Analysis of *Chlamydia trachomatis* serovar distribution changes in the Netherlands (1986–2002)

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 serovars 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 2000–2 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 2000–2, those found CT positive (n = 407) by LCx (Abbott Laboratories, Chicago, IL, USA) were genotyped as described previously. This is the largest CT population typed to date in The Netherlands. The following serovar distribution was found: B = 1%; D = 12%; Da = 0.2%; Dv = 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 serovar B/Ia 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, Dv 1998, n = 305; 7, Morreé, 2000, n = 426; Morreé, 1998, n = 74; 9, Spaargaren, this study, n = 407). C = serogroup C (serovars H, I, Ia/I, J, Jv, K); Int = intermediate serogroup (serovars F, G, Ga); B = serogroup B (serovars D, Da, Dv, E).

Results are shown in figure 1. In general, no statistical 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 asymptptomatically 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) serovar C was found more frequently in Rotterdam: 30 v 19% (p = 0.0001; OR 1.6 (95% CI 1.4 to 2.3)), the most prominent serovar difference was serovar K (10.6 v 3.2%, p = 0.0001; OR 3.6 (95% CI 2.4 to 5.3)); (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 population 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.

**Key messages**

- No statistically significant serovar distribution shifts were observed between 1986 and 2002 in the Netherlands
- The type of cohort did not influence the analyses: STD based, asymptptomatically screened, mixed cohorts
- Geographical serovar distribution differences were observed between Rotterdam and Amsterdam but these were stable in time:
  - 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)
  - the Intermediate serogroup was found less frequently: 21 v 31%, p = 0.0002, most prominent serovar difference was serovar F (15 v 22%, p = 0.0018)
  - serogroup B was stable (49 v 50%)

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**Figure 1** Serovar distribution studies in the Netherlands from 1986 to 2002. The time of cohort collections is shown since the year of publication can be different from the year of cohort collection. Differences in serovar distributions in time were analysed. Each study is indicated by first author, year of publication, and number of isolates included: 1, Wagenvoort, 1998, n = 190; 2, vd Laar, 1999, n = 372; 3, Morreé, 1998, n = 90; 4, Ossewaarde, 1994, n = 289; 5, Lan, 1995, n = 51; 6, v Duynhoven, 1998, n = 305; 7, Morreé, 2000, n = 426; Morreé, 1998, n = 74; 9, Spaargaren, this study, n = 407; C = serogroup C (serovars H, I, Ia/I, J, Jv, K); Int = intermediate serogroup (serovars F, G, Ga); B = serogroup B (serovars D, Da, Dv, E).
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. Smith et al propose repeated panel surveys in general practices to improve surveillance in primary care, monitor changes in prevalence over time, and address the current lack of behavioural data. There are some limitations to this approach. Firstly, prevalence surveys will not measure all 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 genitourinary medicine clinics. 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 clinical data need to be available for infections other than chlamydia for appropriate interpretation of time trends. Routine collection of data on laboratory diagnosed sexually transmitted infections from all clinical settings and linkage to demographic data could complement current proposals.

The Avon Surveillance System for Sexually Transmitted Infections (ASSIST) integrates person based general practice, clinic and laboratory data to provide information for action at local level and to inform national priorities. Data on positive and negative tests for laboratory diagnosed infections taken in any clinical setting are collected from the Health Protection Agency and trust laboratories. Postcode information for geographical mapping and small area analysis is obtained by matching pseudoanonymised data with GPs’ registration databases. These data are also matched to disaggregate data from genitourinary and Brook clinics to identify duplicate tests and obtain geographic data for infections diagnosed in these settings.

ASSIST project data can be used to estimate the population burden of diagnosed infections and explore associations with demographic and socioeconomic characteristics 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 younger individuals.

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 and 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 titres 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 titres 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 460×10^6/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. Larger prospective studies, with cases and controls matched for variables such as the stage of syphilis at diagnosis, the initial RPR titre, and treatment regimens are required.

<table>
<thead>
<tr>
<th>Table 1 Number of patients in each group and the mean four dilution drop in RPR titres 3, 6, and 12 months following treatment in HIV positive compared to HIV negative individuals</th>
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<tr>
<td><strong>3 months</strong></td>
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<tr>
<td><strong>No of patients</strong></td>
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<tr>
<td>HIV positive</td>
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<td>HIV negative</td>
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Accepted for publication 1 September 2003

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 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 350×10^3/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 5366 (80%) of these 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 400). 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, in 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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Funding: None.

Competing interests: None declared.
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) 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 (85%) were in MSM. Fig 1 shows the trends.

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, and HIV is no longer considered a fatal condition.

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Accepted for publication 28 September 2003

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. Most 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/AIDS, the Internet 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 computer access and 86% reported having internet access, defined as access at home, work, or internet cafes. Similar access levels were reported by the subset of respondents (17%) who reported having had no HIV/AIDS training in medical school or in continuing medical education (CME). All 132 respondents reported a willingness to utilize 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 generalization 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 presents 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 web-based program 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 materials, 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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Accepted for publication 18 September 2003

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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, Diclofenac ointment (diclofenac 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 Diclofenac ointment. To demonstrate a 20% difference

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Figure 1 Trend of early syphilis per sexual behaviour 1999, 2000, 2001, and 2002.
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 ethinc committees at 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 –0.5 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 suggests that the aetiology of this syndrome so that appropriate treatment can be targeted more accurately.

Acknowledgements
I wish to thank Glaxo-Wellcome (now Glaxo-Smith Kline) for the supply of the study medication.

Table 1 Treatment outcomes

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<th>Emollient</th>
<th>Dermovate ointment</th>
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References

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 suboptimal with combivir 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 a genotype resistance test performed at presentation in this case a more effective regimen 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 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.

We strongly suggest that immigrants with a new HIV diagnosis should be closely investigated regarding previous drug therapy. We strongly suggest that immigrants with a new HIV diagnosis should be closely investigated regarding previous drug therapy. The baseline CD4 count and viral load were consistent with advanced infection, 20×10⁹/l (2%) and 134,000, respectively.

He was commenced on combination antiretroviral therapy and stavudine, lamivudine, and had a good initial virological response with a drop of his viral load to 1230 (3.09 logs) in 2 weeks. However, his viral load rebounded to 71 000 at 6 weeks. He was thought to be non-adherent to the antiretrovirals at this stage and was questioned extensively regarding adherence. He claimed 100% adherence to his medication and denied any missed or late doses. Interactions with prescribed and non-prescribed medications were excluded.

At this stage a genotypic resistance test was organised from the sample, with a viral load of 71 000 and he was admitted to the local respite unit (The Sussex Beacon) for directly observed therapy (DOT). The viral load after 2 weeks of DOT was 240 000.

A genotypic resistance test revealed the following mutations: K65R, D67N, K70R, K103N, M184V, G190A, T215F, K219Q, suggesting that he had extensive resistance to nucleoside analogues and to all nucleosides. When he was reviewed with his resistance test result, he had vivid knowledge of HIV testing or treatment in Zimbabwe, but identified combivir tablets as part of his anti-tuberculosis medication. Genotypic resistance testing of his archived sample before his commencement of treatment showed: M41L, V118I, M184V, T215F. He was then commenced on a salvage regimen of didanosine, tenofovir, kaletra, and saquinavir HG and had a 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.

References
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 1 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).

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 HIV 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 advisors.

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 result. 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% of all patients (319 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 to reduce transmission of HIV.

The conclusion, however, is that the new system enabled us to exceed the Department of Health target for 2004. The new system enabled us to exceed the Department of Health target for 2004. The new system enabled us to exceed the Department of Health target for 2004. The new system enabled us to exceed the Department of Health target for 2004.
Online HIV/STI Chinese clinician training

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Sex Transm Infect 2004 80: 154
doi: 10.1136/sti.2003.007583

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