Opportunistic screening for genital chlamydial infection. II: Prevalence among healthcare attenders, outcome, and evaluation of positive cases


Objective: To determine the prevalence and treatment outcomes among young women screened opportunistically for genital Chlamydia trachomatis and to evaluate the impact of screening in those participating.

Design: An opportunistic screening programme (1 September 1999 to 31 August 2000) using urine samples, tested by ligase chain reaction (LCR). In-depth interviews were used for programme evaluation.

Setting: Screening was offered in two health authorities at general practice, family planning, genitourinary medicine (GUM), adolescent sexual health, termination of pregnancy clinics and women’s services in hospitals (antenatal, colposcopy, gynaecology and infertility clinics).

Main participants: Sexually active women (16–24 years) attending for any reason.

Main outcome measures: Screening data: prevalence of infection by age and healthcare setting; proportion of positive patients attending for treatment. Evaluation data: participants’ attitudes and views towards screening and follow-up.

Results: In total, 16,930 women (16–24 years) were screened. Prevalence was higher in younger women (16–20) than those aged 21–24 years and was highly variable at different healthcare settings (range 3.4%–17.6%). Prevalence was approximately 9% in general practice. The role of the project health advisers in managing results and coordinating treatment of positive individuals was essential; the vast majority of all positives were known to be treated. Women felt that screening was beneficial. Improving awareness and education about sexually transmitted infections is required to alleviate negative reactions associated with testing positive for infection.

Conclusions: Prevalence of infection outside GUM clinics is substantial and opportunistic screening using urine samples is an acceptable method of reaching individuals with infection who do not normally present at specialist clinics.

 METHODS

A full description of the methodology used has been previously reported. In summary, an opportunistic screening programme was undertaken in two health authorities (HAs), Portsmouth and South East Hants and the Wirral as in existence before April 2002, for 1 year (1 September 1999 to 31 August 2000). Urine screening was offered mainly to sexually active women aged 16–24 years at participating healthcare settings (191 sites in total), including general practices (GP), family planning clinics (FPC), GUM, adolescent sexual health, termination of pregnancy and women's services in hospitals (antenatal, colposcopy, gynaecology and infertility clinics). Repeat attenders were eligible for another test on changing their sexual partner. Screening was offered to eligible attendees irrespective of their reason for attendance and the offer of screening was recorded whether or not the test was accepted. The presence of symptoms (pelvic pain, irregular bleeding, discharge, or cystitis) was recorded at each attendance. Specimens were tested using the ligase chain reaction (LCR, Abbott LCx) and all positive tests were confirmed by repeat LCR using the same urine specimen. PCR (Roche Cobas) was used as arbiter for discrepant LCR results. Participants were subject to external quality assessment at three points during the study to ensure the quality and validity of testing. In each site, project research nurses (PRNs) based at a local coordinating office were responsible for informing all participants of their results by letter or phone. In the Wirral, the PRNs were trained community health advisers and their office was located in a community hospital, 4 miles from the local GUM clinic. In Portsmouth, the office was situated within the same building as the local GUM clinic and adjacent to the main FPC. The PRNs discussed implications of test results...
with participants and advised participants with positive results to attend the local GUM clinic for treatment, partner notification and further management. Alternative options for treatment (either at the coordinating office or at the original site of testing) were also presented; in these cases, the PRNs were also responsible for partner notification. For positive participants, data were sought on the reported number of partners during the past 3 months and where partners attended for treatment. To standardise results, data on treatment and partner notification were censored at 3 months from the original date of screening. In Portsmouth, screening was limited for logistical reasons to five specimens/day in each general practice during October 1999 and in FPCs between September and November 1999.

Quantitative data management and analysis
All results focus on the main target group of women aged between 16 and 24 years. To allow patient-based analyses, episodes belonging to the same participant were matched, based on their identifying details (NHS number, name, date of birth, postcode); full details of the methodology used have been previously described. Population size was determined using mid-1999 population data from the Office for National Statistics and estimates of the proportion of women who were sexually active were calculated using data from the second National Survey of Sexual Attitudes and Lifestyles (NATSAL 2000). The term “community screened/treated” refers to those screened or treated in any setting excluding GUM or where the healthcare setting was unspecified. No formal comparisons have been made between health authorities because geographic differences were confounded with differences in study methodology. In Portsmouth, all participating GPs started screening at the beginning of the survey, whereas in Wirral, GPs were phased in over 6 months. In addition, service provision and the age distribution of the sexually active 16–24 year old female population was different between health authorities. In Portsmouth, there was a higher proportion of older women (aged 20–24 years) in the target group than in Wirral (62% compared to 56%). The study design was dynamic; participants were recruited as they attended different healthcare settings and the probability that a participant was recruited by a setting depended on the order that they visited settings, service provision, area study methodology, and the participant characteristics. Prevalence and 95% confidence limits are therefore reported unadjusted. Prevalence estimates use one test result for each participant; participants with multiple tests where at least one result was positive, were taken as positive. All data were analysed using STATA version 7.0. Logistic regression was used to provide adjusted odds ratios using first tests only to account for the multiple attendances.

Qualitative data collection and analysis
In-depth interviews were used to determine the views of those screened; full methodologies used in patient selection and analysis have been previously described.

RESULTS
Screening data
Characteristics of participants
During the 1 year screening period, 11 999 women in the target age range were screened in Portsmouth and 4931 women in Wirral (see table 1). Those screened were predominantly of white ethnicity in both sites (>97%), reflecting the resident populations.

Prevalence of infection at healthcare settings
In women, the overall prevalence of infection in those screened was 9.8% (95% CI 9.3 to 10.3) in Portsmouth and was 11.2% (10.3 to 12.1) in Wirral. This varied by age and was higher in those aged less than 20 years old (see fig 1); peak prevalence was seen in 18 year old women in Portsmouth (13.0%; 11.4 to 14.8) and 20 year olds in Wirral (13.6%; 11.0 to 16.7). Prevalence decreased rapidly with age and was lowest in the oldest participants (24 years); 6.8% (5.4 to 8.4) in Portsmouth and 7.2% (5.1 to 9.7) in Wirral. Table 2 indicates the prevalence of infection in women screened at specific healthcare settings. The reported prevalence of infection in women within each healthcare setting was not significantly different between the two HAs. In both HAs, prevalence was highest in those attending GUM clinics (13.4% and 17.6% in Portsmouth and Wirral), TOP clinics (14.0% and 13.3%), and youth clinics (16.7% and 12.7% respectively). Prevalence at general practice and FPCs was respectively 8.5% and 9.8% in Portsmouth, and 8.7% and 10.1% in Wirral.

In Portsmouth, 62% of positive episodes from women were recorded as asymptomatic compared to 53% in Wirral (p<0.001). After adjusting for age and healthcare setting using logistic regression analysing first tests only, prevalence of infection was 25% higher among symptomatic women than non-symptomatic women (OR 1.25; 95% CI 1.09 to 1.43) in Portsmouth and 35% higher among symptomatic women (OR 1.35; 1.11 to 1.65) in Wirral. The prevalence of infection in first accepted episodes from women (16–24 years) at defined healthcare settings depending on whether screening could be described as diagnostic testing or truly opportunistic screening are given in table 3. Episodes are grouped as follows:

(1) Those who either reported symptoms of chlamydial infection and attended for this reason or attended for GUM screening ("diagnostic")

(2) Those who attended for another reason but reported symptoms on the form ("opportunistic screening" as would not normally be tested)

(3) Those who were asymptomatic ("opportunistic screening").

Overall, prevalence tends to be higher in those reporting and attending with symptoms (group 1) than those screened opportunistically (groups 2 and 3). Although prevalence of infection is lower in those screened opportunistically, there is still a substantial burden of infection among these women. In general practice, prevalence was significantly higher at both sites in those tested for diagnostic reasons (group 1) compared to those who were asymptomatic (group 3).

In Portsmouth, 92% of women in the target age group (11 043/11 999) were screened only once during the study period; this was similar in Wirral at 91% (4495/4931).
Prevalence among women who had one test only was 8.3% (7.8 to 8.9) in Portsmouth and 9.2% (8.4 to 10.1) in Wirral. Of those who had multiple tests, prevalence was significantly higher at 26.6% (23.9 to 29.5) in Portsmouth and 30.5% (26.4 to 34.8) in Wirral.

Effect of limiting healthcare settings where the screened programme was offered

Table 4 illustrates the proportion of positives that potentially could have been detected if screening had only been undertaken at single healthcare settings during the programme. We have derived the total number of positives among the population attending each setting by adding to those screened and found positive at the setting all positives who were detected through screening elsewhere during the study but who also attended the setting in question. In Portsmouth, over 60% of all positive women could have been detected by screening at general practice only. FPCs were also an important setting in Portsmouth; potentially, 47% could have been detected by screening only at this setting. Despite the phased introduction of general practice to the programme in Wirral, this setting remained the main site for screening; 30% of infections would have been detected by only screening here. Table 4 also shows the prevalence of infection among these populations and demonstrates that period prevalence estimates based only on those tested at specific settings (table 2) underestimates the true prevalence of infection of those attending healthcare settings.
Management of positives: treatment outcomes and partner notification

As some women had multiple positive results, this section refers to results from screen positive episodes not positive women. In Portsmouth, 98% of positive female episodes of infection were known to be treated and 92% in Wirral. The PRNs gave pretreatment advice and counselling to 59% of positive women in Portsmouth (67% of community screen positives and 5% of GUM screen positive episodes). This was similar in Wirral, where advice was given to 59% of positive episodes from women (71% of community screen positive and 2% of GUM screen positive episodes). Table 5 outlines the treatment outcomes for women (16–24 years) at both HAs depending on whether they were initially screened at the local GUM clinic or in the community. In both Portsmouth and Wirral, over 98% of positive women screened at the GUM clinic were also treated there. In Portsmouth, 84% of community screened positives received treatment at the GUM clinic, whereas only 25% of community screened women were treated at the GUM clinic in Wirral. The PRNs in Wirral treated the majority (61%) of community screened positive women at the coordinating office, whereas in Portsmouth the PRNs saw the majority of positive women in their office and then took them to the GUM clinic in the same building for treatment. A minority of women were treated in Portsmouth by the PRNs in their office (1%). In both HAs, approximately 15% of community screened positives were treated at a community setting; this was usually the site where screening had initially taken place.

No information was available on the number of partners from 5% of positive episodes in women from Portsmouth and 16% in Wirral. In Portsmouth, 52% of partners reported by women were verified as having been treated and this was significantly lower in Wirral, where 41% of partners from women were treated. However, it should be noted that not all reported partners were traceable as names or contact details could not be given. Prevalence of infection in partners of positive women was 47.3% (331/628) in Portsmouth and 42.7% (38/89) in Wirral.

Evaluation data

Expectation and management of results

All respondents interviewed had unprotected sex with one or more partners but took the test expecting a negative result. Contrary to expectations, some participants were positive and they were shocked at this (see quote 1 in box). Few women realised that referral to GUM for treatment would involve a full sexual health screen and partner notification and this made some women anxious about attending GUM clinics (quotes 2 and 3). All respondents receiving treatment in GUM clinics accepted full sexual health screening, believing it to be in their best interest because of a high likelihood of concurrent STIs. When questioned, however, women did not recall information or names of infections for which they had been tested. None the less, although the stigma associated with STIs also gave rise to concerns about accessing treatment, others felt GUM clinics offered anonymity and flexibility (quote 4). Women’s responses to their experience at GUM clinics were often bound up with their feelings about having an STI and, consequentially, there was little consistency of response to the quality of care received.

Partner notification

Respondents were not always clear about the mechanics of partner notification—that is, whether they could notify ex-partners themselves or leave contact to GUM clinics. Women created a distinction between current and past partners and expressed reluctance to contact former partners themselves. Most women had told their current partner that they had been screened and felt obliged to inform them of their result, despite being concerned about partner response (quote 5). Common responses to a positive test result included feeling dirty, ashamed at passing on the infection, and suspicion about where the infection had originated. For some, this led to tension and suspicion within relationships but no repercussions within relationships resulted (quote 6). However, most said their partner had been understanding and rational.

Table 5  Management of positive women (16–24 years): treatment outcomes

<table>
<thead>
<tr>
<th>Setting</th>
<th>Positive episodes in women (16–24 years)*</th>
<th>Total screened at setting (% total)</th>
<th>Total untreated (% total)</th>
<th>Treated at GUM (% total treated)</th>
<th>Treated at other community setting (% total treated)</th>
<th>Treated by PRNs (% total treated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portsmouth (GUM screened)</td>
<td>167</td>
<td>16 (8.0%)</td>
<td>151 (91.8%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Wirral (GUM screened)</td>
<td>104</td>
<td>1 (0.9%)</td>
<td>103 (98.1%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Portsmouth (community screened)</td>
<td>1052</td>
<td>16 (1.5%)</td>
<td>866 (98.5%)</td>
<td>10 (1.0%)</td>
<td>158 (15.3%)</td>
<td>0</td>
</tr>
<tr>
<td>Wirral (community screened)†</td>
<td>447</td>
<td>16 (9.2%)</td>
<td>101 (24.9%)</td>
<td>101 (24.9%)</td>
<td>57 (14.0%)</td>
<td>101 (24.9%)</td>
</tr>
</tbody>
</table>

*As some women had more than one positive test, data are presented for each positive episode.
†Excludes those treated where health setting was unspecified in Wirral.
Impact of screening
It is difficult to judge the impact that screening might have on long term behaviour. Several women said the experience of screening had been thought provoking, heightened their awareness of chlamydia, and the need to practise safer sex. They were also aware that they needed to be screened if they changed sexual partner. Overall, women generally felt screening was beneficial and believed it was important for people to be screened and treated (if infected) to protect both their own sexual health and fertility, and to prevent the spread of disease to others.

DISCUSSION
This is the first time an opportunistic screening programme has been piloted on a large scale in England. As such, it forms the largest survey of Chlamydia trachomatis prevalence carried out in England to date, giving estimates of the prevalence of infection of attendees at a range of healthcare settings using the same inclusion criteria and testing methodology. Prevalence estimates from different healthcare settings are broadly commensurate with other studies,14 trending towards the higher end of reported ranges. This is expected, given the relatively young age group screened (16–24 years) and the use of a highly sensitive test. The ligase chain reaction on urine is known to identify 20% more infections than one enzyme immunoassay (Chlamydiazyme) on endocervical swabs,15 which is the most commonly used test/specimen combination in PHLS laboratories.16 Given the similarity in prevalence estimates within healthcare settings in the two areas taking part in this study, it is likely that equivalent prevalence would be found elsewhere in the country in comparable healthcare populations. The highest burden of infection was seen in the young sexually active population (< 20 years) and prevalence declined in older women. However, there was still a major burden of infection in 20–24 year old women at over 6%. Macmillian et al reported similar prevalence and decreasing trend with age, where infection levels only dramatically decreased in women aged 30 and above.16 This suggests that the upper age limit for screening in this study, as proposed by the chief medical officer’s expert advisory group on C trachomatis and thus likely to be used in a national programme, needs to be reviewed. Bias due to the self selection of cases will influence the prevalence seen; however, uptake of testing was universally high among all age groups and healthcare settings. Crude prevalence in Wirral is higher than Portsmouth; this is expected given that 44% of the sexually active 16–24 year old female population are aged 20 years or less compared to 38% in Portsmouth. In addition, the phased introduction of GPs to the programme in Wirral meant that those who would only access health care via general practice were less likely to be recruited.

This screening programme was targeted at women attending healthcare settings for any reason. Although a proportion of women (13% of all accepted first tests in Portsmouth and 11% in Wirral) were known to be screened for diagnostic reasons, it is likely that more symptomatic women were tested than would have been if the programme was not in place. The results of this study demonstrate the significant population burden of this infection; 90% of infections were diagnosed outside GUM in Portsmouth and 86% in Wirral. Analysis of the potential impact of limiting screening to single healthcare settings indicates that general practice is a key site for screening; although prevalence of infection was among the lowest of healthcare settings, service utilisation is by far the highest.11 Planning future screening initiatives will need to take into account the estimated prevalence of infection at healthcare settings, in addition to local service provision and service utilisation. As service utilisation varies with age, a range of services will be required to best reach the younger and older ends of the population. In addition, given the limited population level attendance rates at most healthcare settings, screening is only likely to achieve significant population coverage and reduce long term prevalence if it is offered widely using general practice as the key practice and if attendance at other settings is significantly increased.

Screening was regarded as constructive by participants in the programme, whereby they felt they were safeguarding their own sexual health. The views of participants were in keeping with similar studies,17 18 indicating that improvements in public awareness and greater education on STIs are necessary to help to alleviate perceived stigma and distress associated with positive results. Increased publicity generated by the screening programme aided normalisation of the topic of infection in the target group; this should be maintained and the role of GUM services needs to be actively promoted.

Clinical audits of non-GUM settings have previously highlighted problems associated with management of chlamydia positive patients, both within and between healthcare settings, where poor treatment rates, lack of referral to GUM, and low partner notification rates are commonly seen.19 20 Over 90% of positives were known to be treated during the programme, a significant achievement given the number of women screened. Further follow up of positives at the 3 month cut-off point used for results in this paper indicates that almost all positives did receive treatment. The extremely high levels of treatment suggested that this model of care (utilising coordinating PRNs to manage results and a collaborative, defined management plan between healthcare settings) is very effective in managing infection on a large scale. The majority of community screened positives received pretreatment counselling from the PRNs and it would appear that the actual site of treatment may be determined to some extent by the location of the PRNs. It should be noted that the partner notification rate was lower in Wirral where fewer positives were managed in the GUM clinic and the high prevalence of infection in partners reiterates the importance of effective partner notification to prevent re-infection and onward transmission.

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Although this study provides evidence of the feasibility and acceptability of a screening programme, little meaningful information can be gained on screening intervals, reinfection rates, or the effect of screening on the long-term outcomes and infection because of the study design. A prospective follow up study has now been implemented in the pilot sites to provide reliable estimates of chlamydia incidence and reinfection rates, which will be used to inform whether the proposed national screening programme should incorporate a recall component for groups at high risk of reinfection. Once a national programme has been implemented, further studies will be required to evaluate the effect on rates of pelvic inflammatory disease. Health professionals were financially remunerated in this study to offer testing and this may have influenced the uptake of testing. The extent to which financial inducements to professionals are sustainable in terms of a national programme remains to be seen.

In conclusion, this study has demonstrated that large scale opportunistic screening for genital chlamydial infection is achievable at a wide range of healthcare settings in England. Urine screening is acceptable to patients and professionals and the role of coordinating health advisers was vital in achieving successful treatment of positives, especially in those screened outside GUM. A national screening programme will be rolled out from 2002 and will require the infrastructure for managing large numbers of positives; however, this must be seen within the context of already overstretched GUM services.

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CONTRIBUTORS
JMP participated in protocol development, coordinated data management, and was the lead writer; MC developed the protocol, critical review of paper, and is the guarantor of the study in addition to JH (Wirral) and SR (Portsmouth); PAR participated in protocol development, undertook the statistical analysis of the uptake data (with assistance from JMP) and critical revision of paper; EP, NJ, and CC coordinated, implemented, conducted interviews, and analysed the qualitative study and paper preparation; JH and SR were lead local study coordinators and participated in protocol development, management and implementation of the study; HM, GH, and GU participated protocol development and were responsible for laboratory aspects and service provision; HM and GH were responsible for local data management; LM and TG organised patient coordination and follow up; VH, JT, and AG participated in protocol development and were responsible for GUM patient management along with Mary H earn (clinical research fellow) in GUM Wirral. All authors commented on the paper.

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Up to 19 different Chlamydia trachomatis (CT) serovars which are pathogenic predominantly for the urogenital tract and numerous CT variants have been identified. An increasing number of isolates are typed worldwide and provide a wealth of information on the epidemiology of CT infections, a sexually transmitted disease (STD) for which screening has been proposed. Recent studies have demonstrated an association between CT serovar G and squamous cell carcinoma. A possible shift in the serovar distribution over time in a region or country could reveal information on changes in the epidemiology of CT infections and could potentially have clinical implications.

We therefore determined the CT serovar distribution in a large STD population in Amsterdam in 2000–2002 and compared it together with all published serovar distributions since 1986 in the Netherlands to assess if serovar distribution shifts over time occurred.

Of people attending the STD outpatient clinic in Amsterdam from 2000–2002, those found CT positive (n = 407) by LCx (Abbott Laboratories, Chicago, IL, USA) were genotyped as described previously. This is the largest STD population typed to date in The Netherlands. The following serovar distribution was found: B = 1%; D = 12%; Da = 0.2%; D- = 1%; E = 33%; F = 23%; G = 4%; Ga = 9%; H = 8%; I = 6%; Ia = 1%; J = 3%; K = 2%.

Literature searches identified eight serovar distribution studies in the Netherlands, of which the first was performed in 1986. With the inclusion of the present study, 2204 serovars were available for analyses. In the serovar distributions comparison, we (1) did not distinguish between male and female participants, (2) did not distinguish between serovar distributions based on serotyping or genotyping techniques, (3) excluded serovars B/Ba because of the low numbers, (4) excluded double infections, (5) excluded variants, and (6) classified CT serovars in the three phylogenetically based serogroups: the B group (serovars D, Da, 49%), the intermediate serogroup (serovars F, G, Ga), and the C group (serovars I, Ia, J, IV, and K).

Results are shown in figure 1. In general, no statistically significant serovar distribution trends in time were observed between 1986 and 2002 when all studies were taken together. Of the nine studies, 1 and 6 represent serovar distributions from STD populations in Rotterdam and show no significant changes in general or over time (mean: C group: 30%; Int group: 21%; B group: 49%). Studies 2, 3, 4, and 9 represent serovar distributions from STD populations in Amsterdam and show no significant changes (mean: C group: 20%; Int group: 31%; B group: 49%). Studies 5, 7, and 8 represent serovar distributions from mixed symptomatic and asymptomatic infected people (5 and 7) and asymptatically infected populations in Amsterdam. They show no significant changes in general, over time, or compared to the Amsterdam STD based serovar distribution (C group: 17%; Int group: 30%; B group: 53%).

However, when the two geographically derived serovar distributions were compared to each other, (1) serogroup C was found more frequently in Rotterdam: 30 v 20%, p = 0.0001; most prominent serovar difference was serovar K (10.6 v 3.2%, p = 0.0001; OR 1.6 (95% CI: 1.2 to 2.3)), the most prominent serovar difference was serovar K (10.6 v 3.2%, p = 0.0001; OR 1.6 (95% CI: 1.2 to 2.3)); (2) the intermediate serogroup was found less frequently in Rotterdam: 21 v 31% (p = 0.0002; OR 1.6 (95% CI: 1.2 to 2.0)), the most prominent serovar difference was serovar F (15 v 22%, p = 0.0018; OR 1.6 (95% CI: 1.2 to 2.1)), and serogroup B was stable (49 v 50%).

In conclusion, no changes in serovar distribution differences were found over time in the Netherlands in general or within the two different geographic areas. However, the Rotterdam population differed significantly from the Amsterdam populations in having a larger incidence of C group serovars and a lower incidence of the intermediate group serovars, albeit an identical B group serovar distribution. The findings could be the result of different ethnic compositions of the studied cohorts or other confounding factors between Rotterdam and Amsterdam, a subject that warrants further study.
Surveillance of sexually transmitted infections in primary care

Surveillance for sexually transmitted infections must respond to increases in the provision of sexual health services outside genitourinary clinics. First, prevalence surveys will not measure actual diagnostic activity in primary care and other clinical settings. This is essential for determining whether proposals from the National Strategy for Sexual Health are being implemented effectively. Secondly, periodic surveys in different areas could not readily identify outbreaks. In the Bristol area, for example, most cases in an ongoing outbreak of sexually transmitted hepatitis B infection have presented to general practitioners. Although genitourinary medicine clinics are the main setting for detecting outbreaks their impact in primary care should be monitored. Thirdly, the validity of panel surveys will depend on a high response rate and postal invitations often have low uptake. A single system cannot fulfill all the requirements for infectious disease surveillance. Laboratory reporting remains incomplete and demographic and socioeconomic characteristics are over time. Automating regular data downloads and reporting will improve the timeliness of data collection to facilitate identification and monitoring of outbreaks. The wide coverage of the system can guide local service development and clinical practice and monitor the impact of the Sexual Health Strategy. For example, in 2001 half of all chlamydia tests and 44% of positive results came from GP, family planning, or Brook clinics. Nearly two thirds (62%) of those tested in general practice were over 25 years old in whom the positivity rate was 4% compared with 11% for under 25 year olds.

We propose that, while behavioural data obtained from panel surveys in primary care provide depth, sentinel surveillance of laboratory diagnosed infections in all clinical settings provides breadth, and both are needed for effective surveillance.

References

Comparison of the serological response to treatment of early syphilis in HIV positive versus HIV negative individuals

The effectiveness of treatment for syphilis is evaluated by demonstrating declining titres of the non-treponemal antibody tests—for example, the rapid plasma reagin (RPR). The serological response in HIV co-infected individuals has been the subject of debate, with some studies reporting a similar serological response and others a delayed response in HIV positive patients.

A resurgence of infectious syphilis has occurred in Manchester, United Kingdom, in recent years. From January 1999 to August 2002, 379 cases of early syphilis were
reported and 28% were HIV co-infected (CDSC North West, personal communication). North Manchester General Hospital (NMGH) houses one of the city’s three genitourinary medicine clinics and the regional infectious diseases unit, providing care for approximately 1000 HIV positive individuals. Our aim was to evaluate the serological response to treatment for early syphilis in HIV positive and negative individuals treated at NMGH.

Between January 1999 and March 2002, 75 men (72 homosexual) and three women were diagnosed with early syphilis. Of the 78, 40/75 men were HIV positive. The RPR results 3, 6, and 12 months following treatment for early syphilis were collected by retrospective case note review. Exclusion criteria were syphilis re-infection during the study period (two patients), HIV status undetermined (six patients declined HIV testing), or lost to follow up (16 patients). Patients were divided into two groups—HIV positive and HIV negative individuals. From the sequential RPR results 3, 6, and 12 months following treatment the mean reduction in RPR titre in each group at these points was calculated, and statistical comparison made between the two groups using the Student’s t test.

The results are shown in table 1. We found no significant difference in the reduction of RPR titre in the year following treatment between the HIV positive and negative groups.

Of the 31 HIV positive individuals in this study, 17 were taking highly active antiretroviral therapy at the time their syphilis was diagnosed. The average CD4 lymphocyte count in this group was 460×10⁹/L (range 33–1000) and viral load 83 515 copies/ml (range <50–1 2 million).

Limitations of the study are that it was retrospective, patients in the HIV positive and negative groups were not matched individually for variables such as stage of syphilis or initial RPR titre, and the treatment regimens varied (with at least 10 days intramuscular procaine penicillin or 14 days oral doxycycline, and HIV positive patients prolonging courses of treatment in accordance with the UK national guidelines for the treatment of early syphilis). No account was taken of the patient’s CD4 lymphocyte count, or whether they were receiving antiretroviral therapy. However, the cohort represents a diverse group of HIV positive individuals and we consider them representative of those generally encountered in clinical practice.

We demonstrated that in clinical practice the RPR remains a valid way of assessing the response to treatment of syphilis in those co-infected with HIV. Larger prospective studies, with cases and controls matched for variables such as the stage of syphilis at diagnosis, the

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Mean drop in RPR</th>
<th>Mean drop in RPR</th>
</tr>
</thead>
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<tr>
<td>HIV positive</td>
<td>31</td>
<td>1.71</td>
</tr>
<tr>
<td>HIV negative</td>
<td>23</td>
<td>1.57</td>
</tr>
<tr>
<td>p Value (t test)</td>
<td>0.78</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Is it time to rethink the roles of health professionals in the HIV outpatient setting?

HIV outpatient services across the United Kingdom are seeing large increases in their patient workload. This is fuelled by the success of highly active antiretroviral therapy (HAART), resulting in fewer deaths, and by increases in the number of new diagnoses. A further rise is anticipated in England following implementation of “The national strategy for sexual health and HIV” that plans to increase HIV testing dramatically in order to reduce the number of undiagnosed HIV infections by 50% by the end of 2007. The success of HAART has also changed the focus of many doctors’ patient consultations from prophylaxis and management of opportunistic infections, to issues related to the complexities of HAART, sexual behaviour risk reduction and promoting healthy lifestyles. As a result, HIV service providers need to develop new models of care that can deliver high quality, cost effective care to meet these changing demands. We reviewed the role of the doctor in providing routine outpatient HIV care.

Data were collected prospectively on all HIV infected patients attending for routine care between 24 June 2002 and 17 July 2002. We obtained complete data for 431 of 433 consecutive patient appointments. Of these, 79/431 (18%) did not attend their appointment. Of the remaining 352, the median age was 38 years (range 17–70), the majority were male (291, 83%), of white ethnicity (251, 71%) with a median CD4 count of 350×10⁹/L (range 10–1390) and viral load (VL) of 500 copies/ml (range <50–12 million).

Consultants saw two thirds of attendees, specialist registrars a third. Almost half the consultations (173/352) were with patients who were defined by their physician as being asymptomatic with respect to their HIV infection; 66/173 (38%) of these were not taking HIV therapy and 107/173 (62%) were on HAART with a sustained virological response (VL<50 for >6 months). Over the next 8 months, 53/66 (80%) of those not taking HAART and 68/107 (64%) taking HAART remained well with no significant changes to their health status. Of those on HAART, five required admission to hospital (bacterial pneumonia, three; cholecystitis, one; cryptococcal septicaemia, one), 12 made changes to their therapy (therapy interruption, four; virological rebound, three; toxicity, five) and 12 had intermittent low level viraemia (VL between 50 and 100). Other problems encountered in both groups included shingles (n=7) and raised liver function tests (n=11).

We have identified a high proportion of asymptomatic patients who are currently under regular review by medical staff and could potentially be managed by other healthcare professionals. Increased use of general practitioners and nurse practitioners are two potential options. We should review HIV outpatient service provision and move away from the “acute-terminal” model of care that has prevailed since the beginning of the epidemic and learn from chronic disease management models seen in other areas of the health service. As these new models are developed, in addition to staff requiring training to be conversant with common problems seen during routine monitoring of antiretroviral therapy, it is essential that evaluation is conducted to ensure similar levels of effectiveness, efficiency, and acceptability.

Contributors

SE and DM developed the study; SE, SD, and CG collected and analysed the data; SD and KM wrote the text. SE, DM, and CG provided comments on the text.

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Syphilis outbreak in Milan, Italy

Infectious syphilis has been considered a sensitive marker of risky sexual behaviour. Following a decline of syphilis in Western Europe, there has been a resurgence of infectious syphilis in many countries, with a number of outbreaks in men who have sex with men (MSM). The STD centre of Milan is the biggest in northern Italy with an average of about 6000 patients per year. All patients are offered screening tests for syphilis using treponemal particle agglutination test (TPPA) and rapid plasma reagin (RPR).

The number of cases of early syphilis (primary, secondary, and early latent asymptomatic with probable infection <12 months previously) has increased from 46 to 211 between 2000 and 2002. Over the same time the number of cases of late syphilis (asymptomatic with probable infection >12 months previously) have remained stable. Most cases of early syphilis in 2001 and 2002 (261/306, 85%) were in MSM. Fig 1 shows the trends.

As in other reports of recent syphilis outbreaks in MSM, a proportion of cases (25.8%) are in men with HIV. Of the 74 HIV positive men with early syphilis, 39 (53%) already knew their HIV status. This is an indication that our health promotion messages are not effective with this group at least. The fear of AIDS has declined in Italy: public campaigns are soft, HAART therapy has changed the appreciation of HIV infection for infect patients, and HIV is no longer considered a fatal condition.

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Online HIV/STI Chinese clinician training

The spread of HIV in China is accelerating and many Chinese physicians are poorly trained to address it. We review clinician training and the internet in China, and present the results of a convenience sampling of 136 Chinese clinicians regarding their access and attitudes towards computer based HIV/STI training.

Having been trained in an era of virtual STI eradication, many Chinese physicians are inadequately prepared to respond to the current HIV epidemic. Medical school curricula frequently lack STI coursework, and a European Union-China Project (EUCP) study in 2000 showed as few as 5% of physicians had ever received any HIV/STI training. Coinciding with the spread of HIV in China is the exponential growth of the internet and computer technology, reaching over 68 million internet users as of June 2003. These computer based resources can potentially serve as a powerful medium for the training of clinicians. To investigate this opportunity, we adapted Chinese language HIV/STI materials developed by the EUCP to create an online HIV/STI training page for the website of the Chinese National AIDS Prevention and Control Center (www.aids.net.cn). We then presented the site and distributed paper based surveys to 136 clinicians recruited during STI training courses in several urban areas.

The response rate was 97% (132/136). Among those sampled, 95% reported having had no HIV/AIDS training in medical school or in continuing medical education (CME). All 132 respondents reported a willingness to utilise computer based training.

This study found a surprisingly high level of computer and internet access among a convenience sample of STI specialists from several urban areas in China. The main limitation of this study was the non-representative sampling, which makes generalisation to other Chinese physicians difficult. Despite this, we believe that these results can be cautiously applied to significant numbers of urban Chinese clinicians who share similar levels of access and interest with this study population.

Online CME promises a promising way to take advantage of growing computer/internet access in China. Chinese physicians can already obtain many of their required CME credits online, with the largest site (www.cmechina.net) training over 50 000 users annually. Notably, HIV/AIDS training is not available. Other potential uses of computer/internet resources include creating training centres to serve as clearing houses for up to date training materials. Especially in those areas where extreme geographic barriers limit the scope of traditional training methods, the internet can help remote hospitals and physicians engage in distance learning.

As China strives to control a growing HIV epidemic with a limited budget, low cost/high output resources like computer/internet training cannot be overlooked. While further investigation is needed to show training efforts positively affect outcomes, the computer/internet revolution offers an immediate and cost effective opportunity to train many urban and some rural physicians. This study suggests that the technical access and clinician willingness necessary for such HIV/STI training may already exist.

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Treatment of vulval vestibulitis with a potent topical steroid

Vulval vestibulitis (vestibulodynia) is characterised by penetrative introital pain and erythema and tenderness localised to the vestibular glands. The aetiology is unknown and most treatment strategies are based on anecdote. Some clinicians recommend the use of a topical steroid but there are no published data to support this. We designed a randomised double blind crossover study to compare a potent topical steroid, Dermovate ointment (clobetasol propionate 0.05%), with a very mild steroid, 0.3% hydrocortisone ointment. The hydrocortisone acted as a placebo as it was impossible to obtain a matching placebo for Dermovate ointment. To demonstrate a 20% difference
between Dermovate and hydrocortisone treated episodes if the placebo effect was 40%, 110 patients were needed. Unfortunately, recruitment was slow and the study ended when the expiry date of the medications was reached.

This report describes the outcomes in the patients who participated. The ethics committee of Mount Vernon and Watford Hospitals NHS Trust approved the study; patients gave written informed consent. All patients had introital pain, tenderness, and erythema compatible with a diagnosis of vulval vestibulitis. The study comprised three phases:

1. emollients only for 2–8 weeks,
2. tube one of the study medication, applied to the vestibule each night for 28 nights,
3. tube two of medication used similarly.

The tubes were identical and the study was designed so that within blocks of 10 patients, half would use each medication first. The same clinician assessed each patient at 14 day intervals using a three point scale for each of the parameters—pain, tenderness, and erythema (maximum score 9; minimum score 0 for each visit). The scores obtained at entry (minimum 3) and after each phase were noted.

Twenty two patients were recruited, but some patients withdrew or were excluded for protocol violations. Fourteen patients completed all phases of the study and two completed the first two phases. After emollient use, nine patients had improved (mean score −1.1; range 0.5 to 2), after Dermovate, 11 improved (mean score −2.7; ranges −1.0 to −8); and after hydrocortisone nine improved (mean score −1.8; range 1 to −3) (table 1). Eight patients who used both treatments had a better response to Dermovate and four had a better response to hydrocortisone (p<0.07). Eight patients expressed a definite preference, seven for Dermovate and one for hydrocortisone. There may, however, have been an effect of the order of the treatments as two patients did better on their first treatment whereas nine did better on their second (p=0.06).

Although this study was not completed, some conclusions can be reached. Short term use of a potent topical steroid preparation did not produce a clinically important improvement in all cases but some patients had very good responses, which were maintained. This may reflect the fact that the aetiology of vulval vestibulitis is multifactorial and where may reflect the fact that the aetiology of vulval vestibulitis is multifactorial and where may, however, have been an effect of the placebo effect. A Zimbabwean man aged 47 was admitted to the Royal Sussex County Hospital, in August 2001 with lobar pneumonia. He had excellent response to the appropriate antiviral treatment and also baseline resistance test showed: M41L, V118I, M184V, T215F. He was commenced on combination antiretroviral therapy with combination of NNRTI and resulted in the subsequent rapid accumulation of NNRTI resistance.

Unexpected resistance in an African immigrant: lessons for the unwary

The number of people emigrating from Africa to the United Kingdom has been escalating. They contribute to the increasing number of heterosexuals with HIV in the United Kingdom. Increasingly, developing countries are improving their access to antiretroviral drugs through global funds for AIDS and other sources. It is well known that resistance to antiretrovirals develops where therapy is initiated without prior suppressive therapy or where such therapy is imperfect, and that such resistance is associated with poor outcome.

A Zimbabwean man aged 47 was admitted to the Royal Sussex County Hospital, in August 2001 with lobar pneumonia. He had excellent response to the appropriate antiviral treatment. The baseline CD4 count and viral load were consistent with advanced infection, 20×10³/μl (2%) and 134 000, respectively. He was then commenced on a salvage regimen of didanosine, tenofovir, enfuvirtide, and saquinavir and had a very good virological response with a viral load drop of 1350 (3.13 logs) in 4 weeks.

It remains uncertain whether in this case the individual had been aware of his HIV status. It is possible that antiretroviral medications may have been included as part of an unorthodox anti-tuberculosis regimen, given the high co-infection rate in Zimbabwe, without the individual having been informed. Alternatively, the individual may have been unwilling to disclose his status for fear of rejection of his legal claim to stay in the United Kingdom or for other sociocultural reasons.

Either way, the choice of initial therapy was inappropriate, given the underlying resistance to reverse transcriptase analogues, and resulted in the subsequent rapid accumulation of NNRTI resistance.

While it is known that acquired resistance mutations may disappear with time after discontinuation of therapy1 had a genotypic resistance test been performed at presentation in this case a more effective regimen would have been selected. Current BHIVA guidelines recommend resistance testing before therapy only in the context of demonstrable transmitted drug resistance.

As antiretroviral therapies become increasingly available in developing countries and while stigma regarding disclosure of HIV status for immigrants remains, we believe that similar cases will occur.

We strongly suggest that immigrants with a new HIV diagnosis should be closely questioned regarding previous drug and treatment, and also baseline resistance testing should be routinely considered.

References


Table 1 Treatment outcomes

<table>
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<tr>
<th></th>
<th>Dermovate Ointment</th>
<th>Hydrocortisone Ointment</th>
</tr>
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<tbody>
<tr>
<td>Improved</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Unchanged</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Worse</td>
<td>2</td>
<td>5</td>
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Increased uptake of HIV screening following introduction of “opt out” testing and results by telephone

Rogstad et al showed an increase both in the number of patients who were offered the HIV test and those who took the test following the use of a leaflet. We report the increased uptake rate of HIV testing since the introduction of “opt out” testing and giving results by phone. Before January 2002, patients attending our clinic were offered an HIV test if they belonged to high risk groups such as men who have sex with men or injecting drug users. Pretest counselling was done by our health advisers and patients were required to return to the clinic to receive their test results. In 2001, 904 of 2930 new and re-registered patients (31%) underwent HIV testing.

The UK government’s national strategy for sexual health and HIV set its target for reducing undiagnosed HIV in genitourinary medicine clinics by increasing the uptake of HIV testing to 40% by the end of 2004 and to 60% by the end of 2007.

From January 2002, we introduced an “opt out” system, whereby all patients were offered HIV tests, regardless of risk category. This led to an increase in HIV test uptake in the following 3 months to 37% (272 of 740 new patients), which is an increase of 44%.

This caused an increase in the workload of our health advisers, who were spending much time in pretest counselling low risk patients and giving negative HIV results. It became clear that exhaustive, in-depth pretest counselling was impractical and inappropriate when the majority of those tested were “low risk.” Accordingly, we decided that only high risk patients should be referred pretest to the health advisers.

It was also observed that some patients who initially agreed to undergo HIV testing changed their minds when they learned that they would be required to return to the clinic to collect their results. We decided to offer HIV results by telephone, in line with our policy for all other screening tests. High risk patients, however, were encouraged to attend in person for their result. In the next 3 months 44% (325 of 740 new patients) took HIV tests. Five patients tested HIV positive, but only one received the result by telephone.

The introduction of a telephone HIV results system enabled us to exceed the Department of Health target for 2004. The new system was adopted after consideration of the pros and cons in a departmental meeting in which the opinions of all staff were canvassed. Some concern was expressed about the potential for patients given bad news outside the clinical setting. We tried to minimize such outcomes by encouraging patients to telephone in the presence of their partner, a friend, or a relative. Results were only given by telephone when the patient could be seen in clinic on the following day at the latest.

The telephone results system is very popular. One patient said, he would far rather receive bad news in the familiar surroundings of home, with the support of his partner, than in a clinic. Why do it is psychologically harmful (or indeed beneficial) for patients to receive a positive HIV result by telephone; research is needed to answer this question.

The drive to reduce the number of people who are diagnosed HIV infected, and the demands of working life, we believe telephone results are here to stay.

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CD-ROM REVIEW

Topics in International Health: Sexually Transmitted Infections, 2nd ed

Institutional licence £120; individual licence £30; developing world licence £20. CD-ROMs are not Mac compatible. Disc adviser: Dr M Mahto, Department of Sexually Transmitted Diseases, Royal Free and University College London Medical School, UK, London.

Having previously resisted the temptation to upgrade from printed text to the 21st century, I was suitably impressed by both the technical design and the factual content of this 2nd edition CD-ROM. As a bit of a computer novice I found the software easy to install and navigate with helpful instructions at the touch of a button. The program itself runs on Windows 95, 98, 2000, NT4, or XP and needs 32MB of RAM with at least a 120 MHz Intel Pentium processor (or equivalent).

The CD-Rom provides a vast wealth of information on all aspects of common and tropical STIs that are presented in the form of 18 interactive tutorials, each reviewed by expert authors, and a collection of about 800 images. The material covers ranges from history taking and clinical examination to epidemiology, laboratory diagnosis, and syndromic management of STIs. It includes in-depth tutorials on individual STIs that provide up to date references on management useful both in the developing and developed world. HIV/AIDS is covered in a separate CD-ROM. However, there is detailed mention here of the CD-ROM. It is ambitiously designed for use as an educational resource in both developing and developed countries and I think it serves this purpose well. It appeal spans a broad range: medical students swatting for exams (and SpRs sitting Dip GUM), academic researchers as a useful point of reference and all healthcare professionals involved in direct clinical care of patients with STIs including nurses and health advisers.

Overall, the CD-ROM provides an interactive way of accessing and assimilating a huge amount of information on all aspects of STIs. It is definitely much more user friendly than lugging a huge textbook around and gets a big thumbs-up from me!

K P Prime

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Correction


The statistical calculation of this table combined all women, regardless of age. The authors have recalculated this table, and the revised version is available on the website (http://content.bmj.com/cgi/content/abstract/79/1/22/DC1/1 with the correct age restriction — female participants 16 to 24 years only, as originally specified. The majority of these data (general practice, family planning, and youth clinics) have only changed marginally; the main differences lie within the GUM clinics, due to the wider age of women tested at this setting. The conclusions, however, are unaffected by this error. The authors stand by their assertion that prevalence tends to be higher in those reporting and attending with symptoms than those screened opportunistically.

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