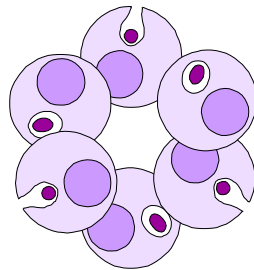


Chlamydia Screening Study



CLASS

Chlamydia Screening Study

Detailed Prevalence Survey Protocol

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This protocol was amended and refined during the course of the study as a result of the findings in the first four practices, and discussion with the funding body. Items which have been substantially changed are listed in section 14, and highlighted in the original protocol with an asterisk *.

1. OBJECTIVES OF THE COMMUNITY PREVALENCE SURVEY

- To determine the prevalence of genital *Chlamydia trachomatis* infections in a general community sample.
- To assess quantitative and qualitative aspects of the acceptability and process of non-invasive testing for genital *Chlamydia trachomatis* infections in a general community sample.
- To provide *Chlamydia* positive cases and *Chlamydia* negative controls for the case-control study.
- To identify individuals with chlamydial infection who will participate in the randomised controlled trial of partner notification strategies.
- To provide sample substrate for the laboratory test evaluation studies.

2. PLAN OF INVESTIGATION

2.1 Selection Of GP Surgeries

- 2.1.1 Twenty-seven practices will be purposively selected from members of two existing GP research networks: the Bristol Primary Care Research and Development Consortium and the Midlands Research Practices Consortium (Appendix 1). Eleven practices will be in the Bristol area and sixteen in Birmingham. In each site selected practices will represent urban, peri-urban and rural areas and include deprived and ethnic minority populations (Appendix 31a, Appendix 31b). Both group and single-handed practices will be represented.
- 2.1.2 For each practice a GP will be nominated to provide liaison with ClaSS (Appendix 2). The signature of the nominated GP (Appendix 3) and a copy of practice headed paper will be obtained from each practice prior to the start of the study (Appendix 4). A computer scan of the signature and the practice headed paper will be undertaken. The signature of the nominated GP will appear on all practice headed correspondence between the patients and the practice in relation to ClaSS. Practices with coloured/detailed headed paper will have correspondence printed directly onto their own paper. This will be obtained prior to their start date.
- 2.1.3 A document containing the Social Research, Prevalence Study, Case Control Study and Partner Notification Trial protocols, Azithromycin, Erythromycin and Doxycycline antibiotic protocols, lead investigator CV, honorary contracts, ethical approval correspondence, frequently asked questions, study team members, Case Report File (CRF) and a Medication/Test Kits Form will be given to each practice prior to the start

of the study (These are referenced at the relevant section of this document). The practice will return a signed approval letter on receipt of this document (Appendix 5) confirming their agreement to undertake the study in accordance with the study protocol and their participation in ClaSS. A copy of the document, and approval letter will be kept at each practice with a matching document held at the respective study centre.

2.1.4 The practice will be provided with the necessary documents and equipment needed to participate in the study (Appendix 29, Appendix 30)

2.1.5 Ethical approval will be sought and obtained from MREC and appropriate LRECs in the West Midlands and Bristol (Appendix 6).

2.2 GP Roll-Out Schedule

2.2.1 A proposed GP schedule for Birmingham and Bristol will be devised (Appendix 7). This schedule will be reviewed regularly with ongoing patient screening to enable appropriate scheduling of the remaining practices.

2.2.2 The order of practice screening will be decided depending on practice size, LREC approval and GP preference and any other considerations arising during the course of the project.

2.2.3 The Study Coordinator, Research Health Advisor and Research Fellow in Birmingham, and the Research Health Advisor and Research Assistant in Bristol will make preliminary visits to each practice one month prior to the start of the practices' participation. These visits will be used to clarify practical arrangements, clarify the study protocol and provide information and advice regarding the study and download data if necessary. The members of the practice team attending these meetings will be the Nominated GP, Practice Manager, Practice Nurse, Head Receptionist and Administrative Manager if requested by the practice.

2.2.4 Precise clinical arrangements, for example decisions as to whether study participants will be seen at designated *Chlamydia* Clinic times or within routine clinic appointments will be at the discretion of individual practices.

2.3 GP Data

- 2.3.1 The following fields will be extracted from the practice database: 1. Sex; 2. Surname; 3. Forenames; 4. Date of birth; 5. Title; 6. House name; 7. No./Street; 8. Village; 9. Town; 10. Postal code; 11. Telephone Number; 12. NHS Number; 13. Registering Doctor; 14. RPP (Rural practice payments); 15. Registration status 16. Dispensing 17. Usual Occupation 18. Practice ID number; 19. GP 'G' Number and 20. "Maiden" name (Females only).
- 2.3.2 Visits will be made to each practice to obtain 'test' data for males and females aged 15-40 years with the fields stated (Section 2.3.1). This age range ensures that the study target sample of patients aged 16-39* is included taking into account any time lag between data download and study packs being sent out. The 'test' data will be used to guide the development of a programme for data cleaning (Appendix 8).
- 2.3.3 The relevant data will be extracted from the practice database and subsequently cleaned according to the data cleaning protocol.
- 2.3.4 All data will be stored in accordance with the Data Protection Act (Appendix 9).
- 2.3.5 Data will be considered current for a period of 3 months from the download date. Where data from practices is older than 3 months repeat data downloads will take place at such practices, where possible (Appendix 32).
- 2.3.6 The rationale behind the approach to data cleaning and randomisation adopted is described in the Data Cleaning and Randomisation Protocol (Appendix 8).
- 2.3.7 There are no fixed exclusion criteria regarding participation in the prevalence study other than age out-with the specified range and residence in a household where another member is a participant. The only other reason for exclusion relates to instances where the practice believes a particular patient would be placed at significant risk of psychological harm through being approached by the study team. Any such cases will be discussed on an individual basis and where it is agreed such a risk does exist the patient will be excluded from the sampling frame. All such exclusions will be documented. Exclusions are discussed at the Preliminary Visit, Section 2.2.3.

*See changes to sampling frame in section 14.3

2.4 Practice Nurse

2.4.1 A nominated nurse(s) from each practice will attend a day and a half training organised jointly by the departments of Genitourinary Medicine and Social Medicine and Primary Care and General Practice in Bristol and Birmingham respectively (Appendix 10). The workshop will address general issues about population sexual health with specific emphasis on the control of genital chlamydial infection. Issues related to partner notification and the randomised controlled trial of strategies for partner notification for patients with genital *Chlamydia* infection will also be covered. All nurses who complete the training days will receive a Certificate of Attendance. The role of the nurse is further addressed in the Partner Notification Protocol (Section 2.1 – 2.3).

3. SAMPLES

3.1 Non-Invasive Samples: Urine And Vulvo-Vaginal Swabs

3.1.1 Women and men will be asked to provide a first void urine sample (FVU). Women will also be asked to provide a vulvo-vaginal swab (VVS). A leaflet with instructions explaining sampling will be enclosed in the study pack (Appendix 12) (see Section 6.1).

4. RANDOM SAMPLE AND RESPONSE RATE

4.1 Random Sample Of Potential Participants And Response Rate

4.1.1 The target sample size is 10,000 men and women (5,000 in Bristol and 5,000 in the West Midlands), drawn from practice populations aged 16 to 39 years.

4.1.2 A response rate of around 70%, based on a pilot study of 200 patients (100 men, 100 women) aged 18 to 45 years who were randomly sampled from a practice list in Bristol¹ is anticipated. A response rate of 82% to a request for urine sample and questionnaire information was achieved, using recorded delivery and telephone reminders. The pilot study suggested that around 20% of patients in this age group will be “ghost” patients who have moved from the address listed on GP registers, a

proportion similar to that found in a larger contemporaneous study carried out in North London.²

- 4.1.3 Taking into account response rate and ghost patients, approximately 18,000 people have been sampled to obtain an estimated 10,000 responders ($0.7 \times 0.8 \times 18,000 = 10,080$). People aged 16 to 25 years who are known to be at higher risk of genital chlamydial infection, will be over-sampled at a ratio of 2:1. *
- 4.1.4 Once the sampling frame has been selected, a 5% random sub-sample of patients will be flagged. Flagged patients whose classification remains “unknown” and “ghosts” following delivery of study packs and reminder procedures will be visited at home (see Section 7.1 – 7.1.4). **

4.2 Sampling

The study protocol specifies that 18,000 people will be sampled in the prevalence study. Of these, 12,000 will be in the 16-25 age group and 6,000 will be in the 26 to 39 age group. Based on the initial list supplied by the practices we estimated that the total number of patients registered with the study practices were approximately 28,000 and 57,300 in the younger and older age groups respectively. We decided to aim for totals of 12,600 and 6,300 in the two groups, to allow for possible errors in the estimated totals. This implies sampling fractions of 0.45 (45%) of the younger age group and 0.11 (11%) of the older age group. The same proportion of patients is sampled from each study practice.

In designing the sampling strategy we also needed to ensure that only one person per household was selected. This was necessary for other parts of the study, and also avoids problems with individuals in households swapping forms or sampling kits. For the younger age group, the required sampling fraction of 45% is clearly not possible for individuals living in households with three or more individuals (since sampling one individual per household means the maximum sampling probability is 0.33). We therefore adopted the following two-stage procedure, separately in each age group:

(i) sample one individual from each household

(ii) sample all individuals from households in which the probability of being sampled is less than the required overall probability.

* See changes to sampling frame in section 14.3

** See changes to follow-up of non-responders, section 14.1 and 14.2

(iii) sample sufficient individuals from the remaining households to ensure that, for each practice, the required proportion of individuals is sampled.*

The final sampling probability for each individual is recorded in the study database. This will allow analyses to be corrected for the sampling procedure, using "inverse probability" weights.

5. DELIVERY OF STUDY PACK

5.1 Introductory letter

Potential participants will be initially contacted at home by post with a GP Introductory Advance letter (Appendix 11a), a Chlamydia Fact Sheet (Appendix 18) and a Chlamydia Study information leaflet (Appendix 17). A study pack will be delivered approximately 7-14 days later.

5.2 Delivery Of Study Pack

- 5.2.1 Following refinement of packaging methods in Bristol for the initial practices, study packs (Appendix 13) will be assembled and sent out in Bristol and Birmingham for their respective practices.
- 5.2.2 The sampling strategy is aimed at providing as close to a uniform rate of laboratory workload as is possible. Evaluation of initial mail-outs and subsequent return of samples from both pilot practices will be ongoing. Initial experience suggests that a 100% mail-out for a single practice is within the capacity of the laboratories. The mail-outs will continue to be phased according to changing response rates and laboratory capacity.
- 5.2.3 Packs will be delivered on any day of the week between 8.00am and 9.00pm.
- 5.2.4 Return addresses on packs are the Bristol study centre for Bristol patients and the Birmingham study centre for West Midland patients.
- 5.2.5 A reminder postcard will be sent out 7 days after receipt of study packs (Appendix 14). The reminder postcard will be sent out from Birmingham study centre for the West Midlands practices and Bristol study centre for the Bristol practices.

* *See changes to sampling frame in section 14.3

- 5.2.6 Experience in the first four practices surveyed identified problems with the use of Royal Mail recorded delivery in relation to survey requirements – in particular the ability to accurately ascertain the denominator for prevalence estimates. There were returns of a substantial number of packs by Royal Mail to the study office where residences were not occupied at the time of delivery AND individuals failed to collect the study pack from their local Royal Mail depot. In most cases it was impossible to ascertain whether these individuals resided at the address in question. Returned packs coded “addressee gone away” were classified as “ghosts”, returned packs coded “refused” were classified as non-participants. Returned packs with any other codes (see appendix 33) were then reissued by standard delivery. Subsequently a proportion responded (indicating that to classify all these subjects as “ghosts” would be inappropriate) however the majority remained unknown. To address this situation follow up contact of ALL these individuals was attempted either by telephone (where a number was available), or home visit where a contact phone number was not available (see Appendix 23). Individuals were then classified as resident at the address (and thus either a non-responder or refuser, depending on the information provided at contact) or a “ghost” (not resident at their GP registered address at the point of survey). Where this distinction could not be reliably made (i.e. an occupied address where details of the current resident could not be obtained) the subject was classified as a non-responder. Given the work-load involved it was not felt feasible to undertake this process in every practice. Consequently it was decided to establish a dedicated courier service. In addition to addressing the issues of denominator ascertainment described above this also gave the opportunity to further “personalise” contact between the study and potential participants and thus, potentially, improve response.
- 5.2.7 Experience in the initial practices surveyed in both Bristol and Birmingham led to the identification of previously unforeseen problems with the use of Royal Mail recorded and standard delivery as described above. These problems related primarily to the ability to ascertain whether the subject named in GP records as being resident at the address actually did reside there and whether or not this person had received a study pack. Royal Mail practice of inviting residents who were not at home when delivery was attempted to collect study packs from a depot also proved problematic. In view of these considerations a private courier will be commissioned to deliver study packs according to a standard protocol. Couriers will receive training on study pack delivery (Appendix 25). A courier delivery sheet will be used to record delivery outcomes (Appendix 26). A maximum of 5 delivery attempts will be made to each subject at each mailing. At least one of these delivery attempts will be after 6pm or at a weekend. Following the initial mailing it will now be possible to classify subjects as having received a pack (receivers); having refused a pack at

the point of delivery (refusers); as not living at the GP registered address/address details incorrect (ghosts); or as status still undetermined. Further action will depend on this classification (Appendix 33). Couriers will also seek to confirm telephone contact details of receivers. There will be ongoing review of the effectiveness of the courier system. A random 5% of addresses will be either telephoned or visited at home to validate the courier reported findings.

5.2.8 During the course of the study some practices will be participating in social research being conducted by the Social Research Workstream. (see Social Research Workstream protocol).

5.2.9 If we are informed that a patient in the sample is now at a new, specified, address in the practice area, we will contact the practice to inform them and ensure that they will accept the patient at the new address, send the patient a new pack, and update the address on our records. If the patient can no longer be registered with the practice at their new address, they become a 'ghost' i.e not at the address at which they are registered with the practice. If we are informed that a patient in the sample is now at a new address, but that address is unknown, they are also a 'ghost'. If the current occupant of a household offers to accept the pack and pass it on, but will not give the new address to the courier, this will be treated as 'address unknown' and the patients classified as a 'ghost'

6. STUDY PACK CONTENTS

6.1 The Study Pack Contains The Following:

- **A covering letter** – this is printed on practice headed paper and signed by the nominated GP. It will cover brief background and purpose of the study, information on how the subject was selected, invites participation and describes what participation entails (Appendix 11b).
- **Two informed consent forms** - one for the patient to sign and keep and one for the patient to sign and return. Informed consent will be sought for both prevalence study and case control study. Subjects have the opportunity to provide correct name and address details on the reverse of the consent forms if this information is incorrect. The consent forms will be bar-coded (Appendix 15).
- **A questionnaire*** - A short questionnaire covering basic demographic details (age, ethnicity) and whether or not the patient is sexually active. Subjects are asked to record the date and time the sample was taken. Following

experience in the initial practices, subjects will also be asked the time they last passed urine and the part of the urine flow from which the sample was taken. Women are to be asked date of last menstrual period. No other sensitive questions are included. The questionnaires will be bar-coded (Appendix 16).

- **A non-participation form** – This is to be completed and returned with the study pack free of charge by subjects who do not wish to participate in ClaSS. The non-participation form will be bar-coded (Appendix 19).
- **Sample taking instructions** – Instructions for males and females for sample taking with diagrams (Appendix 12).
- **Translation postcard** - A prepaid postcard requesting a study pack together with information in alternative languages will be included in the study pack for patients to return to their study centre. The languages included on the postcards are **Arabic, Bengali, Chinese, Gujarati, Punjabi, Urdu, Vietnamese, Kurdish, Kosovan, Italian and Somali**. If requests for alternative language are made these are supplied. The translation postcard will be bar-coded (Appendix 20). Languages included on the translation postcard were decided following consultation with appropriate local and national bodies.
- **Freepost envelope** – For West Midland patients the samples will be returned to 'Dr Sue Skidmore, Public Health Laboratory Service (PHLS), Birmingham. For Bristol patients the return address is 'Dr Owen Caul, PHLS, Bristol' (contained in Appendix 13).
- **Clip top bag** – The urine sample container will be sent and returned in this bag (contained in Appendix 13).
- **Plastic glove** (contained in Appendix 13).
- **Pen** (contained in Appendix 13).
- **Funnel** (Females only) (contained in Appendix 13).
- **Return box** - including urine sample container (male and female), absorbent roll, elastic band and swab container (females only) (contained in Appendix 13).

7. MANAGEMENT OF NON-RESPONDERS

7.1 Non-Responders

- 7.1.1 After approximately 2 weeks from initial mailing of study packs, a reminder letter (Appendix 21a)/study pack (Appendix 21b) will be sent to subjects, classified as “receivers” who have not responded by either return of specimen, consent form and questionnaire or by return of a non-participation letter.
- 7.1.2 After a further 2 weeks, subjects (whose status is classified as “receiver”) who have not responded, either by return of specimen, consent form and questionnaire or by return of a non-participation letter, will be contacted by telephone (where a telephone contact number is available) to confirm receipt of the study pack and to encourage participation. Each patient will be rung up to 3 times with at least one of the calls being after 6pm. The telephone reminder form will be used to record the outcome of telephone contact (Appendix 22).
- 7.1.3 Where a telephone number is not recorded or does not exist no further follow-up will be attempted at this stage.

8. RETURN PROCEDURES OF SAMPLES

8.1 Return and testing samples

- 8.1.1 Participants will return samples to the PHLS laboratory of their area (Birmingham or Bristol) along with the signed consent form and the short questionnaire in a prepaid addressed envelope.
- 8.1.2 At PHLS samples will only be examined if accompanied by a signed consent form. Following experience in the initial practices a protocol for dealing with incomplete returned samples has been devised as below:

No consent returned – Samples frozen, re-issue request for consent form (Appendix 27), tick on sample record sheet that samples need to be frozen

No urine – re-issue entire pack (Appendix 28)

No swab – no action

No questionnaire – Contact patient if possible to confirm the sample was taken and the time of urination prior to sample being taken

Testing procedures are described in the laboratory studies protocol.

- 8.2 The test result, consent form and questionnaire will be sent on by Bristol and Birmingham PHLS to the study centre in Bristol and Birmingham respectively.

9. ASSESSMENT OF METHODOLOGICAL REFINEMENTS

9.1 Methodological Refinements

- 9.1.1 There will be a number of potential refinements to the above methodology that may be associated with logistical or financial advantages to the project overall. However such advantages may be offset by a negative effect on response rate. This issue will be resolved through random allocation of participants to one of two competing strategies. The methodology associated with the maximum response rate will be adopted thereafter.
- 9.1.2 The impact of several methodological refinements will be assessed in the initial practices participating in Bristol and Birmingham.
- 9.1.3 Following evaluation in Bristol, double-headed (rather than single-headed) vulvo-vaginal swabs will be sent to all female subjects.
- 9.1.4 Following evaluation in Birmingham a short questionnaire with no additional question on recent number of new sexual partners (rather than a questionnaire asking about recent partner change) will be sent to all subjects.

- 9.1.5 Evaluation of alternative approaches to the second mailing suggested that a slightly higher response was achieved with a reminder pack rather than a reminder letter 20% vs. 12%, but at a much greater cost because of the large number of reminders that were necessary. Therefore reminder letters were used in subsequent practices, along with the flagging of non-responders in practices (see para 14.1)

10. RECALL OF PARTICIPANTS

10.1 Recall Procedures

- 10.1.1 For each participant with a positive screening test two participants with negative tests will be selected (see case-control study protocol).
- 10.1.2 A second letter signed by the GP will invite participants with positive screening tests along with the sample of non-infected control participants to re-attend their surgeries.
- 10.1.3 The remaining group of negatives not invited to attend the surgery for their result will be informed of their negative result by post.
- 10.1.4 The study centre will prepare a sealed opaque envelope with the test result. Each test result will be validated against the result sheet from the laboratory, and initialled by the person checking. The sealed opaque envelope is sent to the nurses at the study practices.

11 TREATMENT OF CHLAMYDIA POSITIVE PARTICIPANTS

11.1 Treatment Procedures

- 11.2 Treatment for sexually transmitted infections will be provided free of charge in Departments of Genitourinary Medicine under the conditions of the Venereal Diseases Act (1917).
- 11.3 Treatment will be provided, on site, free of charge, and under observation as a single dose of Azithromycin (1 gram; 4x250mg).³ If a participant is known to be Azithromycin sensitive and is not pregnant, Doxycycline 100mg bd 7/7 will be given. Pregnant women will be offered treatment with Erythromycin 500mg bd 14/7. For pregnant women who are allergic to Erythromycin, the practice nurse will consult with a GP in the practice. Antibiotics will be administered as per the Drug Administration Protocol (see Partner Notification Study protocol). Practices will be provided with pregnancy test kits free of charge.
- 11.4 Each practice will be supplied with the antibiotics required as per the Drug Administration Protocol free of charge. Drugs will be delivered to the practice in advance of their start date along with an Antibiotic Therapy Log Book (Appendix 24) to be used as a Stock Register and a record of antibiotic therapy administration. In each practice, drug supplies will be kept in a locked cabinet and a written record of doses dispensed maintained.
- 11.5 Each practice will be provided with a Receipt Book, Lockable Cash Box and a £100 petty cash “float” to be used to reimburse patients’ travelling expenses.

12 PRECISION OF PREVALENCE ESTIMATES

12.1 Prevalence Estimates

- 12.1.1 We estimate that the prevalence of chlamydial infection will be between 4% and 6% in the younger age group and 0.5% to 2% in the older age group. Separate estimates will be calculated for women and men.
- 12.2 The precision of estimates will depend on the number of men and women participating, and on the prevalence found. We anticipate that response rates will be higher among women such that the study population will comprise 60% women and 40% men.

12.3 The clustered nature of the data from practices covering different populations will also influence precision. Large intracluster correlation coefficients (ICC) would lead to inflated confidence intervals. The sample size in each cluster (GP surgery) is relatively large (approximately 300 women and 200 men) and potentially important design effects are therefore possible. The intracluster correlation coefficient is unknown. Based on a recent survey of self-reported hip pain in 40 general practices in Avon and Somerset we assumed ICCs of 0.001 and 0.002. These result in design factors of 1.14 and 1.26 for women and 1.10 and 1.18 for men.

Table 1 shows binomial 95% confidence intervals for different prevalences and ICCs. These calculations indicate that acceptable precision will be achieved.

Table 1: Precision of hypothetical prevalence estimates at differing intraclass correlation coefficients

ICC	Prevalence (%)	95% Confidence intervals		Prevalence (%)	95% Confidence intervals	
		16-25 years Women (assuming n=4000)	Men (assuming n= 2666)		26-39 years Women (assuming n=2000)	Men (assuming n=1333)
0.001	4	3.31 - 4.69	3.18 – 4.82	0.5	0.15– 0.85	0.07 – 0.93
0.002	4	3.23– 4.77	3.12 – 4.88	0.5	0.11– 0.89	0.04 – 0.96
0.001	6	5.16– 6.84	5.00 – 6.99	2	1.30– 2.70	1.18 – 2.82
0.002	6	5.07– 6.93	4.94 – 7.06	2	1.23– 2.77	1.12 – 2.88

ICC intraclass correlation coefficient. Binomial confidence intervals are shown.

13 STATISTICAL ANALYSIS

13.1 Statistical Procedures

13.2 The statistical package Stata (version 6.0, College Station, Texas, USA) will be used.

13.3 Methods for survey data analysis will be employed to produce estimates of the prevalence of chlamydial infections. Design effects associated with the cluster nature of the data will be computed. Estimates for *a priori* specified subgroups (lower socio-economic status, young age and ethnic minority

group) will be obtained. Logistic regression for survey data will be performed for exploratory analyses.

14 Amendments to protocol following HTA monitoring meeting

The following amendments have been made to the Prevalence Survey Protocol as a result of discussions at the HTA monitoring meeting 2nd October 2001 and in the light of preliminary survey data. (see appendix 38 for more detailed explanation about the rationale for these changes)

The reason for these changes relates to several issues.

1. Improving the response rate and consequent external validity of the prevalence survey.
2. Increasing the absolute numbers of Chlamydia positive subjects available to feed into the other components of ClaSS.
3. Assessing Primary Care consultation rates of all subjects sampled in ClaSS to inform comparisons of systematic register based screening with an opportunistic approach and to clarify the wider issue of “ghost” patients on GP lists. Finally, results of comparisons of different approaches to follow-up of non-responders became available
4. Evidence about the impact of sensitive questions in the prevalence questionnaire on response rates

14.1 Improving response rate

The use of incentives

In order to encourage participation, subjects will be offered a £10 voucher and participation in a ‘draw’ if they return a sample. Respondents may opt to have the £10 donated to charity instead on their behalf. Whether or not the offer of a financial incentive improves the response rate will be tested by randomly selecting people to receive the incentive in one practice. However the results will not be available soon enough to inform the procedures used in the other practices, therefore vouchers will be offered to all respondents in these practices.

Flagging of non-responders

In each study practice once “non-responders” have been identified (see definitions) their notes will be “flagged”. Practices will be provided with a list of non-responders by the study centre, a supply of paper flags (appendix) and pre-paid return envelopes. ClaSS practices use a range of systems for keeping medical records (see table below). In practices using paper records the flag will be stapled to the outer cover of the notes of all non-responders. In paperless practices a computer flag will be generated according to the capability of the particular practice system. A supply of paper flags will be kept in each consulting room. Practices using both paper and electronic systems will flag both. Any non-

responder visiting the practice for any reason, identified by their flag, will be given a study leaflet (appendix 11a) and invited to participate in ClaSS. If they agree the “tear off” portion of the flag (appendix) covering current identifier and contact details along with preferred pack delivery time will be completed, torn off and sent by the health professional to the local study centre in a pre-paid envelope. The ‘flag’ will also allow the possibility that the patient was invited and declined to participate. On receipt of cards the study centre will send a study pack to the relevant contact address. Subjects responding will flow through the study as per the normal protocol. Subjects not responding after three weeks will be sent a reminder letter encouraging their participation. No further follow up will be attempted. The flagging scheme will be discontinued at the end of August 2002.

14.2 Follow-up of non-responders other than flagging

In addition to the flagging system described above, non-responders are followed up postally, and by telephone – where telephone details are available. See section 7. Letters are sent by standard delivery postage (since the contact details of non-responders are confirmed as correct).

Following the sending of reminder letters, three attempts at telephone contact are made (for subjects where telephone contact details are available), of which one is made at a time outside normal working hours (i.e. 0800-1800 Monday to Friday). If any of the above follow-up systems results in response the other systems are discontinued. Similarly if an explicit refusal is elicited attempts at follow up will stop. This is coordinated through the study centres in each site.

14.3 Increasing the absolute numbers of Chlamydia positive subjects

Analysis of data collected so far confirms that age is probably the most reliable risk marker for infection.

Prevalence % (95% CI) based on data available 21.10.01

Male 16-25	4.80 (2.77 , 7.69)
Male 26-39	0.68 (0.02 , 3.73)
Female 16-25	6.07 (4.13 , 8.56)
Female 26-39	0.93 (0.11 , 3.30)

Inspection of the distribution of results by age appears to confirm that 25 is the point of inflection. In light of this two changes will be adopted

1. The sample frame will be restricted to subjects aged 16-25 in subsequent survey practices.
2. The sampling fraction will be increased to sample one subject per household within this age group.

This will involve an absolute increase in size of sampling frame along with a focus on the population with higher Chlamydia prevalence. The precise increase

in numbers of positives that will result is impossible to determine accurately (it depends on response rate, prevalence and household structure of participating practices). Assuming a response of 24% (of total sample including ghosts), a prevalence of 5.5% and a household structure that means the number of households is 66% of the number of individuals within a given age-group this approach should provide an extra 366 respondents and an extra 66 positive subjects. This, along with case finding discussed elsewhere, will be adequate to drive the other components of ClaSS.

14.4 Assessing consultation rates of subjects sampled in ClaSS

Knowledge of consultation rates amongst study subjects is crucial to considerations around the comparison of systematic and opportunistic approaches to screening. Published data regarding service use in this age group are limited. It is also important to clarify the proportion of subjects classified as “ghosts” (not resident at their registered address at the time point of the prevalence survey) who are nevertheless still using the practice for Primary Care services. Chlamydia positive cases, and negative controls in the case-control study are already asked about their use of Primary Care services.

The level and means of recording consultations varies in the different study practices, but most practices record all consultations with both doctors and practice nurses on their computers. Six months following the date when packs were first sent out to patients in that practice, those practices which record all consultations with at least their doctors (many record nurse consultations as well) on computer will be asked to provide additional information on service use by all subjects in the sample frame. This information will consist of date of last attendance at the practice prior to the time point of the prevalence survey and date of last attendance at the practice. Reason for attendance or any other sensitive information will not be recorded. The practice will be issued with a list of subjects identified by name, date of birth and practice details (appendix 35), they will complete this form and return to the study centre following removal of names. ‘Attendance’ will be taken to mean a consultation in person or by telephone with any member of the primary health care team. The data collection form will record whether the consultation was with a doctor, a nurse, or ‘other’. Computer records relating to letters or results received about a patient do not count as a consultation.

14.5 Changes to the prevalence questionnaire

From experience in the first four practices it became clear that the inclusion of sensitive questions in the prevalence questionnaire had no significant impact on response rates compared with a shorter questionnaire (22.4% v 24.7% response for long and short versions). Therefore the prevalence questionnaire was modified to include questions on whether the patient had ever had sex and the number of sexual partners in the previous year.

14.6 Validation of the courier delivery status

In the first four practices, extensive attempts were made to verify the delivery status of each individual sampled by telephone calls and home visits. In the remaining practices, a smaller sub-sample will be intensively followed up in order to validate the delivery status recorded by the couriers.

A random sample will be taken of 5% of all those in each practice who were invited to participate in the study. Attempts will be made to validate the delivery status of this sub-sample of patients.

Each patient will be telephoned, if a telephone number is available from the courier, the practice, or the telephone directory (those who have received a pack and not responded will have been telephoned already as part of the reminder process). At least 3 telephone calls will be attempted with at least one being after 6pm or at a weekend.

Where no telephone contact is made, each patient will be visited at home up to 3 times, with one visit being made after 6pm or at a weekend. The home visit will follow the visit protocol appendix 23.

People in the 5% sub-sample will not be followed up by telephone or home visited if:

- They have returned a sample or a non-participation form or have indicated by telephone that they do not wish to participate.
- Those in whom telephone contact was made successfully as part of the reminder process.

Follow-up by telephone and (if necessary) home visit will be made for those:

- Who have received a pack, but not responded, and have not been contacted by telephone as part of the reminder process
- Those the courier could not deliver to i.e. ghosts (including address not found, gone away, not known, address incomplete, boarded up, knocked down, deceased), non-receivers and refusers (those who did not accept the pack from the courier).

Where there are discrepancies between the response coded from the courier sheet and further information obtained by the research team (via telephone reminders or validation visits), appendix 39 describes how people will ultimately be classified.

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14.7 Classification of ghosts and non-responders.

Appendix 33 defines those who are considered to be a participant, a refuser, a non-responder, or a ghost.

People who have been positively confirmed as not being at their registered address are treated as ghosts, and removed from the denominator in calculating response rates (but see appendix 33 for more detailed definitions). For the purposes of this study, people who could not be contacted after repeated home visits (by the research team in the first four practices and by the courier in later practices) are also treated as ghosts. However sensitivity analysis will be conducted to assess the impact on the response rate of treating the latter group

as ghosts (i.e. removed from the denominator) or as non-responders (included in the denominator)

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