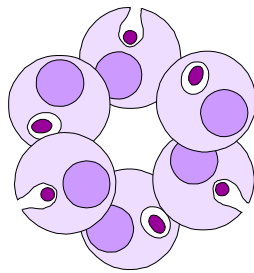


## Chlamydia Screening Study



**CLASS**

Chlamydia Screening Study

# Partner Notification Trial Protocol

This document describes the protocol for the randomised controlled trial of strategies for partner notification for patients with genital Chlamydia infection. All documentation required for the Partner Notification Trial is included here as numbered appendices. Documents are also labelled with a code relating them to the Chlamydia Screening Studies (ClaSS) database. There is some overlap with the case-control study in flow through ClaSS and these areas are included in this document.

## **1. Objectives**

To determine the feasibility, acceptability and effectiveness in GP surgeries of a simple, nurse led partner notification strategy as compared to referral to genitourinary clinics for partner notification undertaken by health advisers.

## **2. Role of the Practice Nurse**

- 2.1. At least one nurse in each practice will be designated to see study participants.
- 2.2. The main responsibilities of the Practice Nurse are; to see all study participants enrolled in the case-control study; give Chlamydia test results; give directly observed Azithromycin or other recommended antibiotic treatment (Drug Protocols, Appendix 1) to participants with positive Chlamydia test results; obtain consent for randomisation, and conduct partner notification for participants randomised to the GP arm of the trial.
- 2.3. Prior to the study the Practice Nurse will have attended a one and a half-day course explaining procedures for the Partner Notification Trial, including obtaining informed consent and randomisation (Practice Nurse Training Manual, Appendix 2). The course also includes training in how to give a positive Chlamydia test result, to ask relevant questions about recent sexual partners and about the principles of patient-led partner notification. Practice Nurses may only conduct partner notification if they attended the training day. If a Practice Nurse leaves the practice her replacement must receive training in the study protocol and partner notification before fulfilling this role. Prior to each practice going live, they will be visited, in Bristol by the Research Assistant and Research Health Adviser, and in Birmingham by the Assistant Program Manager and Research Health Adviser. The purpose of this visit will be to refresh and consolidate issues relating to the protocol. Any issues and questions raised need to be recorded on the Visit to ClaSS Participating GP Practices form (Appendix 3).

## **3. Confidentiality**

- 3.1. On all study forms, subjects will be identified by their study number and on prevalence questionnaire forms also by date of birth. On the consent form subjects will print and sign their name before returning forms to the laboratory. A master file linking study numbers to personal information will be held at the Study Centre but not at any of the participating GP practices. Access to this file will be restricted.
- 3.2. A Chlamydia Test Result Sheet (Appendix 4a and 4b) will be sent to the surgery and will be opened only after the case-control study questionnaire has been

checked (if necessary). The participant will be asked for permission to put the result in their medical notes. If they agree a sticker (Sticker With Treatment Issued, Appendix 5a and 5b) showing study title, result, treatment given and the fact that subjects were selected randomly. For practices that hold computerised records, the Practice Nurse should enter the result and treatment (if any) with ' ClaSS study. See medical notes'. All Chlamydia Test Result Sheets will be returned to the study co-ordinating centre.

## **4. Plan of investigation**

### **4.1. Management of case-control study participants**

- 4.1.1. All positive patients (cases) and the next two sequential negatives (controls) are invited to attend the GP practice for an appointment with the Practice Nurse to be given their result. Controls are matched for sex; GP practice; age range and the date positive patients are issued their letter inviting them to an appointment.
- 4.1.2. Appointments will either be sent out by the study co-ordinating centre or be arranged by the Practice Nurse (ClaSS Appointment List, Appendix 6a and 6b) depending on the preference of each practice. The Study Centre will give a list of patients needing appointments to the Practice Nurse.
- 4.1.3. Where the Study Centre makes the appointment this will be sent with a pack requesting repeat samples. Where the Practice Nurse makes the appointment the Research Health Adviser will send a repeat sample pack prior to the appointment, allowing enough time for the sample to be returned before the appointment. The repeat samples are a first catch urine from males and, from females, a first catch urine and a double-headed vulvo-vaginal swab. Participants will be asked to return samples by first class post to the PHLS, as per case finding in the Prevalence Study Protocol to ensure comparability of results.
- 4.1.4. On attending, participants will see the designated Practice Nurse who will obtain the completed Case-Control Questionnaire (Appendix 7a and 7b) and ask if they need help in completing any parts of it.
- 4.1.5. The Practice Nurse will ask if the patient has returned their repeat samples. If not she will ask the patient to provide samples before giving the result.
- 4.1.6. If any participant has questions about sexual health relating to their participation in the study the Practice Nurse will answer these if she feels confident in doing so, or will give the participant the telephone number of the Research Health Adviser.

### **4.2. Giving out Chlamydia results**

The Practice Nurse will give the Chlamydia test result only after the questionnaire has been obtained.

The health adviser will receive a list of all Chlamydia positive and matched negative patients from the Study Centre every 3 weeks, including name, barcode,

result, address, date of birth and GP practice (List of Patients for Health Advisers, Appendix 8).

#### 4.2.1. Negative results

- 4.2.1.1. Participants with negative Chlamydia test results will be thanked for their participation in the study.
- 4.2.1.2. Purposively selected patients with negative and positive results will be asked for consent to be contacted by a social scientist who will be conducting in-depth interviews about their experience of undergoing testing for genital Chlamydia and taking part in a randomised controlled trial.

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### **The remainder of this protocol is only for participants with positive Chlamydia test results.**

#### 4.2.2. Positive results

- 4.2.2.1. ClaSS project participants with positive Chlamydia tests will be told their result. They will be told that they will receive treatment at the surgery and that there is a further study: the ClaSS Partner Notification Trial.
- 4.2.2.2. **Protocol amendment 1, 17/10/2001** – General Practice patients aged 16 to 39 years who have had a test for Chlamydia taken in a routine surgery for diagnostic purposes are also eligible for treatment and participation in the ClaSS Partner Notification Trial. See Section 5.5. The precise method of referral to the Practice Nurse will differ between practices.

#### **4.3. Antibiotic treatment.**

- 4.3.1. Participants will then be offered free antibiotic treatment. They will be asked about adverse reactions to azithromycin and other macrolides. A history of gastrointestinal upset after taking erythromycin is not a contra-indication to taking azithromycin. Women will be asked if they are at risk of pregnancy, that is if they are not using reliable contraception and have had sexual intercourse since their last period. If they are at risk of pregnancy the Practice Nurse should discuss with a GP whether or not a pregnancy test should be performed and whether or not alternative antibiotic treatment should be offered. Urinary pregnancy tests are available in the surgery.
- 4.3.2. In the absence of antibiotic allergy men and non-pregnant women will be given one gram of azithromycin (four tablets) under direct observation. Men and non-pregnant women with a history of allergy to azithromycin or other macrolides will be offered doxycycline, 100mg twice daily for seven days. Pregnant women will be treated with erythromycin 500mg twice daily for fourteen days. See Drug Protocols (Appendix 1).
- 4.3.3. If a woman has a positive pregnancy test and is upset by the result the Practice Nurse should follow the practice protocol for managing the

situation. The Partner Notification Trial should be discussed and consent for randomisation obtained unless the woman is too distressed to give valid consent.

#### 4.4. Consent

- 4.4.1. After receiving treatment the Practice Nurse will explain the need for sexual partners to be treated and the purpose of the randomised controlled trial (Chlamydia Screening Study 2 Leaflet, Appendix 9a and 9b). Participants will be asked for written consent for randomisation to either of two different partner notification strategies (Consent for Randomisation, Appendix 10a and 10b).
- 4.4.2. Participants should understand that if they agree to be randomised they agree to follow the strategy to which they have been allocated. All participants from the Birmingham area, particularly those in rural areas such as Worcester should be told that they will be asked to attend the Whittall Street Clinic if randomised to the genitourinary clinic arm and that all travel expenses will be reimbursed.
- 4.4.3. Participants who decline randomisation will be referred to their local genitourinary clinic for partner notification according to current guidance. The Practice Nurse will give the patient a card Non-randomised ClaSS Study Form (Appendix 11a, 11b, 11c) with their study identity number on. The card will request the clinic to return it to the Study Centre.
- 4.4.4. In the study Case Report File (CRF, Appendix 12) the Practice Nurse will record the barcode number of each participant, their decision to participate or not and, if they decline, their reason for doing so.
- 4.4.5. **Preference for method of partner notification  
Protocol amendment 2, 31/10/2001**

Section 4.4.3 is replaced with the following:

Participants who decline randomisation will be offered the opportunity to choose their method of partner notification. They may choose to have partner notification done by the Practice Nurse at the GP surgery or be referred to the Research Health Adviser at the genitourinary clinic. Participants who decline to choose will be referred to the local genitourinary clinic, as in Section 4.4.3.

#### 4.5. Randomisation

##### 4.5.1. Allocation

A computer program has been commissioned to generate a centrally held randomisation schedule in permuted blocks stratified by practice. The unit of randomisation is the individual.

#### 4.5.2. Concealment

The computer program permits central randomisation to be performed when the participant attends the practice and has consented to participate in the trial. The Practice Nurse will telephone a number at the co-ordinating centre (0117 928 7336) and will be told the allocation of the participant (instructions in the CRF, p13, Appendix 12). The Practice Nurse will record the randomised method in the CRF. A log of all calls received by the randomisation centre is retained on the computer program.

#### 4.6. Repeat samples at 6 weeks

4.6.1. The Practice Nurse will give index cases in both arms of the trial sample containers and a prepaid envelope. They will be asked to send a non-invasive repeat sample to the PHLS **six weeks** after treatment. The date on which the specimen should be taken will be written on the study pack. Repeat test results will be sent to the Study Centre and given to the Research Health Advisers. The Research Health Advisers will record the result in the Six Week Telephone Follow Up Form (Appendix 13).

4.6.2. People with positive Chlamydia tests who have declined randomisation will also be asked to provide a non-invasive repeat sample to the PHLS **six weeks** after treatment. The date on which the specimen should be taken will be written on the study pack. Repeat test results will be sent to the Study Centre and given to the Research Health Advisers. The Research Health Advisers will record the result and details of partner treatment in the Non-Randomised Telephone Follow Up Form (Appendix 26).

### 5. Partner notification strategies

Participants who agree to randomisation will follow the procedures outlined below for each arm of the trial.

#### 5.1. Practice Nurse led scheme (Partner notification method 1)

5.1.1. The partner notification interview will elicit information about sexual partners in the six months before diagnosis and will inform the participant about the risk of re-infection from an untreated, potentially infected sexual partner. The interview is intended to last no more than 20 minutes. It is possible that at initial consultations may take up to 30 minutes until the nurse becomes more comfortable. Full details of partners will not be sought but they will be asked to give a first name or initials to facilitate follow up.

5.1.2. A fact sheet about Chlamydia and its consequences will be given to each participant (Chlamydia Fact Sheet, Appendix 14).

5.1.3. The index case will be encouraged to inform each identified partner and tell them to attend the Milne Centre for Sexual Health, Bristol, Whittall Street Clinic, Birmingham or a local genitourinary clinic (e.g. Worcester) to receive treatment and investigation for Chlamydia and other sexually transmitted infections.

- 5.1.4. The Practice Nurse will give patients a Study Contact Slip (Appendix 15a and 15b) to give to each of their contacts and record sexual history information and the identifying numbers of contact slips in the CRF (Section O, p14, Appendix 13). To indicate which contact slip relates to which contact, they will be coded in the diagnosis box as C4a<sub>1</sub>, C4a<sub>2</sub>, C4a<sub>3</sub> etc., corresponding with the order they are documented in the CRF. If patient has more than one contact it is important that each slip is given to the correct contact so it may be useful to write the first name or initials on the slip. The CRF will be passed on to Research Health Adviser after completion. Information from Section O will be typed onto the Contact Details Tracing Form (Appendix 16) and passed to the Research Health Adviser in the alternative centre so that outcomes can be ascertained in a blinded manner.
- 5.1.5. If difficult issues about sexual partners or other sexual health concerns arise from the partner notification interview the Practice Nurse can discuss these with a GP or refer the participant to the Research Health Adviser.
- 5.1.6. If the patient has any complaints they should be asked to contact the relevant Study Centre and handled as per the Dissatisfaction Procedure (Appendix 17). This information will be passed to the Qualitative Researcher at the Department of Social Medicine for further action if appropriate.

## **5.2. Management of defaulters of Practice Nurse appointment**

- 5.2.1. Study participants who do not keep the appointment made to receive results at the general practice will be contacted by the Practice Nurse to offer a further appointment.
- 5.2.2. Participants who fail to keep the second appointment will be contacted by the Research Health Adviser.
- 5.2.3. The Research Health Adviser will ensure that results are given and participants with positive results are treated.
  - 5.2.3.1. Negative results – the Research Health Adviser will generate a letter to all participants who have not attended after 4 weeks from the initial appointment ('Negative did not attend GP' letter, Appendix 19). These participants are recorded as non-responders to the Case-Control Study.
  - 5.2.3.2. Positive results – The Research Health Adviser will contact the participant by telephone or home visit, making as many calls or visits as necessary to ensure contact. The participant is no longer eligible for the Case-Control Study but is eligible for the Partner Notification Trial. The Research Health Adviser will give the positive result and will arrange for the participant to attend the practice to receive treatment. The Research Health Adviser will also explain the partner notification trial to the participant during the home visit. If the participant consents to randomisation they can sign the consent form and take this to the practice with them. The Research Health Adviser

will ensure that the Practice Nurse does duplicate information about the trial.

- 5.2.4. In exceptional circumstances participants with positive Chlamydia results who refuse to go to the practice for treatment may be treated at home by the Research Health Adviser. The Research Health Adviser will sign the protocols for drug administration and administer appropriate antibiotic therapy at the participant's home and will initiate partner notification.
- 5.2.5. If patients have moved and registered with a new practice they will be contacted through their new health authority of residence. Health Authorities will forward information and letters to other areas to be forwarded to patients.

### **5.3. Referral to genitourinary clinic (Partner notification method 2)**

- 5.3.1. The index case will be told about the importance of partner treatment and will then be referred to the genitourinary clinic (Milne Centre for Sexual Health in Bristol, Whittall Street Clinic in Birmingham) for partner notification and for examination and investigation for other sexually transmitted infections, if they wish. They will be asked to make an appointment with the Research Health Adviser and given a specially designed ClaSS Study Form (Appendix 20a and 20b) to present to the clinic on arrival. This contains details of the opening times and location of the genitourinary clinics and a direct telephone number for the Research Health Adviser.
- 5.3.2. The Practice Nurse will ask index cases randomised to the genitourinary clinic for permission to be contacted by telephone if they have not presented to the clinic after one week. The Practice Nurse will obtain a telephone number and best time to phone. The Practice Nurse will phone/fax the ClaSS appointment list to the Research Health Adviser and give the name, barcode number and telephone number for all patients referred. The Research Health Adviser will enter these details onto the Health Adviser Appointment Form (Appendix 21). The Research Health Adviser will ascertain attendance either through presentation of the ClaSS Study Form or through daily clinic records.
- 5.3.3. Information about sexual partners will be recorded in section O of the CRF (p14, Appendix 12) and the box ticked to indicate that the Research Health Adviser has filled this in.
- 5.3.4. For outcome ascertainment the following information will be transferred from Section O of the CRF (p14, Appendix 13) onto the Contact Details Tracing Form (Appendix 16) to be used at the 6 week follow-up interview: Barcode, name, date of birth, telephone details, address, contact slip details, identifying details of contact. The Contact Details Tracing Form will be sent to the Research Health Adviser in the alternative centre so that outcomes can be ascertained in a blinded manner.
- 5.3.5. Partner notification procedures at the genitourinary clinics in Bristol and Birmingham will follow Society of Health Advisers in STD guidelines (see Section 6). Partner notification may be undertaken using any of the methods of index-, contract- and provider-referral. The choice of method is

determined between the health adviser and the index case and is not thought to be amenable to randomisation. Outcomes from all methods of partner notification will be considered together but the method used will be recorded in the study record.

#### **5.4 Management of defaulters of Health Adviser appointment**

- 5.4.1. If the index case has not contacted the health adviser within one week of referral the Research Health Adviser will attempt to telephone the patient and will repeat advice about the importance of partners being treated and encourage attendance, making an appointment to see them.
- 5.4.2. If when phoning, the patient is not in, two further attempts to contact should be made at differing times of day. If no contact has been made after three attempts, no further action will be taken.
- 5.4.3. If patient does not attend the booked appointment the Research Health Adviser should phone to make further arrangements. No more than three attempts should be made if the patient cannot be contacted.
- 5.4.4. If patient fails to attend a second booked appointment they should be phoned one more time to offer a final appointment (maximum of three attempts). No further action will be taken after this.

#### **5.5. Patients referred into ClaSS Partner Notification Trial from routine GP surgery Protocol amendment 1, 17/10/2001**

- 5.5.1. **Identification of Chlamydia positive patients** – The Public Health Laboratory Service will 'flag' all positive Chlamydia test results to remind practice staff that the patient may be eligible for the Partner Notification Trial. The Practice Nurse will check their eligibility (see 5.5.2, below) and inform the Coordinating Centre.
- 5.5.2. **Eligibility** – Any patient seen in a routine surgery aged 16 to 39 years who has had a positive test for Chlamydia, who can be managed by the Practice Nurse and who has not previously returned a ClaSS project Non-Participation form to the Study Coordinating Centre in Bristol. The Practice Nurse should ask the patient if they have previously received a ClaSS study pack and declined to participate. Patients who have previously taken part in the Partner Notification Trial and who have a subsequent positive Chlamydia test done by their GP are not eligible to take part in the trial again.
- 5.5.3. **Identification of participants already in ClaSS** – Owing to the changes in sampling procedures in the Prevalence Study (see Prevalence Study Protocol) there will be patients who have been invited to participate in the ClaSS project and who have a Chlamydia test done by their GP for another indication. We want to identify these participants and allocate their ClaSS project barcode number. Each practice will receive a paper list (in alphabetical order, by sex) of people who have been invited to participate in the Prevalence Study. The Practice Nurse should check the name of any

GP referred Chlamydia positive patient against this list. Patients appearing on this list already have a ClaSS project number that can be obtained from the Coordinating Centre. Patients not appearing on this list should have a new barcode number allocated to them.

**5.5.4. Trial documentation** – Each practice will have a Trial Documentation Pack containing a stock of additional ClaSS barcode identification numbers or blank labels, consent forms (see 5.5.5) and registration forms for these patients (Appendix 27).

5.5.4.1. Patients with an existing ClaSS project number – This number will be used for all trial documentation and specimens. The Practice Nurse will write this number onto a panel of labels that will be used for the CRF, contact cards and six week specimen(s). This number will then be used to perform randomisation.

5.5.4.2. Patients without and existing ClaSS project number – The Practice Nurse will allocate a new ClaSS barcode number, using the stock of pre-numbered labels supplied with the Trial Documentation Pack. She will inform the Coordinating Centre as soon as a new ClaSS project number has been allocated so that the patient's details can be uploaded onto the telephone randomisation computer.

The registration form will be collected from the practice by the Research Health Adviser or posted, if necessary. The Practice Nurse should use the same CRF for patients referred through routine GP surgery as for those already in the ClaSS project but should complete only **unshaded** sections of the CRF.

**5.5.5. Study information** –

5.5.5.1. Patients who have had a Chlamydia test done by their GP outside the ClaSS project and have not received a study pack should be informed of the ClaSS project at the earliest opportunity and given the ClaSS Chlamydia Fact Sheet (Appendix 14) and Chlamydia Screening Study 2 Leaflet (Appendix 9a and 9b).

5.5.5.2. Patients who have had a Chlamydia test done by their GP and have also received a study pack, but not returned a specimen should be given the Chlamydia Screening Study 2 Leaflet (Appendix 9a and 9b) and informed that the Partner Notification Trial is part of the ClaSS project.

5.5.5.3. Patients who have had a positive test as part of ClaSS and declined to take part in the Partner Notification Trial, but who subsequently have a positive test for Chlamydia done by their GP should be given the Chlamydia Screening Study 2 Leaflet (Appendix 9a and 9b) and invited again to take part in the Partner Notification Trial.

**5.5.6. Antibiotic treatment** – Patients should be made aware that the trial protocol includes free treatment in the practice with azithromycin (or other appropriate antibiotic) and randomisation to partner notification performed

by the practice nurse or by a specialist health adviser at the local genitourinary clinic. Patients who decline to be randomised will be asked to see their GP for a prescription for antibiotics.

- 5.5.7. **Consent** – Patients who consent to participation in the trial should sign the consent form (Appendix 10a and 10b), which will be printed on pale mauve paper and contained in the Trial Documentation Pack (see 5.5.4).
- 5.5.8. **Randomisation** – The additional ClaSS barcode identification numbers for each practice will be registered on the central telephone randomisation system. Randomisation should be performed exactly as for existing ClaSS project participants.
- 5.5.9. **Repeat samples and follow up** – These procedures will be performed exactly as for existing ClaSS project participants. Patients who decline randomisation will not be registered in the ClaSS project, will not receive antibiotic treatment in the practice and will not be followed up.

## 6. Health advisers partner notification protocol

- 6.1. The index cases randomised to the genitourinary clinic will have been given a ClaSS Study Form detailing a number to ring for an appointment with the health adviser. In the Whittall St Clinic, this number will transfer to an answer phone if not answered. The Research Health Adviser or delegated colleague will respond to messages the same day if within clinic hours. In the Milne Centre, the call will transfer to a mobile phone carried by the Research Health Adviser, or a delegated colleague, during clinic hours. On contacting the Health Adviser an appointment will be offered as soon as possible for the patient to be interviewed during normal working hours within the clinic. The patient should also be offered the opportunity to see a doctor afterwards for a full sexual health check-up. This will require flexibility on the part of the medical staff and the clinic medical rota needs to be adjusted accordingly so that these patients can be fast-tracked. It is **important** that partner notification (PN) strategies are not discussed during this telephone contact with the patient as this could bias the study's findings. As it is routine to discuss Chlamydia and other sexually transmitted infections over the telephone with patients this is permissible but the importance of discussing this in person should be stressed.
- 6.2. Details of telephone calls need to be recorded on the Health Adviser Appointment Form (Appendix 21).
- 6.3. When the patient attends for interview clinic notes will be made up and they should be seen by the Research Health Adviser in an appropriate counselling room. The start and finish time of interview need to be recorded on the Health Adviser Appointment Form. The objectives of the consultation are:

- To ensure that the index patient fully understands the significance of genital tract infection with Chlamydia and the possibility of other infections being present.
- To ensure that the index patient understands the importance of effective treatment of both themselves and their partners.
- To ensure that the index patient understands the relevance and importance of partner notification.
- To inform the index patient about safer sexual practices and so reduce the risk of acquiring a new sexually transmitted infection.
- To assist the patient in undertaking partner notification.

**6.4.** Research Health Adviser should go through the ClaSS Chlamydia leaflet and discuss any concerns the patient has. The following should be addressed:

- What Chlamydia is and how it is transmitted.
- It is a sexually transmitted infection.
- If asymptomatic there is evidence that it could persist for months or even years.
- It can be isolated from the throat and eye without detectable infection in the lower genital tract. It can therefore not always be assumed to be sexually acquired.
- It is often asymptomatic, especially in women.
- The complications of untreated Chlamydia.
- If the patient has not been prescribed azithromycin discuss the side effects of doxycycline and erythromycin, and the importance of complying fully with treatment and what to do if a dose is missed.
- The importance of their sexual partner(s) being evaluated and treated.
- Advice to abstain from sexual intercourse, even with condoms, until either one week after they have taken azithromycin or until they have completed therapy with either doxycycline or erythromycin and their partner has been treated.
- Advice on safer sexual practices.
- Short discussion on other sexually transmitted infections (STIs) and safer sex. The opportunity to see a doctor should be mentioned to check for other STIs, in particular genital warts in both men and women, non-gonococcal urethritis in men and pelvic inflammatory disease in women. Trichomonas and gonorrhoea should also be mentioned but informed that they are relatively uncommon and treatment for Chlamydia is likely to be effective against gonorrhoea. Any other issues raised eg HIV testing, contraception advice, condom provision should be dealt with through normal clinic protocols. All details relating to further STI

consultation to be entered on Health Adviser Appointment Form (Appendix 21).

- 6.5.** Partner notification is a voluntary process and the co-operation of the patient is paramount. It should be non-coercive, confidential and not be seen as punitive. However, there may be circumstances when the wishes of the index patient are overridden. These cases will need to be discussed with the designated Consultant in charge/Senior Health Adviser.
- 6.6.** The patient should be asked details of their contact(s) as required on Clinic Contact Cards (Appendix 22) or Contact Details Sheet - Section O of the CRF, p14, (Appendix 12) and told that this information is used to verify contacts' attendance. Patients should be advised that contacts are not routinely informed (provider referral) unless consent is given by the patient. The importance of contact attendance needs to be stressed. In rare circumstances, if further discussion with patient is not possible, a decision may be made, after discussion with Consultant, to go ahead and inform the contact. This is because we have a duty of care to the contacts, and if they are at significant risk of infection with Chlamydia, we may be obliged to notify them without the consent of the index patient because of the damage Chlamydia may cause. However it should also be stressed that this would be done in such a way that the contact would not be aware of the index case's identity and only after we have made attempts to fully discuss the reasons for doing so with the index case. The Research Health Adviser can offer the patient four options when discussing Partner Notification. In order for this to be effectively undertaken consent to re-contact the index patient must be sought and documented.
- 6.6.1. Index Referral –** The patient agrees to take responsibility to inform contact(s). This should be documented in the Clinic medical notes and noted in the comment box of the Contact Details Sheet – Section O of the CRF (p14, Appendix 12). They will be given specially designed Study Contact Slips (Appendix 15a and 15b) for each identified sexual partner to assist with this and will be urged to ensure that partner(s) present the slips on presentation at a clinic so that trial outcomes can be ascertained. Study Contact Slips are lilac, uniquely numbered and contain information about the location, opening times and telephone numbers of the Milne Centre for Sexual Health, Bristol or Whittall Street Clinic, Birmingham. They have a Freepost address so that they can be returned easily to the study co-ordinating centre. There is a telephone number for GPs seeking advice on how to deal with contacts attending their surgery rather than the local genitourinary clinic. If the contact has attended the genitourinary clinic in the past it should also be documented in their notes. The index patient will be re-contacted in two weeks to establish if contacts have attended. This can take place either by appointment or by telephone. During this consultation the health adviser needs to establish or identify difficulties regarding contact's attendance and offer possible solutions, eg contract referral or provider referral. For follow-up the index patient should receive either

two letters at two-week intervals or, telephone contact attempted. If no response note 'no further action' on card and in notes. In exceptional circumstances further attempts to contact may be appropriate e.g. for pregnant contacts or under 16s. These situations should be discussed with the Senior Health Adviser/ Consultant.

6.6.2. **Contract Referral** – The Health Adviser and index patient negotiate a period of time (usually up to three weeks) for the index patient to inform their contact of the infection and the need to attend. They will be given study contact slips as described above. The index patient gives consent for the Research Health Adviser to initiate provider referral if the contact has not attended within this period of time. Consent for contract referral and the period of time should be clearly documented on the contact cards and in the patient's notes. Also, if contact has old notes, details re index's patient number, diagnoses and date of infection should be documented in these. If contact has not attended within the agreed time, provider referral is commenced.

6.6.3. **Provider Referral** – The index patient gives permission for the Research Health Adviser to inform their contact(s) of the need for tests and possible treatment. Check to see if contact has old notes. If so, write in notes details of index patient's number, diagnoses and date of infection, then mark notes as important in line with individual clinic policy. Mark on card that contact has notes and that these are being reactivated and send contact letter or phone. If contact has not attended within two weeks, phone or send second letter. If contact has not attended within three weeks, a visit may be appropriate (See Home Visit Protocol. Appendix 23). This enables possible verification of the given address, a new address to be obtained, or to speak to the contact in person.

If the contact does not live at given address, attempt to get correct address from Health Authority and contact.

If contact is known to have received a letter or spoken to a Health Adviser and is therefore aware of the need to seek medical tests and/or treatment, ensure discussion is documented on card and leave.

6.6.4. **No Referral** – Study documentation should still be completed - no action should clearly be marked on the Contact Details Sheet and a reason given. This should also be detailed in the notes. Reasons may include patient declined, no available information (i.e. name or address), violence or other risk to index patient.

6.7. Details relating to the GUM consultation of any contacts that attend should be recorded on the appropriate form – STI Consultation for Contacts (Appendix 24).

## 7. Outcome assessment

- 7.1. At six weeks index cases who participated in the partner notification trial will be contacted by telephone and interviewed by a Research Health Adviser using the PN Trial Six Week Telephone Follow Up Form (Appendix 13). To ensure blinding of outcome assessment the Research Health Adviser in Birmingham will carry out follow up telephone interviews with index cases in Bristol and vice versa. The Research Health Adviser will ask about sexual behaviour since treatment and will record details of contact slips handed out and the outcome if known using a standardised questionnaire. Index cases will be asked to return any contact slips that were not handed out.
- 7.2. At six weeks index cases who declined randomisation will also be contacted by telephone (see Section 4.6.2). They will be given the results of their follow up sample and will be asked to provide brief details of whether their sexual partner(s) were notified and treated. This information will be entered on the Non-Randomised Telephone Follow Up Form (Appendix 26). This interview will be carried out by the Research Health Adviser in the same centre as the patient.
- 7.3. Research Health Advisers will require an electronic copy of the PN Trial Six Week Telephone Follow-up Form (Appendix 13) and the Contact Details and Outcome Ascertainment Form (Appendix 25). Each of these will be personalised with the patients' barcode. Research Health Advisers are responsible for ensuring that telephone interviews with these index cases are completed at 6 weeks following appointment attendance.
- 7.4. Prior to this telephone call the Research Health Adviser will contact the laboratory to check if repeat sample has been received. On phoning the patient the Health Adviser will check if and what date a repeat sample was obtained. Participants who have returned a repeat specimen will be given their result. Those who did not will be reminded to send their repeat specimen, if patient does not now have sampling pack the Health adviser will organise this to be posted. Index cases whose repeat Chlamydia test is positive will be asked to attend the genitourinary clinic for treatment and partner notification. Details of this will be recorded in the Repeat Sample 3 Follow-up section of the PN Trial Six Week Follow Up Form (Appendix 13).

At 6 weeks the following outcome parameters will be assessed:

### 7.5. Primary outcome:

- 7.5.1. Proportion of index cases who had one or more partners who received treatment, as confirmed by the return of a study contact slip.

### 7.6. Secondary outcomes:

- 7.6.1. Number of sexual partners reported to have been treated, as determined by telephone follow-up;
- 7.6.2. Number of sexual partners identified;
- 7.6.3. Number of sexual partners notified;

- 7.6.4. Number of regular and casual partners notified and treated;
- 7.6.5. Number of sexual partners infected with Chlamydia;
- 7.6.6. Proportion of index cases randomised to genitourinary clinic arm who present at the clinic for partner notification;
- 7.6.7. Re-infection rate at six weeks;
- 7.6.8. Re-assessment of primary outcome at three months.

## **7.7. Ascertainment of partner outcomes**

- 7.7.1. It is known to be difficult to verify reports from index cases that sexual partners have been treated, particularly if identifying information has not been volunteered. The use of distinctive and uniquely numbered Study Contact Slips will make it easier to identify individuals who present these when attending for treatment and index cases will have been advised that their partners should attend one of the participating genitourinary clinics. Throughout the course of the study, general practitioners and genitourinary clinics not involved in the study in Bristol and Birmingham will be made aware of the study and will be sent examples of the Study Contact Slip. The contact slip will contain information requesting that the patient receive appropriate anti-Chlamydial treatment and will include the address of the Study Centre for return.
- 7.7.2. At the follow up interview patients will be asked for details of partner outcomes. If names have been volunteered, attendance at a genitourinary clinic will be checked against clinic records. To ensure consistent attempts at partner follow up in the two arms of the trial, the primary outcome assessment includes only confirmed partner treatment.
- 7.7.3. The outcome of partner notification efforts for each identified contact will be recorded on the Contact Details and Outcome Ascertainment Sheet (Appendix 25).

## **7.8. Definition of outcomes – Protocol amendment 3, 19/05/2003**

Having reviewed the number of contact slips received (without unblinding the study) it is clear that this method of outcome ascertainment is inadequate. Too few contact slips have been returned to the study centre for meaningful analysis of this as the primary outcome. A combined outcome is therefore required. This is defined as:

- Receipt of a study contact slip confirming partner treatment, or
- Confirmation in genitourinary clinic database of partner attendance, or
- Report by index case at telephone follow up that partner received treatment.

## 7.9. Qualitative assessment

7.9.1. Participants will be asked if they would consent to an in-depth interview with a researcher to assess the acceptability of each partner notification strategy and experience of receiving a positive Chlamydia test result. They will also be asked about the acceptability of telephone contact by health advisers to provide baseline information for future studies of the effectiveness of telephone partner notification by trained health advisers compared with current practice.

## 8. Sample size considerations and statistical analysis

8.1. A pilot study including 50 male and 50 female index patients who attended the Milne clinic in Bristol showed that 32 (65%) of men and 38 (76%) of women ( $p=0.28$ ) had one or more confirmed partners who received treatment. The success rate in the GU clinic arm will be lower in the context of the present study because some index patients randomised to this arm will not attend. The sample size calculations shown in table 3 indicate that the trial will have adequate power across a plausible range of success rates.

### 8.2. Intent to treat analysis

It is recognised that some participants randomised to partner notification by the Practice Nurse may not want to give details of sexual partners to the Practice Nurse and prefer to attend the genitourinary clinic. These patients will be given the telephone number of the Research Health Adviser and will have partner notification done at the clinic, using study contact slips. Outcomes will be ascertained as above and will be analysed in the Practice Nurse arm. These patients will still be telephoned by Research Health Adviser six weeks following treatment.

**Table 1 Required number of index patients to detect differences in primary outcome**

| Success rate in GU clinic* | Success rate in GP surgeries* | Difference | No of index patients in each study arm |           |           |
|----------------------------|-------------------------------|------------|--|-----------|-----------|
|                            |                               |            | 80% Power                              | 90% Power | 95% Power |
| 40%                        | 30%                           | -10%       | 376                                    | 496       | 609       |
| 40%                        | 20%                           | -20%       | 91                                     | 119       | 144       |
| 50%                        | 40%                           | -10%       | 408                                    | 538       | 661       |
| 50%                        | 30%                           | -20%       | 103                                    | 134       | 163       |
| 60%                        | 50%                           | -10%       | 408                                    | 538       | 538       |
| 60%                        | 40%                           | -20%       | 107                                    | 140       | 170       |

\*Proportion of index patients with one or more partners who received treatment, as confirmed by the return of a study contact slip. Based on a continuity corrected chi-square test with a 0.05 two-sided significance level

