A randomised controlled trial of a safer sex intervention delivered through mobile phone messaging

Protocol Version 12

Main Contacts

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Funder: NIHR

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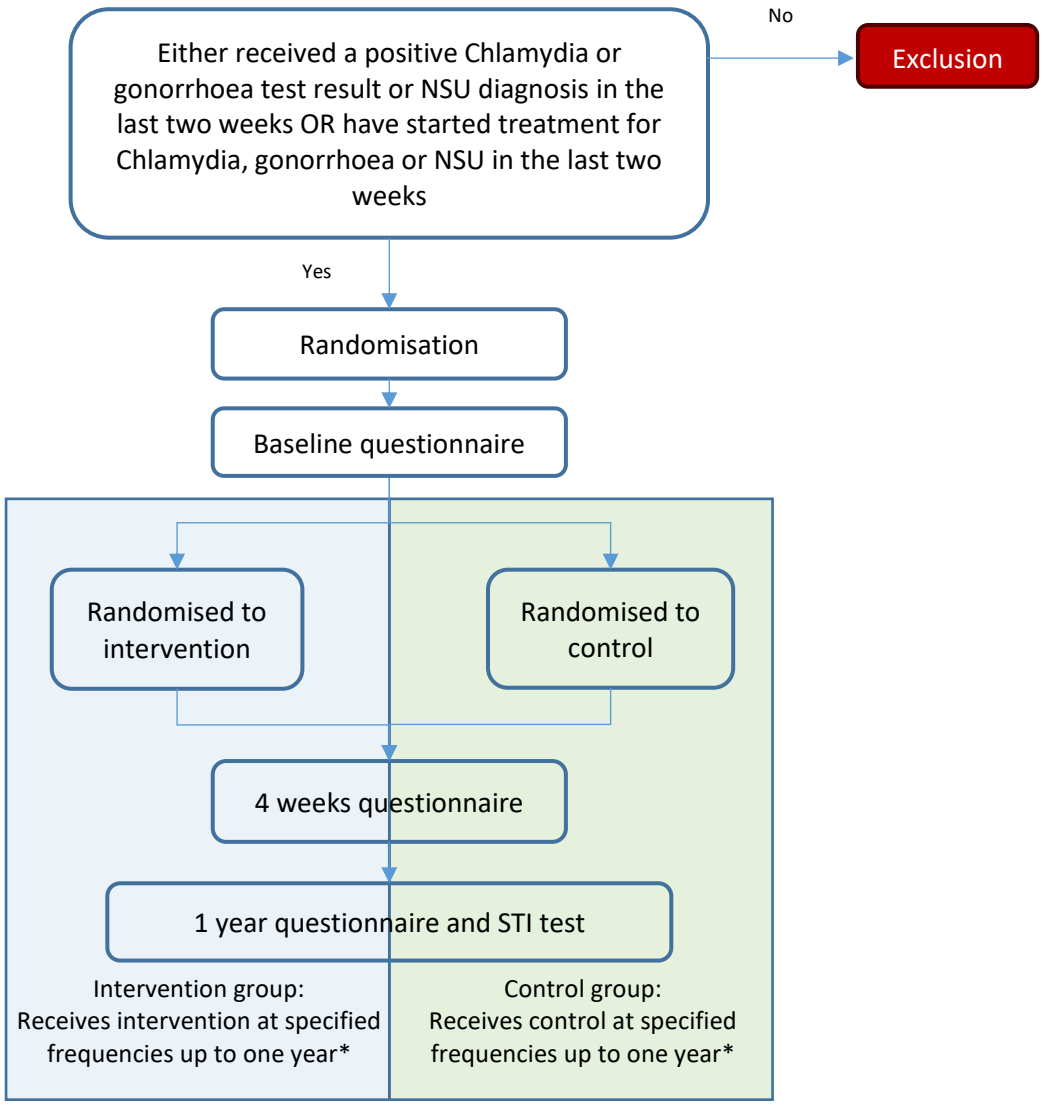
Contents

1. Trial summary

1.1. Protocol summary

Trial title	A randomised controlled trial of an intervention delivered by mobile phone messaging to reduce sexually transmitted infections (STI) by increasing sexual health precaution behaviours in young people.
Objectives	To establish the effectiveness of a safer sex intervention delivered by mobile phone messaging on STI infection at one year. To establish the effect of the intervention on partner notification and condom use at 4 weeks. To establish the effect of the intervention on partner notification, condom use and STI testing at one year. To explore which components of the intervention are effective by collecting data on the theoretical constructs influenced by the intervention components and on the pathway to behaviour change. To establish the costs and cost-effectiveness of the intervention.
Trial design	A single blind randomised controlled trial to establish the effects of a safer sex intervention delivered by text message.
Primary endpoint	Cumulative incidence of Chlamydia and gonorrhoea infection at one year.
Inclusion criteria	• Either; - have received a positive Chlamydia or gonorrhoea test result or have been diagnosed with NSU in the last two weeks - Or have started treatment for Chlamydia, gonorrhoea or NSU in the last two weeks • own a personal mobile phone • be aged 16 to 24 (according to clinic data) • be able to provide informed consent (patients who lack mental capacity and those unable to understand English will not be recruited)
Exclusion criteria	• known to be a sexual partner of someone already recruited to the trial
Sample size and enrolment	Sample size = 6250 Recruitment start date: 1st April 2016 Recruitment end date: 31st December 2018 Follow-up end date: To be confirmed Number of centres: - 30+ NHS trusts, additional GP services to be confirmed

1.2. Trial flowchart



*For specified frequency of intervention and control see section 9.1.

2. Introduction

2.1. Background

Younger people bear the heaviest burden of sexually transmitted infections (STIs) such as Chlamydia and gonorrhoea, and their long-term adverse health effects including ectopic pregnancy and subfertility (1, 2). The risk of adverse health effects increases with repeated infections. Those with an STI are more likely to acquire further STIs and HIV, if exposed. The highest prevalence of STI is in socio-economically deprived areas and among people with larger numbers of sexual partners (1). Re-infection rates following treatment are high: up to 30% for Chlamydia and 12% for gonorrhoea at one year (3).

2.2. Existing research

Partner notification, condom use and STI testing can reduce infection and reinfection. There is some evidence that existing interventions delivered face-to-face that target partner notification, condom use and or STI testing may be effective, but they are limited in their reach or too costly for widespread application(4). Existing interventions delivered via the media have high reach but their effects have yet to be established (5). Effective ways to increase partner notification in specialist and primary care settings are needed (6, 7).

Mobile phones have the potential to provide effective, low cost health behaviour support. However, the effect of mobile phone support for safer sex behaviours such as condom use, partner notification and STI testing is equivocal (8-10). MEDLINE, EMBASE, Global Health, Web of Science, PsycINFO and the Cochrane Library (Jan 1990 – Nov 2014) was searched to identify trials of mobile phone based support to increase safer sex behaviours and identified 7 trials (11-17). Four interventions targeted testing for STI (11-13, 18), one aimed to delay resumption of sexual activity until 42 days after circumcision (17) and four targeted condom use (12, 13, 15, 16). None of the interventions had as its goal to increase partner notification. Interventions included a limited number of behaviour change techniques (BCT) (up to three) (19). No trial had low risk of bias.

2.3. Intervention development work and pilot trial

safetxt builds on the successful intervention development work and pilot trial (ethics reference number 13/LO/1001) (10, 20). The trial was commissioned by the NIHR to develop a safer sex intervention delivered by text message and to evaluate its acceptability to young people and the feasibility of a trial to establish its effects. The messages were developed based on: behaviour change theory; evidence-based behaviour change techniques; the content of effective face-to-face safer sex interventions; the factors known to influence safer sex behaviours; the views of 82 young people collected in focus groups and a questionnaire completed by 100 people aged 16-24 (10). The theory and evidence-based intervention employs 12 behaviour change techniques and is designed to reduce STIs in young people by supporting them in telling a partner about an infection, using condoms and obtaining testing before unprotected sex with a new partner.

Messages were written and adapted based on young people preferences expressed in focus groups. Participants expressed a preference for messages with a non-judgmental and credible tone, short messages written in a positive style and those providing practical information regarding what needed to be done, why and how. Young people wanted messages that were easy to understand, avoided slang and avoided exclamation marks (which were experienced as patronising). They wanted no more than four messages a day and wanted the message frequency to reduce within the first two weeks. Content regarding gender roles, sexual pleasure and relationships were considered too personal and intrusive when delivered via short messages and so were removed from the intervention. Messages encouraging participants to make action plans to carry out behaviour were also considered too intrusive, but were acceptable when modified to provide suggestions regarding when and where risk reduction behaviours could be carried out. Text messages encouraging participants to set goals were also considered too intrusive and were removed from the intervention. One hundred participants completed a questionnaire. All messages were scored ‘easy to understand’ and none were disliked. Six were removed or adapted as less than 40% of participants scored them as ‘relevant’.

The agreed parameters for judging the success of the intervention development work and pilot trial were the acceptability of the intervention, the successful delivery of at least 93% of text messages, the recruitment to the pilot trial on time and achieving 80% or higher follow up for STI tests at 1

year. All the pre-specified criteria for progression to a main trial have been met. In a qualitative trial with young people, recipients reported that the tone, language, content, and frequency of messages was appropriate (20). Messages reportedly increased knowledge and confidence in how to use condoms and reduced stigma enabling them to tell a partner about an STI. Sharing messages with their partner enabled participants to negotiate condom use. Based on their feedback the intervention has been further refined for the main trial. It has been ensured that messages are relevant to men who have sex with men and women who have sex with women, for example by ensuring pronouns used are gender-neutral. Additional content has been included providing examples of how others negotiated condom use in ongoing sexual relationships. New messages have been reviewed by participants who report them to be relevant, easy to understand and acceptable. The pilot trial demonstrates that a main trial is feasible. Over 97% of text messages sent were successfully delivered to participants. Target recruitment was achieved early. 86% (171/200) was achieved for STI tests at 3 months and 81% (162/200) follow up for the cumulative incidence of Chlamydia at 12 months. For self-reported data, 92% (183/200) was achieved follow up at four weeks and 82% (163/200) at 1 year. The pilot trial 1 year data are consistent with the effects that the main trial is designed and powered to detect, for example, the cumulative incidence of Chlamydia in the pilot is RR 0.6 (95% CI 0.29-1.36). The randomised controlled trial is designed to reliably establish the effects of the intervention delivered by text message on the cumulative incidence of Chlamydia and gonorrhoea at one year.

2.4. Risks and benefits

Without new effective interventions the Department of Health is unlikely to achieve its aims in increasing safer sex behaviours and reducing STI. Safer sex behaviours such as condom use, notifying partner(s) about an existing STI and STI testing reduce the risk of STI, but young people may lack the knowledge, confidence and skills needed to adopt these behaviours.

The intervention delivered by text message provides acceptable, broad reach and low cost support which could enable more young people to adopt safer sex behaviours and so reduce STI. In the UK in 2013, 98% of 16-24 year olds personally own and use a mobile phone and mobile phone ownership is high across all socioeconomic groups. In research leading to this application, it was demonstrated that support via text message is particularly acceptable in the area of sexual health intervention (20, 21). Interactive support was delivered to participants wherever they were located and whenever it was needed, facilitating privacy, which is especially important for many young people (20).

The intervention provides support and is unlikely to cause any harmful effects. Even small changes in sexual health behaviour will outweigh any plausible risks from using mobile phones. Road traffic accidents are the only demonstrated hazard of text messaging. Trial participants are advised not to read or send text messages whilst driving and there was no evidence of any increase in road traffic accidents in a previous trial of smoking cessation support delivered by text message conducted among 5800 participants. For the minority of young people in abusive relationships, carrying out partner notification could carry a risk of further abuse. At the time of recruitment participants will be in contact with services which can provide support or refer participants for specialist support. In addition, participants will be provided with a general list of help lines, including help lines offering support for people experiencing violence. A potential risk regarding the intervention is that text messages might be viewed by others without the participant's consent. However, in intervention development work young people were confident they could keep their text messages private by deleting them or using mobile phone password protection. Some intentionally shared messages with friends, partners and younger siblings. In the pilot trial, three people reported that they were

unhappy about someone else reading their messages. Nonetheless, whether other people read messages intended for participants and the consequences of this will be monitored.

If it proves to be effective, the low cost intervention could have an important impact on the sexual health of young people in the UK. A number of service providers have already expressed an interest in implementing the intervention, if proven effective. There is likely to be international interest in the impact of the intervention as short written messages delivered via mobile phones are increasingly used for behavioural support worldwide and sexually transmitted infections remain an important cause of morbidity and mortality. Identifying which intervention components are effective has the potential to generate general principles to inform similar interventions in the future.

2.5. How safetxt attempts to address inequalities

Inequity in health refers to differences in health profiles which are both avoidable and unfair (22). Equity implies that everyone should have a fair opportunity to attain their full health potential (22). Equal quality of care for all is an important aspect of providing everyone with a fair opportunity to attain their health potential (23). Services can be inequitable if they are designed in a way that makes them inaccessible or unacceptable to sections of the population they are intended to serve (22, 23). The intervention is designed to provide equal quality of care and to be accessible and acceptable to the diversity of young people in the UK in terms of age, sexual orientation, ethnicity and gender identity. Since 98% of 16-24 year olds own and use a mobile phone in the UK, the intervention delivered by mobile phone has the potential to be widely accessed. The intervention was developed and tested with young people from diverse gender identities, sexual orientations, ages, ethnic backgrounds and areas of residency, including those at higher risk of an STI and those from socioeconomically deprived areas. These young people reported that the intervention was easy to understand, acceptable and relevant to them.

Differences in health status due to health-damaging behaviours are inequitable when the degree of choice in carrying out those behaviours is restricted (22). Choice in carrying out safer sex behaviours can be restricted due to lack of knowledge of the health consequences of behaviours or lack of knowledge or skills in how to carry out behaviours. Further, some social groups can come under social pressure to adopt potentially health damaging behaviours (22). This is particularly relevant to sexual behaviour where, for example, gender stereotypes can influence behaviour and can make it hard for women to negotiate safer sex behaviours such as condom use (24). The intervention aims to reduce restrictions in choice in carrying out safer sex behaviours by providing information, behavioural support and by demonstrating behavioural skills. Support for participants who may be pressurised into unsafe sex is provided using examples of how others have negotiated condom use and how others told partners about an STI. Information will be provided about how to access helplines or services for those with additional support needs.

Whilst recognising that the trial is underpowered for subgroup analyses, safetxt will identify whether there is any evidence for variation in the intervention effect in specific social groups that could result in inequity in health. These social groups are defined according to: sexual orientation and gender (men who have sex with men, men who only have sex with women, women who have sex with men, women who only have sex with women), ethnic group (Caucasian, black, other) and education over the age of 16: none, full-time education, an apprenticeship/ traineeship, part-time education/training.

2.6. Rationale for current trial

safetxt will reliably demonstrate the effects of the intervention on STIs at one year. The effects of the intervention on partner notification, condom use and STI testing will be reported. Understanding

which intervention components (behaviour change techniques) are effective could generate principles to inform the content of future interventions. Which interventions are effective will be explored by collecting data on the theoretical constructs influenced by the intervention components and on the pathway to behaviour change.

3. Research objectives

To establish the effectiveness of a safer sex intervention delivered by mobile phone messaging on STI infection at one year.

To establish the effect of the intervention on partner notification and condom use at 4 weeks.

To establish the effect of the intervention on partner notification, condom use and STI testing at one year.

To explore which components of the intervention are effective by collecting data on the theoretical constructs influenced by the intervention components and on the pathway to behaviour change.

To establish the costs and cost-effectiveness of the intervention.

4. Outcome measures

4.1. Primary outcome

Cumulative incidence of Chlamydia and gonorrhoea infection at one year assessed by NAAT tests: urine for men with pharyngeal and anal swabs for MSM and self-taken vulvo-vaginal swab for women.

The sensitivity and specificity of self-taken tests, respectively, is as follows (25):

Infection	Test	Sensitivity	Specificity
Chlamydia	Vaginal swab	94.1%	99.7%
	Urine sample	98.1%	99.5%
	Rectal swab	91.4%	98.2%
Gonorrhoea	Vaginal swab	100%	99.8%
	Urine sample	100%	99.5%
	Rectal swab	92.3%	87.9%
	Pharyngeal swab	100%	87.8%

4.2. Secondary outcomes

4.2.1. Secondary outcomes at four weeks

- Clinic attendance by partner for treatment
- Whether participants took the (prescribed antibiotic) treatment and avoided sex for 7 days after treatment
- Whether they told the last person they had sex with before the test that they needed to get treatment
- Whether their partner took the treatment and they avoided sex with this person for 7 days after taking the treatment
- Condom use at last sex
- Data regarding the theoretical constructs underlying the components of the intervention (behaviour change mediators) measured using the items below or existing scales (26).
- Knowledge relevant to the consequences of behaviour and how to avoid infection

- Attitudes towards partner notification
- Correct condom use self-efficacy (27)
- Self–efficacy in negotiating condom use (28)
- Self–efficacy in telling a partner about an infection (29)

4.2.2. Secondary outcomes at one year

- Diagnosed with any STI after joining the trial according to self-report confirmed by postal test results and clinic records
- Condom use at last sex
- Sex with someone new since joining the trial
- Condom use at last sex with someone new
- Sexually transmitted infection testing for self - prior to sex with someone new confirmed by clinic record
- Participant's report as to whether their last new partner was tested for sexually transmitted infection prior to sex with them
- Number of sexual partners since joining the trial
- Number of text messages read
- Whether anyone else read the messages
- Contamination between intervention and control group
- Car accident where the participant was the driver in the past year
- Partner violence in the past year

5. Statistical considerations

5.1. Sample size

Two main factors determine the number of participants needed in a trial, that is: the estimated event rate, and the size of the treatment effect.

5.1.1. Estimated event rate

The estimated event rate for the cumulative incidence of STI at 1 year is 20%, based on the event rate in cohort studies and the pilot trial (3).

5.1.2. Size of treatment effect

Because the intervention can be administered to large populations at low cost, even a modest reduction in treatable STI would be worthwhile. The trial has therefore been designed to detect a reduction in Chlamydia or gonorrhoea infection of 20% versus 16% (RR 0.8), which is similar to the effects of face-to-face safer sex interventions (4).

5.1.3. Numbers needed

In the pilot trial there was 2% contamination between the intervention and control group. If the real difference in STI infection at one year follow up is 20% versus 16% then with contamination of 2% the trial would detect a difference of 19.9% vs 16 %. (Calculated based on 2% of the control group having an infection rate the same as the intervention group = (98% x 20%) + (2% x16%) = 19.9%).

To detect this difference there is a 90% chance that a trial with 5000 participants will achieve $P<0.05$, even allowing for 20% losses to follow-up.

The Public Health Board has requested assessment of heterogeneity in effects of the intervention according to key subgroups. Whilst recognising that subgroup analyses will still be underpowered, a

trial with 90% power for the primary outcome will have greater power for assessing differences in effect of the intervention in subgroups than a trial powered to 80% for the primary outcome.

5.2. Statistical analysis

The relative risk is estimated with a 95% confidence interval for the primary outcome and dichotomous outcomes and the mean difference and 95% confidence intervals for continuous outcomes. All analyses will be based on the intention-to-treat principle. Pearson's chi-squared test will be used to assess differences between intervention and control groups at the 5% level of significance.

For the primary analysis Multiple Imputation by Chained Equations (MICE) will be used in order to account for missing data (30). MICE makes appropriate assumptions for accommodating missing data in the analysis based on the predictors of outcome and the predictors of loss to follow up. MICE is recognised as a way of reducing bias and increasing precision of trial results and is increasingly used as the primary analysis in randomised controlled trials (30, 31). The analyses will be conducted using the "ice" command in Stata version 13. One hundred imputed datasets will be generated and the point estimates and standard errors will be combined using Rubin's rules.

A complete case analysis will also be conducted where any participants with missing information on any covariate or outcome shall be excluded.

Sub group analyses. The trial is powered for the primary outcome measure. Recognising that the trial has limited power and that any inferences would be tentative the chi-squared test will be used for heterogeneity at a 5% level of significance to assess whether the intervention effect differs by: age (16-19, 20-24), sexual orientation (men who have sex with men, men who have sex only with women, women who have sex with men, women who only have sex with women), ethnic group (Caucasian, Black, other) age at which left education (16 or under, over 16). 99% confidence intervals for subgroup analyses of the primary outcome will be reported.

Where sufficiently succinct, existing validated measures of key constructs (such as self-efficacy) will be used in the research instruments. The measures of the theoretical constructs in the pathway to behaviour change will be measured by the items described in the outcomes section and existing scales (26-29). In the evaluation of which components of the intervention are effective the trial data will be used to refine measures using methods described within the Generalised Latent Variable Modelling framework that combine principles of factor analysis and item response theory (32). The reliability of the measures will be assessed using Fisher information, Cronbach's alpha and Omega in the first 1000 participants. Regression models will be used with appropriate link functions to explore the relationships between predictor and dependent variables as well as changes between groups and t-tests to compare changes between groups. In the final stage of the analysis methods described within the modern causal mediation framework will be employed using causal pathway analysis to quantify the mechanisms (mediation and moderation effects) and explore dependencies and associations within the systems that underlie the associations between predictors (knowledge regarding how to prevent reinfection, knowledge regarding how to use a condom, attitudes to partner notification, self-efficacy in how to use a condom, self–efficacy in negotiating condom use, self–efficacy in telling a partner about an infection and outcomes (condom use, STI testing, partner notification and cumulative incidence of STI at one year) (33).

6. Research design

6.1. Trial design

safetxt is single blind randomised controlled trial to establish the effects of a safer sex intervention delivered by text message on the cumulative incidence of Chlamydia and gonorrhoea infection.

Potential participants testing positive for Chlamydia, gonorrhoea or diagnosed with non-specific urethritis (NSU) will be identified from STI testing services by research staff based at the service. They will provide potential participants with information about the trial at one of three time points:

1) When potential participants attend the service and are diagnosed with Chlamydia, gonorrhoea or NSU

2) When potential participants receive positive test results for Chlamydia or gonorrhoea by phone

3) When potential participants collect treatment for Chlamydia, gonorrhoea or NSU from services

Research staff will provide potential participants with verbal and written information about the trial. Written information about the trial will be viewed on the website or emailed to potential participants. Participants will be able to join the trial either by providing informed written consent to the research staff providing the written trial information, by texting their consent or by providing consent online at the trial website (according to their preference).

Research staff may telephone, email or text eligible participants identified from clinic records with information about the trial. The may simply provide information about the trial to be followed up at in-person visit or may direct participants to the website and encourage them to sign up.

Site staff are also able to ask eligible participants if they are happy for their details to be given to GCP trained staff at LSHTM CTU. Participants will then be contacted by LSHTM CTU to recruit to the trial.

In accordance with the Public Health Research Programmes request that studies collect long term outcomes using routinely collected data, participants' consent will be obtained for this. Participants will be able to contact the trial Clinical Trials Unit (CTU) by text message to the short code number or by telephone call.

6.2. Allocation

Participants will be randomly allocated, using a remote computer based randomisation system, to a safer sex intervention delivered by text messaging, or to a control group.

An electronic link to the computer based randomisation programme will result in the generation of a research number and allocation to the intervention or control group. The system will then automatically deliver intervention or control group texts according to the allocation. All participants will be free to use any existing services or interventions.

6.3. Protecting against bias

Due to the nature of the intervention, participants will be aware of treatment allocation. The intervention will be delivered by computer ensuring that investigators are unaware of the allocation sequence (allocation concealment). Both laboratory staff assessing STI and the statistician will be blind to treatment allocation.

6.4. Centres

Each of the collaborating services is listed on the trial website at http://safetxt.lshtm.ac.uk/

6.5. Compliance issues

Anticipated compliance issues:

The IT system will monitor discontinuation; it is anticipated that a similar proportion of participants will discontinue the intervention in this trial as in the pilot trial, about 8% (16/200) (10).

Losses to follow up: In the pilot trial 81% follow up was achieved for the cumulative incidence of Chlamydia at one year and 92% and 82% follow up for self-reported data at 4 weeks and one year, which is higher than previous trials where follow up for post STI tests has been 50% or lower (34).

Incentives were provided to all responders. Non-responders were contacted using phone call, text message, email and/or post according to their preference. Similar methods will be used in this trial to minimise losses to follow up. Participants will be asked to provide contact details of someone that can be contacted if they cannot be reached at four weeks or one year.

7. Trial population

7.1. Inclusion criteria

Participants will:

- either;
  - have received a positive Chlamydia or gonorrhoea test result or have been diagnosed with NSU in the last 2 weeks, or
  - have started treatment for Chlamydia, gonorrhoea or NSU in the last two weeks
- own a personal mobile phone
- be aged 16 to 24
- be able to provide informed consent (patients who lack mental capacity and those unable to understand English will not be recruited)

7.2. Exclusion criteria

- known to be a sexual partner of someone already recruited to the trial

7.3. Withdrawal criteria

Acting on participants' requests to withdraw from the trial: participants' status will be changed to 'withdrawn' on the web based data entry form. This will automatically result in the text messages stopping and the withdrawer being excluded from lists of participants due follow up. Participants will be able to stop text messages, but continue with the trial follow up.

To withdraw, participants can send the text message 'stop' to the short code number to automatically stop the sending of messages. Alternatively, the participants can call the CTU who will arrange for the messages to stop. Participants will be encouraged to notify the CTU of any changes to their mobile phone number.

8. Ethical considerations

8.1. Consent

Fully informed consent: Participants will be provided with trial information and given the opportunity to ask questions. For participants joining the trial the recruiting staff will check that participants understand that they may or may not be allocated to receive the intervention prior to entry into the trial.

8.2. Participants' rights

Participants will be able to contact the CTU by text message to the short code number or by telephone call. Anonymity will be maintained as participants will be identified by a research number only.

The recruiting clinic will be notified of any positive test results for a participant. They will follow their standard clinic procedures to discuss STI test results and arrange treatment with the participant. Participants are asked provide confirmation that they are happy for their clinic to be notified of their test result as part of the informed consent process.

In addition, participants will also be informed about their test results by text message using standard wording used in clinical practice. Participants will only be notified of a positive test result via text message once their clinic has been informed.

Positive test

Your (insert test) showed you need treatment. Please go to your local clinic and show them this message. You can find details of your nearest clinic here http://www.nhs.uk/service-search/sexual-health-information-and-support/locationsearch/734

You tested negative for (insert test) (if one of their results is negative)

Thank you for taking part in the study

Negative test

You tested negative for Chlamydia and gonorrhoea.

Thank you for taking part in the safetxt study.

8.3. Data management

Data are held on a secure system and are password protected. Any paper data will be locked in a cabinet within a room which is locked unless staff are working in the room. Access to the building is only by LSHTM identification cards. All trial procedures are in accordance with the principles of Good Clinical Practice. Essential documents of the sponsor/trial organisers and investigators will be retained for at least ten years after completion of the trial. In accordance with LSHTM's retention requirements, primary research data will be retained for 10 years following trial completion. In accordance with the Data Protection Act of 1998 (35), participant personally identifiable data will not be kept longer than necessary and will be deleted within three months after the participant is discharged from the trial. If a patient withdraws, attempts will be made to contact the patient to determine if they are still happy for their data to be used. If no contact can be made, it will be assumed that they are withdrawing from the whole trial and do not wish their data to be used.

All data systems will be set up with checks to alert the Trial Assistants if data being entered are illogical, inconsistent or incomplete.

8.4. Declaration of Helsinki and Good Clinical Practice

The trial will conform to the spirit and the letter of the declaration of Helsinki, and in accordance with Good Clinical Practice Guidelines.

8.5. Ethical committee review

The National Research Ethics Service Committee London - Riverside have reviewed and approved the trial (REC reference 15/LO/1665).

8.6. Socio-economic position and inequalities

8.6.1. How safetxt takes into account the socio-economic position of research participants and potential participants

The trial will recruit participants across the UK. Services involved in recruitment include those serving socio-economically and ethnically diverse populations (such as in inner city areas of South East London and the London Borough of Brent as well as rural areas (Cambridgeshire) and clinics providing services to young people with diverse sexual orientations including men who have sex with men (MSM) such as Mortimer Market Centre in central London. All eligible participants will be invited to join the trial irrespective of their social position. The trial information is designed to be easy to read and understand.

9. Planned interventions

9.1. Planned intervention

Intervention: regular messages delivered by text message to influence safer sex behaviours.

The intervention aims to increase safer sex in three ways:

1. Encouraging participants to correctly follow STI treatment instructions and inform partner(s) about infection

2. Promoting condom use with new or casual partners

3. Encouraging participants to obtain testing for STI prior to unprotected sex.

The intervention employs educational, enabling and incentivising behaviour change functions and twelve behaviour change techniques identified in effective face to face safer sex interventions: information about health consequences of behaviour, instruction on how to carry out the behaviour, demonstrations of risk reduction behaviour, social support, emotional support, social rewards, non-specific incentives, encouragement to add objects to the environment, anticipated regret, problem solving, action planning techniques and reframing (10, 19). The information on safer sexual practices is in accordance with existing guidelines.

The intervention text message content has been developed in collaboration with young people, and has been shown to be acceptable, comprehensible and relevant.

Frequency of messages:

Time period	Frequency of messages
Days 1-3	Four messages per day
Days 4-28	1-2 messages per day
Month 2	2-3 messages per week
Months 3-12	2-5 messages per month

The messages will include the following information tailored by gender, sexual orientation and according to the STI diagnosed.

- Explain to participants that many people with an infection have no symptoms
- Explain to participants that infections are easy to treat
- Provide suggestions about when, where and how to tell partners about an STI and examples of how others (in casual and long term relationships) informed partners
- Cover the difficulty of assessing STI risk by appearance
- Emphasise positive aspects of condom use
- Prompt participants to carry condoms
- Provide tips on how to avoid condom use problems
- Give examples of how others resolved problems using condoms and of how others negotiated condom use
- Prompt to think about how they have successfully carried out safer sex behaviours in the past, times they had taken risks and what they could do differently in the future
- Include advice regarding getting tested before unprotected sex with a new partner
- Include links to services and support for those concerned about relationship violence and abuse
- Include links to web based information regarding how to use a condom, contraception, alcohol and sexual risk and general communication about sex

9.2. Control treatment

Control: a monthly text message asking participant to provide information about changes in postal or email addresses.

All participants will receive usual care and will be free to seek any other existing support they wish. For participants recruited from community and sexual health clinics usual care will be delivered in accordance with standards set by the British Association of Sexual Health and HIV. Those recruited from general practices will receive the usual care provided by the practice.

9.3. Delivery of intervention

The IT system used successfully in the pilot trial will be used to deliver the intervention. All messages are sent automatically from a large database to an aggregator. The aggregator has contractual agreements with all the mobile phone network operators and sends messages to each participant via their network. Incoming messages from participants are sent to the short code via the networks and aggregator and can be viewed on the computer system. During the trial the system will be housed in the CTU. The success of delivery of messages at each step is monitored by the networks the aggregator and computer system that generates and receives the messages. A member of the trial team will automatically be notified if there is any failure in the delivery of messages. All participants will be able to set embargoed times when they do not want to receive messages.

10. Data collection and follow up

10.1. Data collection

	Baseline	4 weeks	One year
Baseline questionnaire at randomisation	X		
Postal questionnaire		X	X
Posted STI kit			X

The primary outcome measure will be assessed using Chlamydia and gonorrhoea tests collected by post at one year and clinic records of completed tests. STI Test kits will be posted (in P650 standard packaging) to respondents. Directions in the pack will ask participants to provide a vaginal swab (women), a urine sample (men), oral swab (men who have sex with men) or anal samples (men who have sex with men) and then replace it in the packaging before posting it in the prepaid and addressed envelope to the laboratory. Test kits will be identified by lab number only, rendering the laboratory staff blind to the participant's allocation. Results of the STI testing will be reported on the secure trial lab site by lab code only. Self-reported data will be collected by post or any method the participant agreed to at enrolment (mobile phone, email).

Clinic records will be checked by clinic staff to confirm self-reported STI tests and diagnoses after joining the trial and partner attendance for treatment.

At 4 weeks and one year postal questionnaires will be sent to all participants. Non-responders will be contacted by any method the participant agrees to at enrolment (post, email, text message, telephone call). The current contact details of non-responders will be checked with the person nominated by participants at randomisation.

Participants will be sent a £5 unconditional incentive with each postal request i.e. when sending the 4 weeks questionnaire and 1 year test and questionnaire. Participants who return the test sample will be sent £20.

Participants can directly enter self-reported outcome data via a web based data entry form. Paper based self-reported outcome data is directly entered into the web based data entry form by a trial assistant blinded to treatment allocation.

10.2. Assessment of efficacy

Efficacy of the intervention will be assessed by STI tests posted to participants and by self-reported data collected by questionnaire.

10.3. Assessment of harms

Harms will be assessed by self-reported data. Car accidents are the only demonstrated harm resulting from text messaging, hence the intention to collect data regarding involvement in road traffic accidents.

The safetxt intervention aims to increase partner notification of STI status. Fear of partner violence has been reported to be a barrier to partner notification and partner notification has been identified as a factor which may trigger partner violence. However, no randomised controlled trials targeting increased partner notification detected a difference in partner violence between the control and

intervention groups. Data will be collected regarding the experience of partner violence at 12 months.

In cases where a participant under the age of 18 reports partner violence, the Chief Investigator for the trial will contact them via telephone. Information about any reported partner violence will then be reported to the appropriate social services agency. All, participants will be signposted to local support agencies to ensure that they have access to appropriate support.

Participants will also be invited to provide information regarding any other negative effects of involvement in the trial. Data will be collected regarding whether other people viewed messages and whether the participant was happy/unhappy or unsure about this.

11. Research governance

11.1. Sponsor

London School of Hygiene & Tropical Medicine is the main research sponsor for this trial. For further information regarding the sponsorship conditions, please contact the Research Governance and Integrity Office:

London School of Hygiene & Tropical Medicine
Keppel Street
London WC1E 7HT
Tel: +44 207 927 2626
Email: patricia.henley@lshtm.ac.uk

11.2. Adverse events

Information on adverse events will be collected in the follow up data. If the CTU were to become aware of an adverse event, it would be immediately reported to the sponsor.

11.3. Quality control/assurance

The trial is of a behavioural support intervention unlikely to cause harm so analysis will be conducted once at the end of the trial. The sponsor may audit the trial per their own risk assessment and schedule.

12. Economic evaluation

Mobile phone based support is inexpensive, and could be provided to large numbers of people. The costs of subfertility, ectopic pregnancy and STI infection, are high. In the UK, the estimated direct costs of treating Chlamydia and gonorrhoea in 2004 was £70 million and the estimated total costs to the NHS of treating STI and their sequelae in 2003 was about £700 million (36, 37). In 2009, estimated costs of in vitro fertilisation were between £5,000 and £20,000 per additional birth, and the costs per live birth are higher in older women where success rates are lower (38). When a low-cost intervention is effective it is likely to be cost-effective since in addition to health benefits there are likely to be savings in future NHS costs (9).

In order to assess whether an intervention offers acceptable value for money decision makers need to know its costs, and have some quantification of the likely health benefits and cost savings. In this case the primary benefits are in terms of fewer STIs following the intervention, and consequently the main challenge is to either translate fewer STIs into Quality-adjusted life years (QUALYs) gained, or

to identify a monetary value per STI prevented. The former approach will be followed on the grounds that it can facilitate comparison with the evaluation of other interventions. Valuations of the relevant health states will be literature-based as opposed to collected directly from trial participants.

The economic modelling required to assess the cost-effectiveness of the intervention will estimate the annual probability of members of the target group acquiring Chlamydia, gonorrhoea and NSU with and without the intervention (based on the experience of those in the control and intervention arms of the trial). Detailed information will be collected on the costs of delivering the intervention. Secondary sources will be used to estimate the future NHS costs avoided as a consequence of avoided infections.

Parametric uncertainty will be explored with both deterministic and probabilistic sensitivity analyses. Scenario analyses will be performed in order to explore the sensitivity of the estimates of cost-effectiveness to a range of alternative assumptions regarding the extent of any enduring effect and the rate at which it is likely to diminish over time.

13. Trial organisation

13.1. **Trial Steering Committee (TSC)**

Professor Pippa Oakshott (St George's Hospital) - independent chair

Colum McGrady - A service user

Dr Andrew Copas (UCL)

Dr Michael Brady (King's)

Professor Michael Ussher (St George's Hospital)

Dr Caroline Free (LSHTM)

Observers

Rosemary Knight (Senior Manager of the CTU)

Kimberley Potter (Assistant Trial Manager)

The role of the Trial Steering Committee is to provide overall supervision of the trial and ensure the trial is conducted to the rigorous standards set out in the Good Clinical Practice guidelines. The Trial Steering Committee will meet approximately every six months.

As this is a behavioural intervention unlikely to produce adverse effects, it is not planned to convene a Data Monitoring and Ethics Committee. The TSC has agreed to take on the monitoring of ethical aspects of the trial.

13.2. **Trial Management Group (TMG)**

Dr Caroline Free

Ona McCarthy

Melissa Palmer

Kimberley Potter Assistant Trial Manager

Lauren Jerome Trial Assistant

Irrfan Ahmed Data Manager

Rosemary Knight Senior Manager of the CTU

The TMG will meet fortnightly at the beginning of the trial and then monthly once trial is up and recruiting. All co-applicants will be invited to bi-yearly meetings regarding trial progress.

14. Appendices

Appendix 1: Acronyms

BCT	Behaviour Change Techniques
CTU	Clinical Trials Unit
MG	Management Group
MICE	Multiple Imputation by Chained Equations
MSM	Men who have sex with men
NAAT	Nucleic Acid Amplification Test
NHS REC	NHR Research Ethics Committee
NSU	Non-specific urethritis
QUALYs	Quality Adjusted Life Years
STI	Sexually Transmitted Infection
TSC	Trial Steering Committee

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