Health Technology Assessment Programme

NIHR HTA Programme

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An interactive computer-based intervention to increase condom use: intervention development and pilot trial

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Planned investigation

Overall aim: To undertake all necessary development work to address the question: "What is the clinical and cost effectiveness of a computer-based condom use intervention to prevent recurrent sexually transmitted infections (STI) in men?"

Hypotheses
We hypothesise that an interactive computer-based intervention offered to men after diagnosis of a sexually transmitted infection will be more effective than usual care alone in increasing their motivation and capability to use condoms correctly, resulting in more consistent and correct condom use and consequent reduction in future STI acquisition.

This proposal is for developmental research to
1) Design an **interactive computer-based intervention** to increase correct condom use in men 16 and over, recently diagnosed with an STI
2) Assess the **feasibility and optimum design** of a **randomised controlled trial** to test the intervention

Detailed objectives:
• Clarify the barriers and facilitators affecting condom use for men
• Develop and optimise a targeted, theoretically-informed, interactive computer-based intervention (ICBI) to increase correct condom use in men recently diagnosed with STI
• Refine our existing sexual health outcome measure (for self-reported sexual health behavioural outcomes)
• Conduct a pilot trial to optimise the parameters for a Phase 3 randomised controlled trial of usual clinical care plus the ICBI compared to usual care only
• Conduct a qualitative process evaluation to explore men's experiences of participating in the pilot RCT
• Optimise the data collection and analysis procedures for a health economic analysis for a future Phase 3 RCT

Existing research

Sexual health crisis for men
Sexually transmitted infections (STI) and unwanted pregnancy are major public health problems, with high social and economic costs.[1] Men aged 20-34 are at particularly high risk of STI acquisition, with particularly high rates of STI and HIV in men who have sex with men.[2]

Problems with condoms as prevention
Condoms are effective for prevention, but there are many barriers to successful use, for example decrease in sensation, interruption of sex, incorrect size or fit, use of alcohol/recreational drugs, anxiety affecting sexual performance, and stigma associated with carrying condoms.[3] The prevention of pregnancy is often a stronger motivation for condom use than prevention of STI.[4] Condoms may be perceived as barriers to intimacy and trust,[5] and use is often lower in established relationships.[6] Gendered sexual scripts and power imbalance militate against successful condom use, reinforcing taboos about discussing and negotiating sex in advance.[5] It is men who experience most of the disadvantages of male condoms, and who have more power to influence condom use for penetrative sex, so prevention efforts should target the obstacles that they face.[3]

Men may be reluctant to discuss their sexual health with health professionals, partners or friends.[7] Men are less likely than women to visit health professionals and generally have shorter clinic appointments, so are less likely to be offered health promotional advice or risk reduction counselling in the context of routine appointments. The National Chlamydia screening programme has been less successful in reaching men than

women under 25 (22.6% of men vs. 42.7% of women in 2010-11). A computer-based intervention therefore offers an alternative avenue to reach men who are not accessing face-to-face health services.[8]

Why men recently diagnosed STI?
People who have had one sexually transmitted infection are at high risk of acquiring another in future:[9] re-infection rates within one year were 8.4% for Chlamydia and 8.9% for Gonorrhoea at St Bartholomew's sexual health centre in London in 2011. The time of diagnosis represents an opportunity for health promotion since the diagnosis (especially a first diagnosis) may represent an event which prompts reflection on future behaviour.[10] Whilst STI diagnosis and treatment is managed increasingly in general practice or community settings such as pharmacies, most sexually transmitted infections are diagnosed in genitourinary (GU) clinics,[2] so GU clinics are an ideal setting for participant recruitment.

Why a computer based intervention?
We define interactive computer-based interventions (ICBI) as 'Computer-based programmes that provide information and one or more of decision support, behaviour-change support, or emotional support for health issues'.[8] ICBI require contributions from users to produce personally relevant tailored material and feedback. ICBI are highly suitable for sexual health promotion because access can be private, anonymous and self-paced,[11] which may be particularly important for men who may be reluctant to disclose a lack of knowledge or skill. Interventions can be targeted for specific groups (e.g. by age, gender or sexuality), and content can be tailored for individuals.[12]

Our Cochrane systematic review of ICBI for sexual health promotion has shown that they can improve sexual behaviour (including condom use) as well as increasing knowledge, self-efficacy and safer sex intention.[8] Noar et al. also found that ICBI are effective in increasing condom use.[13] More evidence is needed to establish effects on biological outcomes (STI) and cost-effectiveness. ICBI can be expensive to develop but offer the advantages of intervention fidelity[14] and the potential to reach large audiences at relatively low dissemination costs.

What works face-to-face?
Guidance from the National Institute for Health and Clinical Excellence recommends that people at high risk of STI are offered one-to-one structured discussions to address risk-taking,[1] and this is increasingly being offered as part of routine care in GUM and other health care settings. Whilst interventions such as motivational interviewing can impact on sexual behaviour,[1] in practice it is resource intensive to train and support staff, and to difficult find time for structured discussions in busy clinical services.

There is now a large body of evidence on face-to-face sexual health interventions for men. Interventions such as one-to-one or group counselling have proved disappointing, with systematic reviews of trials showing contradictory outcomes and at best only modest results on outcomes such as condom use and STI incidence.[15;16] In the face of contradictory results from trials, it is difficult to define the 'active' components of face-to-face interventions.[17;18] The most effective trials in men attending GU clinics used extensive formative research with users[16] – user input into intervention development is therefore a key component of our proposal.

Components of internet interventions
ICBI are complex interventions, with multiple components which may interact, and evidence is emerging about which components are necessary to promote behaviour change. A meta-analysis of computer-based interventions for health behaviour change indicates that interventions which make more extensive use of behaviour change theory and behaviour change techniques are more effective.[19] ICBI efficacy is also enhanced with the use of mobile phone prompts,[19] so we will augment our online intervention with text message prompts to promote safer sexual behaviour. Less is known about the efficacy and appeal of mobile phone applications (apps) to promote sexual health: smart phones are increasingly popular, so this proposal will assess the feasibility and appeal of sexual health promotion in the form of a mobile phone app.

Our team have already developed an **interactive website for sexual health promotion** for young people aged 16-20 (www.sexunzipped.co.uk), and this will be adapted to specifically target men. Sexunzipped was

developed in partnership with young people, and aims to give them the tools to make informed decisions about their sexual health. The site features information, self-reflection activities and decision-making activities in three main domains: Safer Sex, Relationships and Sexual Pleasure. Specific behaviour change techniques[20] are used to encourage safer sex behaviour (active decision-making to avoid regretted sex, increased communication with partners, condom use, contraception use, and STI testing).

Summary
Clinical services are failing to cope with rising rates of STI, and we urgently need **innovative ways of preventing sexual ill-health**. There are several compelling reasons for developing a computer-based intervention to increase condom use which is targeted for **men with a recent STI diagnosis**: they are at high risk of recurrence, and the majority of the disadvantages of condom use particularly affect them. A computer-based intervention offers private, entertaining, self-paced learning which can be tailored specifically for individuals.

Our experienced, multi-disciplinary team are ideally placed to deliver this programme of work which will result in a **computer-based intervention** which is engaging as well as educational, and pilot/feasibility testing of the parameters for a randomised controlled trial to compare the computer-based intervention to 'usual care'.

Project plan

The study design will follow the MRC Framework for developing and evaluating complex interventions[21] and NICE principles for planning, delivering and evaluating public health interventions.[22]

Pre-trial preparation:

Updating literature reviews:
Before the formal beginning of the project, we will **update existing literature searches**, using the best available evidence to inform the intervention content:

- Barriers and facilitators to condom use;
- Computer-based interventions for sexual health (efficacy and mechanism of action);
- Face-to-face condom use interventions (efficacy, mechanism of action and content);
- Psychological theoretical models applicable to sexual health behaviour change
- Behaviour change techniques effective in web-based interventions;
- Economic outcomes related to condom use and STI acquisition.

We will also have sought **ethical permission** for the whole programme of work from COREC, and **Research and Development approval** from the hospital trusts where the genitourinary medicine clinics (GUM) clinics are situated.

Programme of work

- Please see **Project tasks and timelines** (page 14) **Study flow diagram** (page 17)

Part 1- Intervention development and pilot trial set-up
Month 1:   Project set-up, staff training
Months 2-4:   Views on barriers to condom use and intervention content
                        - Men's views (n=20 interviews);
                        - Health advisor views (1 workshop)
Months 5-10:   Computer-based intervention development (n=48 men in focus groups)
Months 8-10:   Refine online outcome measurement instrument (n=12 interviews)
Months 11-12: Final intervention user testing (n=10 interviews) and pilot trial set-up

Part 2- Pilot randomised controlled trial
Months 13-18: Pilot trial recruitment (172 men from 2-3 GU clinics)
Months 25-30: 12 month online outcome data (self-reported), clinic notes review and postal STI testing
Months 25-30: Qualitative process evaluation (n=24 interviews with trial participants)
Months 31-32: Quantitative data analysis
Months 32-33: Dissemination of findings, protocol for Phase 3 RCT

PART 1: Intervention Development and pilot trial set-up- 12 months

Aims:

- To develop a targeted, theoretically-informed **interactive computer-based intervention** which tackles the barriers to effective condom use for men recently diagnosed with a sexually transmitted infection.

- To set up a **pilot randomised controlled trial** including refining our online **outcome measurement instrument**

Our interactive website for sexual health promotion for young people (Sexunzipped) will form the basis of the computer-based intervention targeting condom use skills for men. We already have the software frameworks for online registration, computer-generated randomisation, automated emails to prompt intervention use and follow-up. We also have a fully user-tested online sexual health outcome measurement instrument (the Sexunzipped sexual health outcome questionnaire).

Intervention development process
We will run a **workshop with sexual health advisors** and conduct **interviews and focus groups with men** to:
- Clarify the barriers and facilitators affecting condom use for men
- Work out how best to apply theoretical models for behaviour change
- Design and develop an interactive computer-based intervention (ICBI) to help men to negotiate consistent and correct use of condoms for penetrative sex

Health advisor workshop
We will recruit five **health advisors** who work in genitourinary or sexual health clinics and hold a **one-day workshop** to explore their perceptions of barriers and facilitators to correct condom use and their views on intervention content. Those participating will be offered £100. Discussions will be audio-taped with permission, and emergent themes coded. Health advisor views will inform the **sexual health content** of the intervention.

Men's views
We will consult users (men who are sexual health clinic users) at every stage of the intervention development process. We will model condom use behaviour using a 'behaviour change wheel'[23] to establish the capabilities, opportunities and motivations that men need in order to increase their condom use. From this starting point, we will plan the necessary components of a computer-based intervention.

Men's views on barriers and facilitators to condom use
We will conduct **20 one-to-one interviews** with **men recently diagnosed with STI**, recruited from participating GUM clinics. We will sample purposively, to ensure a diverse sample in terms of age; sexuality ('heterosexual', 'bisexual' and 'homosexual'); first or subsequent episode of STI; and ethnicity. The research associate will conduct semi-structured interviews to ascertain men's experiences and perceptions of barriers and facilitators to condom use, and views on how a computer-based intervention might help them to change their condom use behaviour. Interviews will be conducted in side rooms in GU clinic settings at the time of a visit, or another time in a mutually agreed location (e.g. at University College London). Men will be offered £15 as an incentive for participating.

Men's views on design and content of a computer-based intervention
We will conduct **6 focus groups** with 6-8 men in each group, to establish men's views on successive design templates for the computer-based intervention components, especially website look and feel, site architecture and interactive features. The content of email and text messages to prompt behaviour change will be tested with users to establish acceptability. Focus groups will be facilitated by JB and the project research associate, audio-recorded with permission, and data will be analysed thematically,[24] with ideas feeding in to the next software design templates. We will hold three groups with 'heterosexual' men and three with 'homosexual or bisexual' men in age bands 16-20; 21-25; and 26 and over. These participants do not have to have been diagnosed with a recent STI. Focus groups will be conducted in a central London location, and participants will be offered £20 as an incentive.

Health Technology Being Assessed:
The intervention will comprise a targeted, tailored, theoretically-informed, **interactive computer-based intervention** (ICBI) to encourage condom use in men recently diagnosed with STI. This intervention will be delivered via three platforms: A) The Internet B) touch-screen laptop activity and C) via mobile phone (text messages +/- smart phone 'app')

A. The Internet
The Sexunzipped website already features the following content pertaining to condom use, which can be adapted and expanded in the light of the views of men 16 years and over.

- **Information**, including sexually transmitted infections and their treatment; condom types and sizes; eroticising condom use; erections and condoms; sensation and condoms; how to be a better lover.
- **Self-reflection/self-score activities**: STI myth busting; STI quiz; Condoms are crap (reflection on barriers); Condoms- it's not my problem; Condom confidence; Condom skills; Regretted sex
- **Decision-making activities**: Reducing my risk; How to use condoms more

Sexunzipped content is informed by behaviour change theory. For example, four behaviour change techniques were used in the 'Reducing my risk' activity: 1) Information about behaviour-health link; 2) Information on consequences 3) Prompting intention formation and 4) Prompting barrier identification.[20]

The website tackles the wider social significance of condom use or non-use,[5] and discusses communication and negotiation skills. We will expand information and activities to emphasise assessment of personal risk, choosing condom size, correct condom use, and other specific barriers to condom use which users indicate are important to them. The intervention is likely to feature activities to increase motivation to use condoms; detailed communication skills training; and exercises to boost self-efficacy. Safer sex health promotion will be integrated with other topics, for example 'Sexual pleasure and condoms'.

All of the content will be written with user input at every stage, ensuring that content is relevant and appealing to men who have sex with women as well as men who have sex with men. The website can easily show different content to different demographic groups if this is desired by users. All of the sexual health content will be edited by the research associate using a **software content management system** we have already developed for the Sexunzipped study.

B. Touch-screen condom skill interactive activity
This will be a newly developed touch-screen interactive activity focusing on key condom use skills (e.g. seven points to remember with correct condom use, including size and fit; expiry date; direction of unrolling; expelling air; use throughout sexual intercourse; holding the base on withdrawal; and no re-use of condoms). This 5 to 10 minute game/activity will replicate in a virtual environment the practical skills that are needed for condom application. Participants will be encouraged to access this part of the intervention in a clinic side-room immediately after their clinic appointments. The touch-screen platform will also allow access to the website content described above.

C. Mobile phone platform
Text message content and acceptability will be established in interviews and focus groups with the target group. This part of the intervention may comprise reminders to use condoms at time of high probability of unsafe sex, e.g. Friday and Saturday nights. We will also develop a software application suitable for a smart phone (with mobile Internet access), for example an app which addresses issues such as condom use and erectile dysfunction, and condom use and sexual pleasure.

Pilot randomised controlled trial preparation

Online outcome measurement instrument refinement
We generated the **Sexunzipped online outcome measurement** instrument with user input in qualitative and quantitative validity testing. The measure captures mediators of behaviour change (cognitive outcomes such as knowledge, self-efficacy, intention) and psycho-social outcomes (such as relationship and sexual satisfaction), as well as behavioural outcomes (including condom use, service use). The questionnaire has proved acceptable and comprehensible in the Sexunzipped pilot trial (involving more than 2000 young people aged 16-20 from all areas of the UK).

There is no consensus on the best ways of measuring condom use, and there are a multitude of condom-related outcome measures available.[4;18] For the Sexunzipped study we selected condom use at last vaginal or anal sex; correct condom use (from start to finish, without splitting or coming off); and numbers of occasions of unprotected sex in the last 3 months, but we will review which behavioural outcomes are most appropriate for this study. We will conduct **12 one-to-one interviews** with **men**, to test the relevance, comprehensibility and acceptability of condom-related outcome measures to this older age group, sampling men who have sex with women and men who have sex with men. We will also test the relevance, comprehensibility and acceptability of any newly derived economic outcome measures. Men will be recruited from participating GU clinics or other sexual health clinics, and offered a £15 incentive for participating. Structured interviews will be conducted by the research associate, asking participants to 'think-aloud' whilst completing survey items. These discussions will be audio-recorded, and emergent themes will inform the re-design of survey question items (if this is necessary). The structure of the survey (e.g. skip patterns) and content of individual items will be edited using a **software content management system** which has already been developed for the Sexunzipped study.

Final intervention and trial software testing
Trial procedures (participant registration, consent, randomisation and self-reported outcome data collection will all be online, submitted via the study laptop). We will test the **usability and functionality** of this computer-based trial software framework. **Ten men** (new to the project), aged 16 years and over will be recruited from participating GU clinics or other sexual health clinics, and offered a £15 incentive for participating. **Structured interviews** will be conducted by the research associate, asking participants to 'think-aloud' whilst interacting with a study laptop as if they were trial participants. We will assess the usability and functionality of our procedures for presenting study information online, registering, providing informed consent, automated study arm allocation, touch-screen activity and intervention website access. We will not seek comments on the intervention content at this point. Interviews will be audio-recorded, and findings will feed directly into the final design of the study software framework, and intervention functionality. We will also check systems for automated emails, text messages, and data collection and export (questionnaire responses and patterns of site use).

PART 2: Phase 2 Pilot Randomised Controlled Trial- 21 months.

Aim: to establish the feasibility and best design of a full-scale trial of the computer-based intervention, comparing usual clinical care plus the intervention to usual clinical care only

We will run a pilot randomised controlled trial, recruiting 172 men from sexual health clinics, allocating them either to usual clinical care only, or to usual care plus ICBI, and measuring outcomes immediately post-intervention and at 12 months.

Target Population:
Men recently diagnosed with STI including men who have sex with men (a high risk group with high STI incidence rates) and men who have sex with women (a majority population).

Inclusion criteria
Men aged 16 years and over, with no upper age limit, able to read and write in English, with an active email account and access to the Internet. Participants will be men with a **new diagnosis** of Chlamydia, Gonorrhoea, genital warts, genital herpes, trichomoniasis or non-specific urethritis. We will also include men who receive treatment as contacts of partners with Chlamydia or Gonorrhoea, and those treated presumptively on the basis of their symptoms.

Exclusion criteria:
HIV positive men, diagnoses of syphilis, hepatitis B or C, since patients with these diagnoses are likely to receive more intensive input in the course of routine clinical care.

Setting:
We have chosen to recruit patients in three of London's busy **genitourinary medicine (GUM) clinics**: The Homerton Hospital Department of Sexual Health, the Ambrose King Centre at the Royal London Hospital and the Mortimer Market Centre for sexual health and HIV. These GUM clinics serve a diverse range of patients in terms of age, sexuality, socio-economic status and ethnicity. A genitourinary clinic setting will facilitate recruitment since there are large numbers of new or suspected diagnoses per week.

Methods used to ensure recruitment to the study
We already have excellent links with staff in the proposed GUM clinics (through JA, MS, GH and CE). We will present the research at clinic staff meetings, and the presence of a researcher in clinic waiting rooms will help to remind clinicians to refer participants. We will offer a token prize to the clinician who refers the largest number of eligible participants to the trial each month.

Recruitment procedure
A project researcher will be present in the waiting rooms of participating GUM clinics. Clinic staff (doctors, nurses, and health advisors) will refer potentially eligible men to the researcher after their clinical appointment/s. The researcher will explain the study, check eligibility, obtain informed consent (for the study and to check medical notes), and collect baseline (demographic) data on a laptop. We will also put up posters and hand out flyers to men in the clinic waiting rooms, so that men can refer themselves to the study. The researcher will ensure that men under 25 are offered membership of the 'Come Correct' free condom scheme, and will give free condoms to those who did not receive them as part of their clinical care.

Randomisation and allocation of participants to trial groups
Once baseline data is submitted on the laptop, participants will be allocated by computer algorithm to either the intervention or control group. The participant will be informed with an automated message on the laptop, and this allocation will be unalterable. The control group (usual care) will be asked to complete self-reported sexual health outcome questionnaire straight away. The intervention group (usual care plus ICBI) will have access to the touch screen condom training intervention (in private) and will then be invited to complete the self-reported sexual health outcome questionnaire on the laptop.

Proposed sample size
There are two key outcomes for this pilot RCT: one to assess the potential efficacy of the ICBI intervention using a safer sex intention outcome measure and the other to assess the feasibility of a phase III trial with STI and self-reported behavioural endpoints. The latter will be assessed by the follow-up rate in both arms at 12 months for online self-reported outcomes and postal STI testing.

We have powered the study to allow estimates of the effect of the intervention on mediators of sexual behaviour change (self-efficacy and intention) immediately post-intervention. A sample size of 172 men (86 intervention, 86 comparator, randomised 1:1 between experimental and control conditions) is adequate to find a 1.65 difference in safer sex intention, and a one-point difference in self-efficacy on Likert

scales, with a conventional two sided alpha of .05 and power (1-beta of .9). We anticipate low rates of loss to follow up for the measurements made immediately post-intervention.

Statistical analysis

Analysis of sexual health outcomes will be based on all participants according to their initial experimental allocation (intention to treat analysis). Comparisons of sexual health at 12 months between intervention and control groups will include the baseline value of each outcome as subject level explanatory variables, so that analysis is of differential change according to allocation. For binary outcomes this will be based on logistic regression, for ordinal outcomes on ordinal logistic regression and for continuous outcomes on linear regression. These techniques will lead to the adjusted odds ratio, odds ratio and mean difference as the effect measure, respectively. All effect measures will be presented with 95% confidence intervals. P-values will also be quoted based on 2-sided tests, and a 5% significance level will be used. Estimates of effect sizes derived from the pilot trial will be used to calculate sample sizes for a full scale RCT.

Recruitment rate

We have estimated that 5-6 people per day will be eligible to participate in the research and that 1-2 per day will join the study. We have allowed up to 26 weeks to recruit 172 people.

Planned interventions

Trial arm 1

Comparator arm – usual care

'Usual care' comprises normal clinical care offered in a GUM setting – i.e. clinical diagnosis, treatment if judged appropriate, information about sexually transmitted infection and its treatment, and health promotion as offered routinely. Clients with a new STI diagnosis will usually be offered a more detailed discussion and health promotion counselling with a clinic health advisor: some clients will see more than one staff member as part of routine care. Pressures on services at different times will mean that some clients will receive more time and attention than others. **All study participants will receive usual care**, with allocation to comparator or intervention group after this.

Participants in the comparator arm will receive **mobile phone text messages with trial-related content** only (e.g. emphasising the importance of participating in the trial). Participants in the comparator group will be offered access to the web-based intervention once the trial has ended.

Trial arm 2

Usual care plus Interactive Computer-Based Intervention

Participants in the intervention group will receive usual care as detailed above, plus an Interactive Computer-based intervention delivered via three platforms: 1) touch-screen laptop activity, 2) online via users' usual Internet access routes, and 3) via mobile phone (texts messages, and access to a smart phone 'app')

Proposed duration of the intervention

1) Laptop condom skill interactive activity – duration 5-20 minutes in a side-room in the clinic
2) Website with information, self-reflection, self-score, decision-making activities – password-protected access, with monthly automated email prompts to access the site over 12 months
3) Texts by mobile phone – content and frequency to be chosen by participants – e.g. condom use reminders on Friday and Saturday nights.
4) Smart phone application, e.g. self -help exercises for sexual problems

For men who have a landline telephone but not a mobile phone, we will offer the option of sending text messages to the landline to be read out loud electronically. Many participants may not have home Internet access, or may not own smart phones (i.e. phones with mobile Internet access): they will not therefore be able to access content via these means. All participants will be asked their opinions of these alternate platforms for accessing intervention content –access to digital technology is a major factor in assessing the feasibility of a future trial (and any future dissemination of effective interventions).

Qualitative process evaluation

We will conduct a **qualitative process evaluation**[29] to explore men's experiences of participating in the pilot trial. We will recruit a diverse sample of men who have participated in the pilot trial (diverse in terms of age and sexuality) (n=24 interviews). Men will be invited to participate by email, and interviewed in person using a semi-structured topic guide. Interviews will be audio-recorded with permission, transcribed and coded thematically using Atlas.ti software for data retrieval and coding. The findings of this study will help us to understand how the intervention was perceived and used in practice, and will inform the design of a future definitive randomised controlled trial (including optimising procedures for recruitment and retention).

Training of researchers and collection of data
We will ensure that all researchers are up to date with Good Clinical Practice training, and have the skills and training to conduct high-quality research, for example interview and focus group skills, qualitative data analysis, best practice in trial conduct.

Methods to protect against sources of bias
Once eligibility for the study is established, allocation to intervention or control group will be automatically randomly assigned by computer algorithm, and this will not be changeable by participants or researchers. Participants will be aware of their allocation to intervention or control group because only the intervention group will receive the computer-based intervention. Participants will provide baseline and initial outcome data on a laptop in private, with the researcher available only to clarify research procedures. Subsequent outcome data (at 12 months) will be collected online using an emailed link to the online outcome questionnaire. Data will be saved and exported using ID numbers only. Data collection procedures are therefore automatically blind to allocation to intervention or control group, since they are automated.

Data management
All data will be safeguarded according to the principles of the Data Protection Act 1998, with participant personal details such as name, address, email address, mobile phone number saved on an encrypted, secure external server. Automated exports of outcome data will provide an audit trail to ensure data integrity.

Measurement of cost and sexual health outcomes:
We will report intervention development costs and recruitment and retention rates. We will measure mediators of behaviour change (cognitive outcomes such as condom-related **knowledge**, **self-efficacy**, **intention**) and psycho-social outcomes (such as **relationship and sexual satisfaction**), as well as behavioural outcomes (**including condom use, STI testing, communication with partner/s**), and **STI incidence** (self-reported and laboratory sampling), and outcome measures for a cost-effectiveness analysis.

Self-reported sexual health outcomes will be collected online immediately post-intervention and at 12 months. We will use automated email reminders which provide a web link to the online questionnaire for the 12 month follow-up. We will post a paper version of the questionnaire to any participants who do not have email and Internet access. STI diagnoses will be recorded from GU clinical notes at 12 months as well as laboratory testing of urinary samples returned by post for Chlamydia and Gonorrhoea. We will also record participants' **patterns of engagement with the intervention site** over 12 months, and responses to automated text messages.

Proposed frequency and duration of follow-up

Participants in Sexunzipped research found the sexual health questionnaire interesting and thought provoking, with some reporting that they contemplated behaviour change simply after completing the baseline questionnaire. In the light of evidence that measurement alone may prompt behaviour change,[25] we will measure **condom use, self-efficacy and intention only** immediately post-intervention with a full range of outcomes at 12 months.

Recruitment – Baseline measures	Time 1 – immediately post intervention	Time 2 – 12 months
		Knowledge
Demographic details	Self-efficacy (for condom use and communication with partners)	Self-efficacy (for condom use and communication with partners)
Email address	Intention (for condom use, communication with partners, STI treatment and testing)	Intention (for condom use, partner communication, STI treatment and testing)
Mobile phone number	Condom use at last sex/ over the last 3 months	Behaviour: condom use, partner communication, STI testing
		Wellbeing, relationship and sexual satisfaction
		Economic outcomes: e.g. service use, quality of life

Maximising retention

Our experience with Sexunzipped research indicates that follow-up by email is totally acceptable to participants with email accounts. Participants found it simple to access the online questionnaire by following a weblink within the email. The Text-to-Stop smoking reduction trial obtained their excellent follow-up using multiple methods of contacting people – we will use similar methods:

1) Automated email, with 3 further prompts
2) Texts to mobile phones, with 3 further prompts
3) Telephone call from the researcher with completion over the phone
4) Paper questionnaire by post

Cost- effectiveness analysis

The primary aim of the economic component will be to determine the **feasibility and validity of collecting cost and outcome data** for a cost effectiveness analysis within a full trial. We will conduct an initial **cost-effectiveness analysis** (CEA) of incremental cost per gain in outcome, looking at cost per STI prevented (Chlamydia or Gonorrhoea), comparing intervention participants with controls from the NHS perspective. This will include one way, two and parametric sensitivity tests.

The aim of the analysis will primarily be to test whether information collected is fit for purpose, and to inform information collection in future trials. We will test the feasibility of collecting cost data for intervention and control participants including costs associated with STI tests and treatments, and contract tracing, testing and treatment. Trial subjects may access sexual health services from a range of providers, so information from GU clinic notes alone may prove unreliable. We will therefore ask participants about sexual health related health service contacts over the past 12 months as part of the self-reported outcomes. Personal Social Services Research Unit (PSSRU) reference costs, British National Formulary and other national sources of costing information will be used to calculate unit costs. Costs associated with the maintenance of the internet site and updating the site will also be included.

STIs prevented will be calculated by taking account of laboratory diagnoses at 12 month follow up as well as self-reported episodes for the previous year. We will calculate the cost per episode of Chlamydia or Gonorrhoea prevented for the intervention group versus controls. We will determine whether there are other suitable outcomes for use in the cost-effectiveness analysis.[26] The National Institute of Health and Clinical Excellence (NICE) recommends that quality adjusted life years (QALYS) are used as the outcome in cost-effectiveness analysis, to allow for the comparison of results for different cost-effectiveness analyses across disease areas. QALYs are calculated by multiplying health related quality of life (HRQoL) by the amount of time spent in the HRQoL state. The EQ-5D is the questionnaire recommended by NICE to calculate HRQoL.[27] It is a 5 item, 3 level questionnaire, with the 5 items being self-care, usual activity, anxiety and depression, pain and mobility. It has been recognised though that the EQ-5D may not be suitable for economic evaluations of public health interventions as it does not capture the relevant information on the full psychosocial impact of public health interventions.[26;28] As part of the literature review and focus groups we

will explore suitable outcomes for assessing the impact of the internet based intervention versus controls, including whether there is a possibility of including HRQoL as an outcome in the CEA in a full trial.

Incidence of STI has significant cost and QALY impacts that may occur beyond the end of the trial, so it is important this information is accounted for as part of the model. This is commonly achieved by a decision analytical model that has a time horizon beyond the end of the trial and combines cost and outcome data from a range of published sources in addition to trial information. As a result we will begin the process of designing a decision analytical model that will take account of costs and QALYs for the lifetime of the service users. The values in the decision analytical model will come from a comprehensive review of the literature including the efficacy of condoms, research to increase condom use and the incidence and prevalence of STIs. The quality of each of the type of evidence and relevance to the UK context will be assessed to determine the best coefficients to use in the cost-effectiveness model.[26] We will also aim to determine utility values for the long term QALY outcomes associated with STIs. The final model will compare the incremental cost per QALY gained and cost per STI prevented of the internet based intervention versus the control group. It will be subject to one way, two way and probabilistic sensitivity analyses (PSA) and a cost effectiveness acceptability curve calculate to determine the probability that the internet based intervention is cost effective for a range of values of willingness to pay for an outcome gained.

Project Outcomes

- Optimised interactive, computer-based intervention for men with STI
- Model for intervention mechanism of action
- Pilot trial recruitment rates
- Robust mechanisms for randomisation and concealment of allocation until the point of randomisation
- Feasible and valid sexual health and economic outcome measures
- Cost-effectiveness model
- Retention rates at 12 months
- Estimated sample sizes for a substantive RCT
- Optimised protocol for a phase 3 randomised controlled trial

Assessment of trial feasibility
Engagement with the intervention, retention in the trial, quality of outcome data obtained and the potential cost effectiveness of an intervention will be used to decide whether a future **large scale randomised controlled trial** (powered to assess effectiveness and cost-effectiveness) is desirable and feasible.

Ethical arrangements
Risks and anticipated benefits for trial participants and society including how benefits justify risks
This project aims to encourage behaviour change to reduce morbidity and the social and emotional costs of STI acquisition. This will benefit trial participants as well as wider society.

There is a risk that the study may unintentionally exacerbate the stigma of STI and risky behaviour for participants. We strive to be non-judgemental about choices of lifestyle or behaviour, respecting others' autonomy. It could be that participants' partners or others see the intervention website, text or email messages and that this leads to relationship difficulties in some way. A component of the intervention will focus on communication with partners, so it is hoped that the intervention will improve the quality of relationships rather than cause harm.

Informing potential trial participants of benefits and risks
Detailed information about the study including risks and benefits will be presented on the study laptop which will be in a side-room in participating GU clinics. Participants will have the chance to ask the researcher any further questions.

Obtaining informed consent

All participants included in the trial will be asked for their consent to take part and for their data to be used in communications to them, and for any subsequent monitoring data obtained as a result of their use of the NHS services to be used for research purposes. The consent form will be saved on the study laptop. We will ensure that all research procedures meet the highest standards for data protection and confidentiality. 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.

Sex, sexuality and sexual health can be controversial topics. Our approach is based upon the principle of harm reduction, aiming to mitigate potential dangers whilst acknowledging that some people will continue to engage in behaviours which carry risks. This approach to sexual health may conflict with the views of some. We have the resources of the UCL media relations office, and will communicate openly about the content and aims of our project to try to pre-empt controversy and adverse publicity.

Proposed time period for retention of relevant trial documentation
10 years

Research governance
University College London is the trial sponsor. UCL will ensure that there are robust, high quality arrangements for initiating, managing, monitoring, and financing the study in accordance with the Research Governance Framework for Health and Social Care (2005).

Steering Group and Pilot Trial Management
The entire programme of work will be overseen by a **Steering Group** that will meet quarterly. All co-applicants will be members of the Steering Group, and their role will be to advise about all issues to do with the design and conduct of this programme of research.

The pilot trial will be run through the UCL **PRIMENT Clinical Trials Unit**. The Principal Investigator (JB) will maintain day to day responsibility for the pilot trial, working in close collaboration with the Trial Manager (Research Associate, to be appointed) and Tatiana Salisbury from PRIMENT to ensure that the trial is conducted, recorded and reported in accordance with the protocol, good clinical practice guidelines, and essential standard operating procedures for running randomised controlled trials (including all aspects of trial management, quality control and data analyses).

A **Trial Management Group** consisting of JB, EM, GR, JS and the trial statistician (NF) will meet monthly at the start of the study and then quarterly on completion of recruitment to monitor the conduct and progress of the trial. JB and NF will monitor data to identify any unusual patterns. Preliminary analyses of study outcomes and adverse events will be presented to the Trial Management Group when 25%, 50% and 75% of the data are collected.

4. Project timetable and milestones

Pre-project preparation:

Milestones
By month 0:
- Ethical and R&D permissions in place
- Literature reviews complete
- Research Associate recruited

Part 1 – Intervention development

Month 1:	Project set-up, staff training
Months 2-4:	Health advisor views (one-day workshop)
	Men's views on barriers (n=20 interviews)

Months 5-10:	Computer-based intervention development with user input: touch screen activity, website and mobile phone text message content
	(n=48 men in 6 focus groups)
Months 8-10:	User views on sexual health and economic outcomes (n=12 interviews) Refine online outcome measurement instrument
Months 11-12	Final intervention user testing (n=10 men)
	Finalise RCT software frameworks: online information and consent, automated randomisation, email prompts, intervention usage data, data export

Milestones:

By end month 12:

- Fully tested computer-based intervention
- Software framework for trial conduct (registration, randomisation, data collection and export, email and text message systems in place)
- Clinical settings ready for pilot trial to commence

Part 2 – pilot RCT

| Months 13-18: | Pilot trial recruitment (172 men from 2-3 GU clinics), touch-screen activity |
| | Baseline data, outcome data immediately post-intervention (self-reported) |

Milestone:

By end month 18:

- 172 men recruited

Months 13-23:	Intervention delivery: 1) usual clinical care plus interactive website, sexual health promotion via mobile phone prompts or 2) comparator: usual clinical care, mobile phone messages regarding trial participation
Months 25-30:	12 month online outcome data (self-reported), clinic notes review and urinary Chlamydia and Gonoccocal sampling
Months 25-30:	Process evaluation (n=24 interviews with trial participants)

Milestones:

By end month 30:

- Final (12 month) quantitative follow-up data collected (self-reported outcomes, laboratory STI tests)
- Process evaluation interviews and data analysis completed

| Months 31-32: | Quantitative data analysis |

| Months 32-33: | Dissemination of findings, protocol for Phase 3 RCT |

Milestones:

By end month 33:

- Protocol for Phase 3 randomised controlled trial
- Final report

Project tasks and timelines

Phase 1 - Intervention development

Month		1	2	3	4	5	6	7	8	9	10	11	12
Tasks	Project set-up		Interviews on barriers x 20 men			Focus Group 1	Focus Group 2	Focus Group 3	Focus Group 4	Focus Group 5	Focus Group 6	Intervention user testing	
		HA workshop	Refinement of sexual health content of touch-screen application, website, and text messages										
						Intervention Development (Touch-Screen Application) Intervention Adaptation (Website)						Trial-related software set up–randomisation, automated emails and text messages	
									Outcome Measurement Instrument Refinement				

Phase 2 – Pilot trial

Month		13	14	15	16	17	18	19	20	21	22	23	24
Tasks		Participant recruitment in GU clinics n=172, touch-screen intervention, immediate outcome data						Trial monitoring					
		Intervention delivery (website, text message prompts)											

Month		25	26	27	28	29	30	31	32	33
Tasks		Access to intervention (website, text messages)						Data analysis		Dissemination, submission of publications
		12 month outcome data collection								
		Qualitative process evaluation – interviews x 24								

5. Expertise

Roles and responsibilities of the named investigators

Our team is ideally placed to carry out this work our track records of internationally recognised **high quality research** and **successful development and evaluation** of interactive computer-based interventions.
We already have an intervention website and an outcome questionnaire which can easily be adapted, and the software structures for trial procedures (registration, consent, randomisation, automated email follow-up, and outcome data collection). This study will build on the successes and lessons learnt from the MRC funded Sexunzipped intervention development and pilot RCT which was led by JB.

Our team has expertise in **sexual health** research (JB, GR, JS, JA, EM, CE) especially **male sexual health** (MG, GH); sexual health **clinical work** (JB, EM, GR, JS, MS); consultation and **collaboration with users** (JB, EM, MG, JAng); developing and applying **models of behaviour change** (SM, EM, JB); developing **interactive computer-based interventions** (JB, EM, JAng, GR, GH, MG); developing and evaluating **complex interventions** (JB, EM, JS, GR, GH, MG) sexual health **outcome measurement** (JS, SM, JB); **qualitative methodology** (JB, JA, MG); **randomised controlled trial design and conduct** (GR, JS, JB, EM, NF, JA); **statistical analysis** of RCTs (NF) and **economic assessment and modelling** (RH). We will also consult Mike Flood Page (who has extensive experience of design and development of educational packages delivered online and via mobile phone) for **expert advice on interactive intervention design** and software commissioning.

JB is the **principal investigator** with overall responsibility for the study. All of the **co-applicants** and two **user representatives** will sit on the **study steering group** which will meet every three months. The steering group will help to make strategic decisions as well as ensuring that the project is delivered on time and within budget.

Roles and responsibilities of the staff employed on the grant
Research associates – JB will directly supervise the two research associates. One **full-time research associate** will be involved throughout the project, and will conduct interviews, run focus groups, write intervention content, recruit participants, coordinate quantitative data collection and analysis, and write up findings. A second **part-time research associate** will be employed at 0.4 WTE to carry out the qualitative (process) analysis, including conducting interviews, collecting and analysing data and writing up findings. A **part-time statistician** will be employed to plan the quantitative data collection and statistical analysis, and to carry out the analyses, supervised by NF.

The **PRIMENT clinical trials unit** is supporting this study and will provide support for the **health economic analysis** (RH), **statistical expertise** (NF), advice on **study management**, **database development** and **trial methodology** (Tatiana Salisbury).

6. Service users

The **views of young people** are integral to the development of the intervention, and we will also seek their views on the pilot trial design. We have two men on our project steering group, and men's views will also be represented through the qualitative ground work (views on barriers and facilitators, and views on intervention content and design). We have ensured that users are in a position to shape the project through clearly defined roles and adequate reimbursement. We also have active links with **policy makers** (including the Department of Health), **website developers**, sixth form **teachers** and **sexual health clinicians**, and their views will continue to shape the direction of our work.

7. Justification of support required

Sexually transmitted infection rates are rising the in the UK, incurring very substantial NHS costs in treatment and health promotion.[1] This proposal represents a **good investment**, since a computer-based

intervention could have substantial impact on NHS resources if STI prevention is self-directed online instead of requiring clinical staff time.

This project is costed at **£507,017** over 2 years and 9 months (80% of the full economic costing), allowing for 12 month follow-up of participants.

Most of the cost is **staff cost.** JB is costed at 20% WTE to oversee all aspects of the study as **principal investigator**. **Co-applicants** are costed at 0.75% to 2.5% which keeps costs minimal whilst reflecting the work that will be involved in maintaining an active role in the study conduct. The cost includes one **full-time research associate** to conduct interviews, run focus groups, write intervention content, recruit participants, and coordinate data collection and analysis. Another **research associate** is needed for 6 months to carry out the qualitative process evaluation (months 25-30), and a Grade 7 **statistician** for a total of 12 months. Please note that % full time for SM, EM, RH, JAng, NF, JS and TS have been rounded up since the application form does not permit fractions.

The **computer-based intervention** will cost **£91,820** in total (£70,000 for software coding including adapting trial-related software for registration, randomisation and data collection, a novel touch-screen component and novel mobile phone 'app'; £12,560 for the mobile phone text message component including messages, £2,800 for secure server rental, £2,500 for advice on software commissioning, £2,460 for images and logo design, £500 for domain name registration and £1,000 for two laptops for participant use).

An important cost component is for **user involvement**, which will cost **£5,670** for incentives (£15-£20 for men's involvement in interviews, focus groups, participation in the pilot trial or participation in the qualitative process evaluation), with **£500** for user involvement in study conduct (steering group meeting attendance). **Research costs** come to **£21,780** including IT and other equipment, transcribing, consumables, insurance, library costs, travel and research dissemination costs. Postal **Chlamydia and Gonorrhoea sampling** with results by text message will cost **£4,951**.
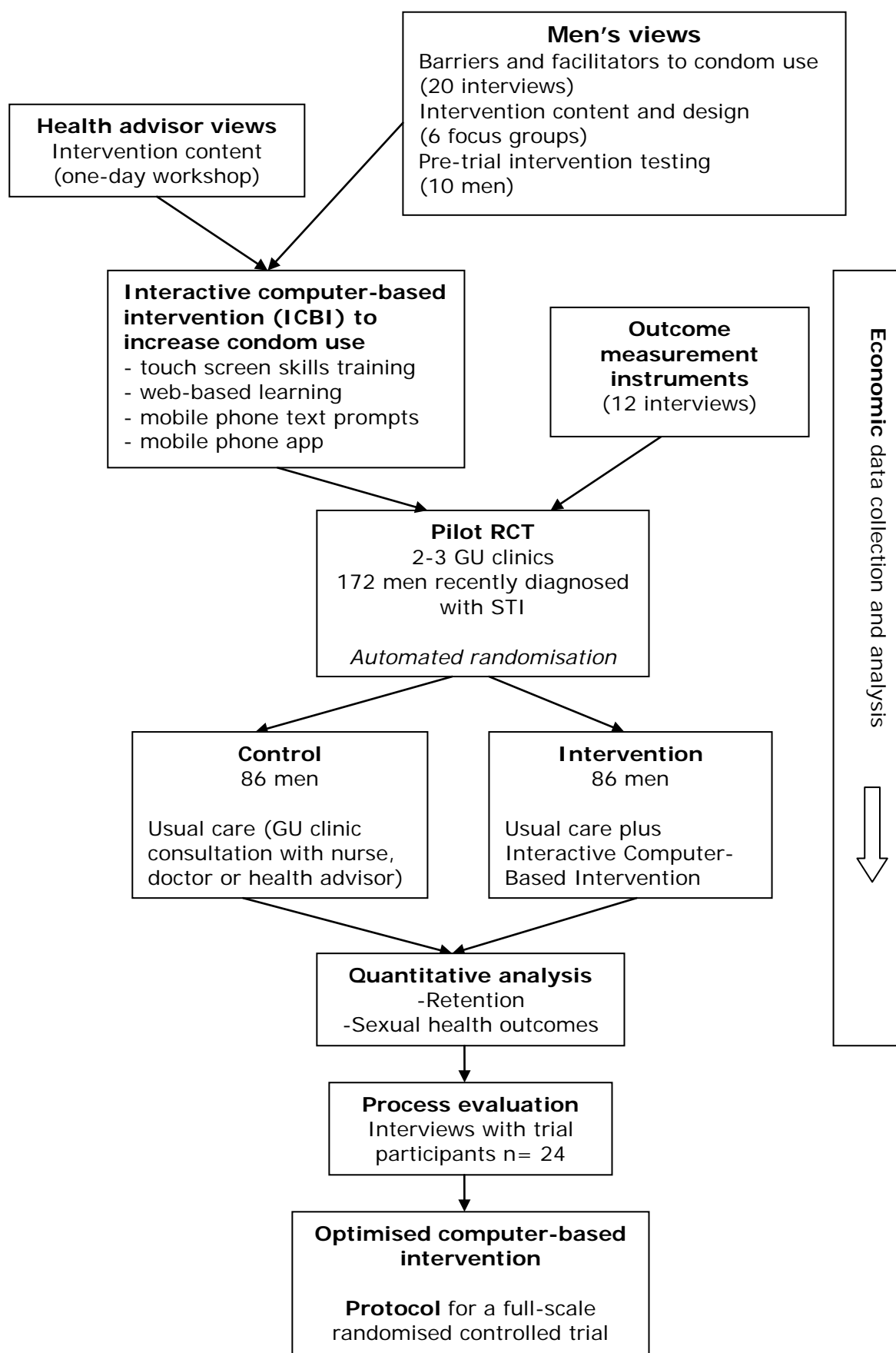
The **NHS service support** costs are **£9,386** per recruitment site (3 GU clinics): we may need to recruit in only two of the three GU clinics identified which will reduce the overall cost. The service support cost includes adequate funding to cover **staff time** (for the clinic manager, doctors, nurses and health advisors) to set up the research and maintain good communication to ensure referral of eligible participants (£3,496). The total for each setting also includes £5,300 for a 0.4 WTE Band 5 **research nurse** for 4 months which will minimise the impact on GU clinic staff workloads. We have also included £206 for admin time to record STI diagnoses from clinical notes, and £384 to cover the cost of possible additional consultations following new diagnoses of STI, but it is also possible that this study will reduce consultation rates by reducing STI incidence.

Publication and dissemination

We will post study information and anonymised findings on the trial website to ensure **free and open access** to our findings.

We will define a dissemination strategy for the website and mobile phone application to maximise patient benefit. We anticipate that except during any times that they are subject to further evaluation, they will be freely available under Open Source software licences. The copyright and intellectual property rights for the intervention will rest with the intervention authors (at the University College London e-Health Unit).

8. Flow diagram - Computer-based intervention to increase condom use

Men's views
Barriers and facilitators to condom use
(20 interviews)
Intervention content and design
(6 focus groups)
Pre-trial intervention testing
(10 men)

Health advisor views
Intervention content
(one-day workshop)

Interactive computer-based intervention (ICBI) to increase condom use
- touch screen skills training
- web-based learning
- mobile phone text prompts
- mobile phone app

Outcome measurement instruments
(12 interviews)

Pilot RCT
2-3 GU clinics
172 men recently diagnosed with STI

Automated randomisation

Control
86 men

Usual care (GU clinic consultation with nurse, doctor or health advisor)

Intervention
86 men

Usual care plus Interactive Computer-Based Intervention

Economic data collection and analysis

Quantitative analysis
-Retention
-Sexual health outcomes

Process evaluation
Interviews with trial participants n= 24

Optimised computer-based intervention

Protocol for a full-scale randomised controlled trial

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