condom use to their users (2). To replicate this level of health promotion, and to provide an equivalent 'intervention' experience for those in the control group, we will create a stand-alone Wordpress website that presents comparable basic information. This will be akin to information provided by NHS choices (https://www.nhs.uk/live-well/sexual-health/#have-safer-sex). Participants in the control group will be directed to this website, instead of the Wrapped website, following randomisation. The same basic information will also be duplicated within the Wrapped website.

Intervention type

Behavioural

Primary outcome measures

- The proportion of participants recruited to the feasibility RCT per day (assessed as the number of participants randomised) out of those using freetest.me in the four areas (RO i)
- The percentage of randomised participants with valid primary outcome measure (cumulative incidence of chlamydia measured using biological samples) at 12 months (RO ii)

Secondary outcome measures

- The mean deprivation score for users of freetest.me over the 3 month recruitment period, compared to the mean deprivation score of the final sample, within each of the four recruitment areas (RO iii)
- The percentage of randomised participants with valid primary outcome measure at 12 months by group (gender, ethnicity, sexual identity, deprivation, randomised groups, chlamydia diagnosis at baseline) (RO iv)
- Cumulative incidence of chlamydia in the intervention and control groups (RO v)
- Attrition curves comparing the percentage of valid participants in the trial at randomisation, M3, M6 and M12 plotted for the intervention and control arms (drop-out attrition) (RO vi)
- The percentage of valid participants in the two arms that don't achieve pre-determined intervention 'goals', and the bounce rate for home and content pages (RO ix)
- Completeness of data from outcome measures that would be needed in a definitive trial (including self-report of chlamydia result at baseline, results from biological samples, demographic information, self-report of condom use, and data needed for cost-effectiveness and cost utility analyses) (RO vii)
- The number of participants randomised as a direct result of each of the different recruitment messages employed (RO viii)
- Completeness of data on costs and resource use that would be needed for the economic evaluation in a definitive trial (RO x)
- Proportion of participants in the control group who report (at 12M) any exposure to Wrapped (RO xi)
- Proportion of participants who report (at M12) having experienced an adverse event during the course of the study (inadvertent disclosure that sexually active/testing for STI if overseen using Wrapped, initiation or change in the consumption of pornography, or other) (RO xii)

Assessment of compliance with treatment

Participant engagement with intervention and control materials will be monitored using Matomo analytics. All interaction that participants have with the intervention or control material (as assigned) will be recorded automatically. There is no minimum acceptable level of engagement – all participants will be allowed to continue in the trial regardless of their level of interaction with the material.

For each participant in the intervention condition we will record:

- Which components were allocated
- Which component pages were accessed (how many times and how long each visit was)
- Whether order placed for condom sample pack (event)
- Whether order placed for condom carrier (if allocated; event)
- Whether (first) order placed for condom delivery (if allocated; event); and whether any subsequent orders placed (frequency)
- Whether a condom review left
- Whether 'using condoms' video watched in full (or time watched for)
- How many of 'discussing condoms' videos watched (in full; or in part how long for)
- How many of 'real life' videos watched (in full; or in part how long for)

Minimising bias

See 'randomisation' section above. To minimise bias, blinding will also be in place. Participants will be blind to condition. Those in the control group will be directed to a website on STIs to provide an equivalent 'intervention experience'. Researchers performing the analysis (KN, KB and SB) will be blinded to participant condition.

Statistics

Sample size and estimated recruitment rate. At least 60 participants per arm is recommended to allow proportions to be estimated with good precision (62). This is inflated to allow for an estimated 25% non-return of initial chlamydia self-test sample (based on freetest.me statistics; 60/0.75=80) and a further estimated 30% drop-out over the course of the feasibility trial (a conservative estimate based on 19% drop out achieved in Free et al's sexual health feasibility RCT (51); 80/0.7=114 per arm). Based on this, the total sample size required for the feasibility RCT has been calculated as 230 participants. Within our four partner areas, an average of 50 orders per day in total are fulfilled by freetest.me thus providing a reasonably large pool to draw from. Dr John Saunders (clinical champion for the National Chlamydia Screening Programme and collaborator on this bid) has advised that a reduction from 10% to 6% in chlamydia positivity as a result of the intervention would be clinically meaningful. With 90% power for 5% (two-sided) significance, and accounting for a 25% dropout at baseline (based on non-return of self-sampling kit) and a further 30% drop-out by 12 months, we have calculated that 3864 participants would be necessary to detect this reduction. Over a 12-month period, we would therefore need to recruit about 11 participants per day in the full trial to achieve our recruitment target (3864/365 days). On average, 18,500 self-sampling kit orders are placed via freetest.me per month (616 per day). Based on this, we would need to recruit 1.8% of total users to the study per day (11/616). To demonstrate within the present feasibility study that we can recruit at the required rate for the full trial, we would therefore need to recruit at the same rate within the pool of freetest.me users living within our four partner local authority areas over the 3 month recruitment period.

Statistical analysis plan. We will calculate the recruitment rate as the proportion of participants recruited per day (from the total using freetest.me in the four areas) to our feasibility RCT. Using analytics data, we will be able to identify the proportion of participants recruited to the study as a direct result of the different value propositions we post as study invitations on the freetest.me thank you page, and therefore draw conclusions about which will work best for the definitive RCT. We will also be able to examine analytics data to better understand the online participant sign-up/consent process and identify any potential 'friction points'. We will calculate the attrition rate as the percentage of randomised participants without a valid primary outcome measure (cumulative incidence of chlamydia measured using biological samples) at 12 months. Attrition rates will be provided for both the intervention and control groups. Non-response both to surveys (at 3M, 6M and 12M) and to requests to provide chlamydia outcome data (at 0M and 3M) will additionally be calculated. We will report on numbers of higher versus lower SES participants retained in the final sample as well as gender, ethnicity, sexual identity, trial group and chlamydia diagnosis at baseline, comparing proportions to make an assessment of whether these factors may be associated with attrition. Attrition will be further examined by plotting attrition curves comparing the percentage of valid participants in the trial at different time points: M0, M3, M6 and M12. This will be plotted for both the intervention and control arms so that comparisons can be made. We will also examine engagement with our intervention and control group material using analytics data. Engagement by demographic group will be compared to identify evidence of any differential engagement.

Engagement will be measured by examining the proportion of participants who achieve pre-determined goals (e.g. complete tailoring questions, view pages for all allocated components, spend more than *x* minutes on site at first visit, order a product, play a video), and also the 'bounce rate' for the home and content pages (the proportion of participants that leave a page without any interaction). Our analytics data will give meaning to any trends observed and help us to draw conclusions about which retention strategies work best and how we might be able to reduce drop-out within the definitive RCT. We will examine the level of completeness of all measures and run missing value analysis to assess whether any missing data are missing at random or whether patterns indicate a possible problem with measures. This will help us to understand changes that we need to make to our measures to reduce non-response. We will look at the observed difference between intervention and control groups for the cumulative incidence of chlamydia and use this data to support estimates for the required sample size for a definitive trial. Clinical significance will also be used in these estimates and a comparison of the two will help to determine feasibility of the future definitive trial. The percentage of participants in the control group who report at M12 that they were exposed to any Wrapped content will be calculated in order to assess contamination. The percentage of participants who report (at M12) that they have experienced an adverse event related to their involvement in the study will be calculated.

Socio-economic position and inequalities. Preliminary data analysis indicates that whilst users of internet chlamydia self-sampling websites are from across the deprivation spectrum, those from the lowest quintile may be slightly less well represented (8). Our feasibility RCT will examine whether a future definitive trial could recruit and retain participants from across important demographic groups (see objectives) including across deprivation. This is vital to determine whether the intervention has a differential effect on chlamydia incidence and therefore may exacerbate health inequalities. Our measures of engagement with the intervention and control material (captured by analytics data) will also be examined by group to identify evidence of differential engagement.

Procedure for reporting deviations from statistical analysis plan. Any deviations to analyses as specified in this protocol will be made in agreement with our statistician from Brighton and Sussex CTU. These deviations will be logged by the research team and fully described and justified in our final report.

Quality control and Quality assurance

Preceding qualitative study. The PI will oversee all data collection. Audio will be digitally recorded and transcribed by an external transcription agency. These transcriptions, along with researcher notes and photos, will form the research data. All research data will be stored on the PIs R drive. Only members of the UH research team (KN, KB, KK and LS) will have access to this data.

Trial. All trial data will be collected in REDCap. This is a secure data management programme hosted on UH server. Only the UH research team (KN, KB, KK and LS) and the trial statistician (SB) will have access to data on REDCap. SB will be limited to having 'view' access to the randomisation module so that during the recruitment period he can check that participants are being randomised according to the pre-defined randomisation list.

During project set-up, all members of the research team will receive training in how to enter data into REDCap for this project.

Data will also be directly entered into REDCap project instruments by participants themselves (i.e. 0M, 3M, 6M, and 12M surveys, and the 0M chlamydia test result). Instructions on how to complete

these will be reviewed by the PPI group to ensure that they are clear and easily understood. Text will be kept to a minimum. The survey items themselves will also be tested by the PPI group.

Prior to moving the REDCap project into production, it will be thoroughly tested. This will involve:

- Entering test data using all fields in all instruments and all events to validate instruments and event definition, branching logic and calculated fields. Test data must include different cases that will allow testing all scenarios of branching logic, calculated fields and minimum/maximum ranges. This will be performed by the UH research team and PPI group. The research team will also simulate the entry of results from 3M and 12M chlamydia testing into REDCap to test that process.
- Reviewing test data by opening data entry forms, creating reports, and exporting data. This will be performed by the UH research team
- Review data and check that i) all planned data analysis to achieve research objectives can be performed, and ii) there is no redundant/unnecessary data collection. This will be performed by the PI and statistician.

Analytics data will be stored within Matomo and only accessible by the UH research team. Data collection using this software will also be thoroughly tested by the UH research team and involve:

- Creating test data for both the intervention and control websites. Test data must allow testing of all scenarios of use
- Checking that unique participant IDs are captured by Matomo for both sites (through direct access from survey link and through link in email/SMS)
- Reviewing test data to check that all planned data analysis to achieve research objectives can be performed

Data handling and record keeping

A SOP for REDCap data entry will be developed by the UH research team. Training for those responsible for entering data will also be provided. Data will be downloaded from REDCap and stored on the PIs R drive for the purpose of analysis. Access to the relevant folder on this R drive will be restricted to the UH research team and the statistician (SB). As/when data is transformed during processing, a new version will be created and named with a version history used to record these transformations. This will ensure that it is always be possible to compare the original data with the processed data.

See data management plan (appendix C) for details on the archiving of research data.

Issue log

We will record all arising issues in an issue log. If action is required, an owner will be assigned and the outcome recorded. The issue log will be used to provide an audit trail of key events and decisions made. This will facilitate transparency, the production of reports/publications, and post-project learning.

Adverse events

We have identified two potential adverse events that could occur as a result of participation in the feasibility trial: 1) inadvertent disclosure to another person that the participant is sexually active/testing for an STI as a result of them being overseen using Wrapped, and 2) initiation or change in the consumption of pornography by the participant. At each follow-up time point, we will ask participants to tell us whether either of these events (or other event; details requested) has

occurred for them. There is also the potential for us to be alerted to these adverse or other unexpected adverse events outside of these time points e.g. by direct contact by participants via our study email address. All adverse events (regardless of origin) will be recorded in an adverse events log and the PI alerted. The PI will discuss each event with the research collaborators, and seek advice from the sponsor, ethics committee and steering committee on the most appropriate course of action.

Safeguarding

On completion of each survey, all participants will be sent an email that contains links to further sources of information and support relating to sexual health, including sources of help and support for those who may have been the victim of sexual abuse, assault or coercion.

The baseline questionnaire contains items that if endorsed would indicate that a participant had been, or is a victim of sexual assault, abuse, and/or coercion. What action would be taken as a result depends on the age of the participant. If they are 18 + years, an additional email would be triggered which acknowledges their responses and encourages them to make contact with these organisations. If they are under 18 years of age, then participant confidentiality will be broken in order to keep them safe. Specifically, their responses to these items, along with their contact details, would be passed on to the relevant local authority/trust where they reside so that contact can be made, and support offered as appropriate. This limit to confidentiality will be clearly outlined in the participant information and reiterated within the survey just prior to completion of the relevant questions (which are optional).

During the course of the research, it is possible that a participant may directly disclose that they are experiencing, or have experienced, sexual coercion, assault or abuse to member of the research team. In this eventuality, the UH safeguarding lead would be contacted and the case discussed. If the individual is deemed to be at immediate risk of harm, then confidentiality would be broken, and their contact details passed on to this lead so that appropriate support can be offered. As before, this is clearly explained within the participant information.

Trial website

Under development.

Participant information sheet

The participant information sheet for the preceding Qualitative study has been developed and received institutional ethical approval. The participant information sheet for the trial and nested qualitative study is under development.

Known risks/benefits

Risks. Participating in all aspects of the above proposed research has limited risk associated with it for participants. Participating in the focus groups (preceding qualitative study) will require individuals to comment on trial recruitment and retention strategies. Participating in the feasibility RCT will require individuals to complete questionnaire measures and to access either online information about STIs or the Wrapped intervention. Those in the intervention group will be given access to resources to encourage and support condom use. Users will be free to choose whether they order products and/or view the material. Trial participants will also be given the option to take part in a follow up interview (nested qualitative study) during which they will be asked about their experience of participating in the trial. Risks associated with these actions are in line with normal everyday risk and we will provide all study participants with information about how to access support for anything related to their participation in the study. As a result of participation in the

feasibility RCT, some people may attempt to use condoms and fail, and this may have some negative psychological impacts in the short-term. The same participants will also need to provide consent for sensitive personal data held about them by freetest.me to be accessed (result of their M3 and M12 chlamydia test result). This, along with all other data collected as part of the project, will be handled in accordance with the latest data protection legislation and anonymised for the purposes of data analysis and reporting.

Benefits. We will emphasise to participants in all aspects of the study, the value of participation in terms of the contribution to science and the potential benefit of the overall project to the health and wellbeing of society. Participants in the intervention group will be given access to free resources. All will receive samples of different types of condoms, some of which they may not have tried before. Depending on which components of the intervention they are allocated, participants may also be able to make monthly orders of condoms and/or receive a free keyring (with a 'hidden' condom). As a result of exposure to a sexual health intervention, there is the potential that some young people may increase their condom use (and reduce their STI risk) which has benefits to them and society.

Stopping rules

All members of the research team are responsible for alerting the PI if there is any reason to believe that there is risk to 1) the safety or welfare of a research participant or member of research team, or 2) the reputation of UH. In this event, the PI will discuss this with Co-I Prof Katherine Brown and if necessary, the project will be halted whilst further discussions/investigations proceed. If required the PI will seek advice and input from the project's governance groups i.e. Study Steering Group, The Brighton and Sussex Clinical Trials Unit (BSCTU), CRN Eastern, and UH (e.g. departmental head, Pro-VC (research), institutional ethics committee, and the Clinical Trials Support Network). Clear documentation about the decision will be kept in the Trial Master File, including justification and rationale for this, and communicated to sponsor and institutional ethics committee.

Randomisation codes

There are two experimental arms in the trial: intervention and control. The trial statistician (Stephen Bremner) will produce a randomisation list (in .csv). This list will determine the order in which participants are randomised into each of the two trial arms (stratified by group to maintain balance across key demographic criteria). KN will upload the randomisation list into REDCap. As/when participants are recruited to the trial, a member of the UH research team (KN, KB, KK or LS) will perform manual randomisation within REDCap (on a rotational basis).

Due to the nature of the intervention, it is very unlikely that there will be a need to break the randomisation code (see known risks/benefits above). However, if this is necessary then any member of the UH research team will be able to identify/confirm the allocation of an individual participant using the REDCap system. Contact details of all members of the team are available within the Personnel folder of the Trial Master File. The PI should be contacted in the first instance (including if out-of-hours).

Assessment of Efficacy (Progression criteria)

1) An average of 1.8% of freetest.me users (out of those who place an order for self-sampling kit in our four areas) per day recruited over 3 months (estimated rate required to recruit sufficient numbers to the definitive RCT over 12 months), and 2) 80% of participants (those randomised) followed-up for the definitive RCT primary outcome measure at 12 months, 3) mean deprivation score of final sample is +/-10% that of users of freetest.me in each of the four areas (as measured over the 3 month recruitment period) and 4) absence of serious/frequent adverse events. Progression decision determined by our independent Study Steering Group (SSG) based on

achievement of the criteria or convincing evidence that either/both are amenable to sufficient improvement.

Eligibility

Participant inclusion criteria: Participant type

Mixed

Participant inclusion criteria: Description

Young people aged 16-24 years living in one of our four recruitment areas.

Participant inclusion criteria: Age group

Mixed

Participant inclusion criteria: Gender

Both

Participant inclusion criteria: Target number of participants

Preceding qualitative study: 15-20
Feasibility trial: 230
Nested qualitative study: 60 (30 primary participants plus their sexual partners)

Participant exclusion criteria

Feasibility trial: no internet access; those whose sexual preferences mean that they are unlikely to have penetrative sex (penis in either vagina or anus) over the trial period.

Participant withdrawal criteria

An individual will be considered to have been recruited (and therefore a participant in the trial) if they are randomised. The process of randomisation will be performed by hand (within REDCap) for all those who complete the baseline (M0) survey.

Subsequently there will be a number of further data collection points: a self-report of baseline chlamydia test result (M0), three follow-up surveys (M3, M6 and M12), and two chlamydia self-sampling tests (M3 and M12). Participants will be invited to participate in all data collection points regardless of whether they began/completed prior activities unless they request to be withdrawn from the study. At each data collection point, a limited number of reminders (SMS/email) will be sent to participants who have not provided data (number frequency to be determined by our preceding qualitative study).

Participants will be informed about how to withdraw from the study within the participant information sheet (the process will be to notify the research team by email using wrapped@herts.ac.uk). Our position (as specified in the participant information) will be to keep all data provided by the participant up to the point at which they withdraw unless they request otherwise.

Recruitment start date

November 2020

Recruitment end date

End January 2021, or when have 230 participants randomised (whichever is sooner)

Locations

Countries of recruitment

United Kingdom

Trial participating centre

All participants will be recruited from the online STI self-sampling provider freetest.me. All data will be collected remotely using online surveys and through the return/analysis of postal STI self-sampling kits.

Project timetable

Months	**Calendar months (inclusive)**	**Activities**	**Associated milestones** (to be achieved by end of time period specified)
-3-0	Feb 2020- April 2020	Protocol development, ethics application, invitations to committee and advisory group members, study set up	• Ethics approval (preceding qualitative study)
0-6	May-Oct 2020	Updates to Wrapped intervention Creation of comparator website	• Stakeholder database • University-based project website set-up, along with linked Twitter account • Comparator website created • Updates to Wrapped complete
0-2	May- June 2020	Development of provisional recruitment and retention strategy	
3-4	July-Aug 2020	Focus groups	
5-6	Sept-Oct 2020	Finalisation of recruitment and retention strategy	• Finalised recruitment and retention strategy • Submit trial protocol paper for publication • Ethics approval (trial and nested qualitative study)
7-9	Nov 2020-Jan 2021	Recruitment of participants to feasibility RCT and M0 survey	• Recruitment target met
10-12	Feb–April 2021	M3 survey and distribution of M3 chlamydia self-sampling kits	
13-15	May-July 2021	M6 survey	
19-21	Nov 2021-Jan 2022	M12 survey and distribution of M12 chlamydia self-sampling kits	• Follow-up target met
9-22	Jan-Feb 2021	Nested qualitative interviews	

0-22	May 2020 – Feb 2022	Consult with Implementation and sustainability group	• Change package
22-23	Feb–March 2022	Feasibility RCT data analysis	• All data analysis complete
0-28	May 2020 – Aug 2022	Conference presentations (x3)	• Conference presentations delivered
24-28	April 2022 - Aug 2022	Report writing and dissemination	• Submission of paper reporting on findings of feasibility trial for publication • Lay summary (written and video) • Final report submitted to NIHR

Plain English summary

What is the problem?

Last year in England, 210,000 15-24 year olds were diagnosed with a Sexually Transmitted Infection (STI), half of all total diagnoses. If individuals experience symptoms, they can be unpleasant and painful. Often though, STIs have no symptoms and individuals unknowingly pass them on to others. Without treatment, STIs can have serious consequences such as infertility which negatively impact on quality of life. The cost to the National Health Service (NHS) of treating STIs is estimated to be £620 million per year. Each individual case of STI is preventable. The only way for sexually active people to avoid STIs is to use a condom, but young people report inconsistent use.

It is important that we look for ways to reach young people at risk of future STIs and identify what will help them to increase their condom use. One way of reaching large numbers of young people at risk of STIs, that has been almost entirely overlooked, is through STI self-sampling websites. Through these sites, young people can request a free self-sampling kit that is received and returned via post. Demand for this service is rising rapidly. Users include groups known to be most at risk of future STIs, such as those from poorer backgrounds.

What have we done so far?

Together with young people and health professionals, we have developed a website called 'Wrapped'. It aims to reduce future STI diagnoses amongst users of STI self-sampling websites through increasing their condom use. After placing an order for a self-sampling kit, users are immediately directed to Wrapped. Here they are asked to identify their main barriers to condom use before being allocated up to six different components. Components include a condom sample pack, access to a free monthly condom ordering service, a free condom carrier, a condom demonstration video, videos of young people giving tips on communicating about condoms, and videos of real couples discussing and using condoms.

What are we going to do?

What we want to know is whether Wrapped works. To find this out, we need to run a type of experiment called a Randomised Controlled Trial (RCT). RCTs are time consuming and expensive, often involving thousands of participants. In line with good practice, to prepare for this we are going to run a feasibility study. The primary aim is to identify whether we can recruit and retain the numbers of participants required for an RCT.

How are we going to do it?

Throughout this study we will work with users of a chlamydia self-sampling website (our Patient and Public Involvement (PPI) group). Initially, we will work with this group to develop materials and procedures that we think will work well to attract people to an RCT and keep them engaged throughout. The materials and procedures we select will be based on evidence of what has worked in the past but also on feedback from other young people sought via focus groups. We will then test these out by running a mini version of a full RCT. Throughout, we will carefully monitor engagement and interview participants, including those who drop-out, to see what we can learn about what it is like to be a participant in our study. Working again with our PPI group, we will use this evidence to adapt our materials and procedures so that we are ready to carry out a full RCT.

Results and publications

Publication and dissemination plan

At project inception, we will create a database of stakeholders (updated throughout) who we will communicate with via a university-based project website and linked Twitter account. We will use these media to promote our work, enable two-way discussion with our stakeholders, provide updates throughout the project (e.g. milestones achieved and highlights) and provide information on study outcomes. We will work with our PPI group on all materials used to disseminate findings to our participants and the public. As a minimum, these will include a written and video lay summary. We will communicate with the academic community via Twitter and also via the more traditional academic routes of conference presentations (e.g., Public Health England conference, British Association for Sexual Health and HIV) and peer-reviewed, open access journal articles. We will communicate with the wider public via press releases; resulting media will direct interested individuals to our website and social media channels. The NIHR will receive regular updates via MIS and a detailed scientific report at project end. The anticipated short-term impact of these dissemination activities is an increase in public engagement with research and related societal issues, and an increase in the knowledge economy (e.g. evidence regarding the effectiveness of recruitment/retention strategies, and lessons learnt from the feasibility study).

Intention to publish date

Publication of trial protocol – November 2020

Publication of results – August 2022

Participant level data

See data management plan (appendix C)

Basic results (scientific)

[leave blank]

Results (plain English)

[leave blank]

Publication list

[leave blank]

Version history

Version number	Effective date	Reason for change
0.1	17.02.20	This version was appended to the Collaboration agreement and reflects the Detailed Research Plan V6 11.02.20 approved by NIHR just prior to final sign-off. Within V0.1, three sections still needed work on them namely, 'participant level data', 'minimising bias', 'adverse events' and 'data handling and record keeping' – these sections weren't included in V 0.1 but are in V0.2
0.2		Absent sections have been populated, namely: 'participant level data', 'minimising bias', 'adverse events' and 'data handling and record keeping'. The project timetable has been adjusted slightly from that provided within the funding application. The table in version 2 reflects the Gantt chart supplied to NIHR as part of project start-up (MIS task) NB changes have been made to appendix A (consort diagram) – see changes on version history of Appendix A.
0.3		Removed plan to use Facebook for dissemination purposes.
0.4		Safeguarding section added to page 20 (also referenced on page 6). Safeguarding procedure reviewed and approved by DMEC and SSC; see meeting minutes 08.09.20. Members of SSC updated, and members of DMEC added (p7-8). Clarification made that the intervention condition consists of Wrapped *plus usual care* (p8, p12 and p15). This was always planned but, whilst was correctly described in the consort diagram, was not clear in the protocol text. Replaced one of our local authority areas (Croydon) with East Sussex as it was no longer commissioning freetest.me (p9) Added exclusion criteria (with approval of DMEC and SSC; see meeting minutes 08.09.20) re sexual preferences (p 9 and p22) Added that we will exclude (not randomise) participants who are identified as responding randomly to items within the baseline survey (with approval of DMEC and SSC; see meeting minutes 08.09.20) (p9). Our intention to send SMS to participants asking them to confirm postal address for sending out test kits 1 week prior to distribution has been added (P11).

		Further detail added about the use of email/SMS to collect data on treatment for 0M, 3M and 12M chlamydia tests (p11-12) Rather than Freetest.me accessing REDCap to enter test results at 3M and 12M we will now instead be given access to a secure service area when the lab will record these. We (UH) will also be responsible for inputting the data onto REDCap (not freetest.me) and also sharing positive test results with the four LAs/trusts. This new arrangement is outlined on p11-12 and p18-19. Our intention to use stratification to achieve balance at randomisation (instead of minimisation) stated on p12 (with approval of DMEC and SSC; see meeting minutes 08.09.20). Change to Wrapped content stated on (p14-15 and p21): headphone carrier replaced with faux leather keyring. Decision made in consultation with PPI who felt that headphone case no obsolete as earphone buds now the market leader (and they have moulded charging cases)
1	19.11.20	Changes made to version 0.4 (using track changes) approved by the NIHR (also this was the version approved by the REC). As a result, a new clean copy (V1), with all changes accepted, was created for display on the NIHR website and to guide the study going forward.