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A prediction rule for selective screening of *Chlamydia trachomatis* infection

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Background: Screening for *Chlamydia trachomatis* infections is aimed at the reduction of these infections and subsequent complications. Selective screening may increase the cost effectiveness of a screening programme. Few population based systematic screening programmes have been carried out and attempts to validate selective screening criteria have shown poor performance. This study describes the development of a prediction rule for estimating the risk of chlamydial infection as a basis for selective screening.

Methods: A population based chlamydia screening study was performed in the Netherlands by inviting 21 000 15–29 year old women and men in urban and rural areas for home based urine testing. Multivariable logistic regression was used to identify risk factors for chlamydial infection among 6303 sexually active participants, and the discriminative ability was measured by the area under the receiver operating characteristic curve (AUC). Internal validity was assessed with bootstrap resampling techniques.

Results: The prevalence of *C trachomatis* (CT) infection was 2.6% (95% CI 2.2 to 3.2) in women and 2.0% (95% CI 1.4 to 2.7) in men. Chlamydial infection was associated with high level of urbanisation, young age, Surinam/Antillian ethnicity, low/intermediate education, multiple lifetime partners, a new contact in the previous two months, no condom use at last sexual contact, and complaints of (post)coital bleeding in women and frequent urination in men. A prediction model with these risk factors showed adequate discriminative ability at internal validation (AUC 0.78).

Conclusion: The prediction rule has the potential to guide individuals in their choice of participation when offered chlamydia screening and is a promising tool for selective CT screening at population level.

Chlamydia trachomatis (CT) infection is the most prevalent sexually transmitted bacterial infection. It is usually asymptomatic and persistent of nature, and distributed widely in the population, particularly in young people.[1] The prevalence of chlamydial infection has increased recently in many countries, including the Netherlands.[2–5] In women, chlamydial infections are a major cause of pelvic inflammatory disease (PID), ectopic pregnancy, tubal infertility, and chronic abdominal pain.[1] Active case finding and early treatment are crucial strategies to reduce transmission. Systematic screening of women has been shown to reduce the incidence of PID and ectopic pregnancy.[6 7] Simple screening strategies (for example, home based) to detect people with an asymptomatic infection has become feasible by improved detection methods of *C trachomatis* in urine[8–11] and by the availability of effective single dose treatment. Universal screening is not likely to be cost effective in a population with relatively low chlamydia prevalence. Selective screening, incorporating risk assessment, may increase the cost effectiveness and confronts fewer individuals with an unnecessary test. However, it could lead to an unacceptably high proportion of missed infections. Selective screening criteria for women have been applied in various clinic based, opportunistic chlamydia screening programmes, but their effectiveness has not been evaluated sufficiently.[12 13] Selection criteria for both sexes have been studied recently in population based screening programmes, but these have not led to practical guidelines for selection.[14 15]

The objective of our study was firstly to describe risk factors for chlamydial infection among sexually active responders in a large population based chlamydia screening pilot study, including men and women aged 15–29 years from both urban and rural areas in the Netherlands (**see p 17, this issue**).[16] Secondly, we wanted to identify a combination of risk factors that discriminated adequately between those who are infected and those who are not.

METHODS

Study population

The data of this study were collected in a national probability survey in the Netherlands, which was implemented in four Municipal Public Health Service (MHS) areas and stratified according to area address density (AAD). From September 2002 through March 2003, 12 000 women and 9000 men aged 15–29 years received a package by post with a urine sampling kit and a questionnaire concerning demographic data (sex, age, self assigned ethnicity, education), symptoms, history of STI, and sexual behaviour. Urine analysis was done by nucleic acid amplification test (PCR, Roche, Basel, Switzerland). The method of sampling and screening as well as response rates, non-response, and weighted prevalence among all participants are described elsewhere.[16] The present analysis is restricted to those participants who reported sexual activity in the last six months, because risk factors were only available for this group. The Medical Ethics Committee of the Free University Amsterdam approved the study.

Statistical analysis

Univariate logistic regression analyses were performed, with self reported characteristics as independent variables and

Abbreviations: AUC, area under the receiver operating characteristic curve; AAD, area address density; MHS, Municipal Public Health Service; PID, pelvic inflammatory disease.

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diagnosis of *C trachomatis* as the dependent variable. For the odds ratios, 95% confidence intervals (CI) were calculated. Variables showing an association of $p<0.2$ were included in the multivariable analysis. Backward stepwise selection was performed with a p value for the likelihood ratio test >0.10 as the criterion for elimination of variables from the model. Interactions between predictors and sex were assessed to study whether effects of predictors were different for men and women. The goodness of fit (reliability) of the model was tested by the Hosmer-Lemeshow statistic. The model's ability to discriminate between participants with or without a chlamydial infection was quantified by using the area under the receiver operating characteristic curve (AUC). AUC values 0.7–0.8 are considered acceptable, 0.8–0.9 excellent, and >0.9 outstanding.[17] Calibration was assessed graphically by plotting observed frequencies of chlamydial infection against predicted probabilities.

The performance of screening criteria in a study population, from which the model is developed, is known often to be too optimistic. The internal validity of the regression model was therefore assessed to estimate the performance of the model in new participants, similar to the population used to develop the model. We used bootstrapping techniques: random samples, with replacement, were taken one hundred times from the study population. At each step predictive models were developed, including variable selection.[18–20] Bootstrapping may help to reduce the bias in the estimated regression coefficients, and give an impression of the discriminative ability in similar participants of screening. The outcome is a correction factor for the AUC, and a shrinkage factor to correct for statistical over-optimism in the regression coefficients and to improve calibration of the model in future participants.[18 21 22] External validity was assessed by leaving out the four MHS in the sample one by one, and fitting regression models, including variable selection, on the remaining data. The discriminative ability of this model was assessed externally on the MHS data not included in the fitting procedure. This procedure replicates the situation in which the prediction model is applied in another MHS region with a population that may to some extent be different.

For the presence or level of each characteristic in the regression model, a score was calculated, based on the regression coefficients with rounding to simplify the calculation in practice. These scores are an immediate reflection of the logarithm of the odds ratios.[23] For each individual these scores were added into a sum score, on the basis of which a regression formula was calculated, taking into account the shrinkage factor derived from the bootstrap procedure. An estimate of the probability for chlamydial infection can be calculated through the regression formula

$$p(Ct) = 1/1+\exp^{(-LPS)}$$

where LPS is linear predictor for score. All possible sum scores and their corresponding predicted probabilities of chlamydial infection were combined in a graph with 95% CIs of the predicted probabilities. The confidence interval was calculated, based on a covariance matrix. The average standard error (SE) of the rounded linear predictor values was used to calculate the 95% CIs of the predicted probabilities $(1/1+ e^{-(LPS +/- 1.96\times SE)})$.[24]

For consecutive cut offs of the sum scores, sensitivity, specificity, fraction positive, and positive predictive values were calculated. Statistical analysis was done with SPSS statistical software version 10.0 (SPSS Inc, Chicago, IL, USA) and with the Design Library for S-plus 2000 (Insightful Inc, Seattle, WA, USA).

RESULTS

Prevalence among sexually active participants

The participation rate was 41% and the prevalence of chlamydial infection among sexually active responders was 2.3% (160/7005).[16] Among the 6303 participants who reported being sexually active in the previous six months, 153 tested positive (2.4% (95% CI 2.1 to 2.8)). The prevalence was 2.6% (95% CI 2.2 to 3.2) in women and 2.0% (95% CI 1.4 to 2.7) in men.

Performance of predictive model and development of prediction score

Multivariable logistic regression analysis showed that chlamydial infection was associated with high urbanisation, young age, ethnicity (Surinamese/Antillian), low/intermediate education, multiple lifetime partners, a new contact in the previous two months, no condom use at last sexual contact, and complaints of (post)coital bleeding in women and frequent urination in men (table 1). The only statistically significant interaction term in the model was sex and the number of lifetime partners.

The Hosmer-Lemeshow goodness of fit test had a p value of 0.12, indicating adequate goodness of fit. The model discriminated well between participants who were and were not infected by *C trachomatis*, with an AUC of 0.81 (95% CI 0.77 to 0.84). Internal validation showed optimism in the AUC of 0.03, resulting in a correction of the AUC from 0.81 to 0.78. In the external validation similar sets of predictors were selected. When tested in each separate MHS, the AUC varied from 0.74 to 0.80. When leaving out the MHS representing mainly AAD 1 and 2, ethnicity did not remain in the model developed from the three other MHS areas. This is related to the finding that the majority of non-Dutch participants in our study population were from this particular MHS area.

Table 2 shows the scores of the prediction rule. The sum score for a 16 year old Surinam woman living in an moderately urbanised area, with intermediate education, three lifetime partners, and a new contact in the previous two months, no postcoital bleeding, and condom use during last intercourse, is 11 (1 + 2 + 2 + 2 + 3 + 1 + 0 + 0). The predicted probability of chlamydial infection for this participant is 11% (95% CI 6 to 20) (fig 1). The discrimination on the basis of the sum score was as good as the discrimination of the original model (AUC 0.80 (0.76–0.84)).

Plots of observed frequency of infection against predicted probabilities showed that calibration of both the model and the score were good for the predicted probabilities up to 10% (see http://www.stijournal.com/supplemental for fig 2).

Application of the prediction rule

The probability of chlamydial infection according to the prediction rule can be used for selection in chlamydia screening. Table 3 shows the results for different cut off levels of sum scores. The first row gives the scenario for performing screening in our whole study population and therefore identifying all patients with a *C trachomatis* infection (sensitivity 100%). When screening is performed in all sexually active participants with a sum score ⩾8, the number to be screened in our study population would be reduced to 33%. However, 21% of the cases would then be missed (sensitivity 79%). The expected prevalence in the screened group would be 5.7%, in contrast to 2.3% on average. By lowering the cut off from a sum score from ⩾8 to ⩾6, one would have to screen an additional 30% of the population to find 93% of the cases. By doing this, the percentage of unnecessarily screened people in the study population would increase from 32% to 62%.

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Table 1 Prevalence of *C trachomatis* infection and risk factors among participants sexually active in the previous six months in a screening programme

				Univariable			Multivariable		
	n	N	%	OR	95% CI	p LR	OR	95% CI	p LR
Sex									
Men	39	1999	2.0	1.0					
Women	114	4304	2.6	1.4	0.9–2.0	0.088		–	
Age group (years)						0.030			0.084
15–19	45	1440	3.1	1.2	0.8–1.8		1.4	0.9–2.1	
20–24	43	2359	1.8	0.7	0.5–1.0		0.8	0.5–1.2	
25–29	65	2504	2.6	1.0			1.0		
AAD*						<0.001			<0.001
Very high urban (AAD 1)	57	1344	4.2	5.8	3.0–11.1		3.9	1.9–7.7	
Low/moderate/high urban (AAD 2–4)	85	3507	2.4	3.3	1.7–6.1		2.6	1.4–4.9	
Rural (AAD 5)	11	1452	0.8	1.0			1.0		
Ethnicity						<0.001			0.005
Dutch	125	5802	2.2	1.0			1.0		
Surinamese/Antillian	15	116	12.9	6.7	3.8–11.9		3.2	1.7–6.2	
Other	12	370	3.2	1.5	0.8–2.8		1.0	0.5–1.9	
Education†						<0.001			<0.001
Low	55	1508	3.6	2.8	1.8–4.4		3.0	1.8–4.9	
Intermediate	66	2567	2.6	1.9	1.2–3.0		2.2	1.4–3.6	
High	29	2151	1.3	1.0			1.0		
Women's complaints, previous 4 weeks									
(Post)coital bleeding						0.004			0.053
Yes	12	184	6.5	2.7	1.5–5.1		2.0	1.0–4.0	
No	102	4120	2.5	1.0			1.0		
Intermenstrual bleeding						0.002			
Yes	18	321	5.6	2.4	1.4–4.0				
No	96	3983	2.4	1.0					
Abnormal vaginal discharge						0.025			
Yes	29	741	3.9	1.7	1.1–2.6				
No	85	3563	2.4	1.0					
Painful urination						0.228			
Yes	14	385	3.6	1.4	0.8–2.5				
No	100	3919	2.6	1.0					
Frequent urination						0.014			
Yes	21	465	4.5	1.9	1.2–3.1				
No	93	3839	2.4	1.0					
Lower abdominal pain						0.025			
Yes	29	741	3.9	1.7	1.1–2.6				
No	85	3563	2.4	1.0					
Men's complaints, previous 4 weeks									
Frequent urination						0.016			0.051
Yes	6	102	5.9	3.5	1.4–8.6		2.8	1.1–7.2	
No	33	1897	1.7	1.0			1.0		
Painful urination						0.060			
Yes	4	71	5.6	3.2	1.1–9.3				
No	35	1928	1.8	1.0					
Urethral discharge						0.103			
Yes	2	26	7.7	4.4	1.0–19.1				
No	37	1973	1.9	1.0					
Age at first sex (years)						<0.001			
⩽15	61	1413	4.3	3.0	2.0–4.6				
16–17	57	2433	2.3	1.6	1.0–2.5				
⩾18	32	2315	1.4	1.0					
Lifetime partners (women)						<0.001			<0.001
1	8	1633	0.5	1.0			1.0		
2–5	55	2045	2.7	5.6	2.7–11.8		4.6	2.4–8.9	
⩾6	49	597	8.2	18.2	8.5–38.6		13.5	6.8–27.1	
Lifetime partners (men)						<0.001			<0.001
1	4	567	0.7	1.0			1.0		
2–5	13	919	1.4	2.0	0.7–6.2		2.6	1.1–5.9	
⩾6	20	491	4.1	6.0	2.0–17.6		5.3	2.4–11.7	
Partners in previous 6 months						<0.001			
1	103	5509	1.9	1.0					
2–5	43	717	6.0	3.3	2.3–4.8				
⩾6	7	77	9.1	5.2	2.4–11.7				
Sexual preference						0.194			
Heterosexual	148	6179	2.4	1.0					
Homo/bisexual	5	110	4.5	1.9	0.8–4.8				
New contact in previous 2 months						<0.001			0.004
Yes	47	765	6.1	3.3	2.3–4.8		1.9	1.2–2.8	
No	106	5515	1.9	1.0			1.0		

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Table 1 Continued

	n	N	%	Univariable OR	95% CI	p LR	Multivariable OR	95% CI	p LR
Condom use at last sexual contact						0.204			0.029
Yes	26	1330	2.0	1.0			1.0		
No	126	4954	2.5	1.3	0.9–2.0		1.6	1.0–2.6	
Contraception at last sexual contact						0.169			
Yes	124	5312	2.3	1.0					
No	28	895	3.1	1.4	0.9–2.0				
History of self reported STI						0.005			
Yes	18	371	4.9	2.2	1.3–3.7				
No	132	5894	2.2	1.0					

*AAD 1, very high urban (>2500 addresses/km^2); AAD 2, high urban (1500–2500 addresses/km^2); AAD 3, moderate urban (1000–1500 addresses/km^2); AAD 4, low urban (500–1000 addresses/km^2); AAD 5, rural (<500 addresses/km^2).
†Low: primary school, lower vocational, or lower general secondary education; intermediate: intermediate vocational education, intermediate, or higher general secondary education; high: higher vocational education or university education.

DISCUSSION

In this large, population based study demographic, behavioural, clinical, and geographic risk factors in 15–29 year old women and men were identified from which a prediction rule for *C trachomatis* infection could be developed. This study has led to a promising tool for selective chlamydia screening at population level.

Risk factors identified

Young age predicted chlamydial infection independently, as has been reported by others.[25] Surinamese/Antillian ethnicity proved to be a strong predictive factor, confirming previous findings in Amsterdam.[15 26] Contrary to other population based studies, we observed low and intermediate education to be predictive for chlamydial infection in both sexes.[15 25 27] Ethnicity and level of education as a risk factor may merely reflect risky sexual behaviour. Nevertheless, we assume the independent character of these variables to reflect risks involved in sexual partner choice: in case of unsafe sex, acquisition of a chlamydial infection is related to chlamydia prevalence background rates within particular sexual networks. Area address density, a geographic factor, remained an independent risk factor for chlamydial infection. As expected, people living in very highly urbanised areas (AAD 1) have the highest risk. However, living in less urbanised areas (AAD 2–4) was also associated independently with chlamydia infection. This finding may be important for decision making regarding future screening programmes. Incorporating AAD score points in selective screening decisions takes care of variations in prevalence within and between regions.[28] Although symptoms of frequent urination and (post)coital bleeding in the previous four weeks symptoms were relatively infrequent and have probably not led to healthcare seeking behaviour, they predicted chlamydial infection. The number of lifetime partners was a strong independent predictor for chlamydial infection, but with a difference in the strength of association for men and women. Other indicators of sexual behaviour that proved predictive

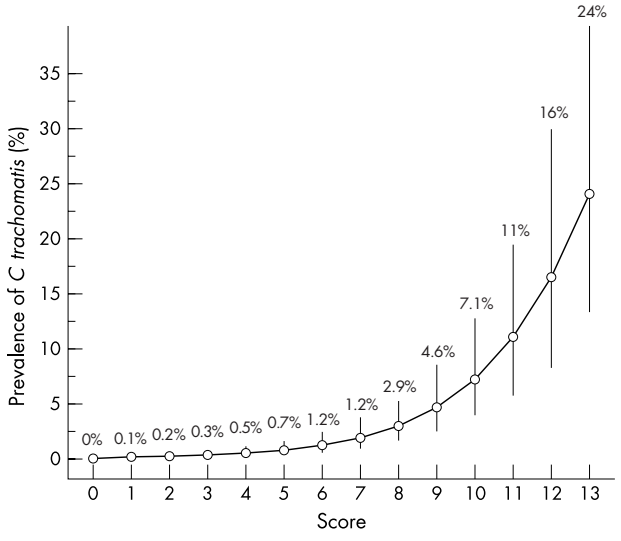

Figure 1 Predicted probability of *C trachomatis* infection as a function of the sum score. The sum score (horizontal axis) was derived from the prediction rule (table 2). On the vertical axis the predicted prevalence of *C trachomatis* is depicted. Vertical lines represent 95% CIs. Since only eight participants had a sum score of 14 (predicted prevalence 33% (18–55), this score is not shown.

Table 2 Prediction rule for quantifying the probability of *C trachomatis* infection

Predictor	Score Women	Men
Age group (years)		
15–19	1	1
20–24	0	0
25–29	0	0
AAD		
Rural (AAD 5)	0	0
Low/moderate/high urban (AAD 2–4)	2	2
Very high urban (AAD 1)	3	3
Ethnicity		
Dutch or other	0	0
Surinam or Antillian	2	2
Education		
Low or intermediate	2	2
High	0	0
Urogenital symptoms*	1	2
Lifetime sexual partners		
1	0	0
2–5	3	2
⩾6	5	3
New partner previous 2 months	1	1
No condom last sexual contact	1	1

*Women, (post)coital bleeding previous 4 weeks; men, frequent urination previous 4 weeks.
An estimate of the probability of *C trachomatis* infection can be calculated using the formula p(Ct) = 1/1+exp (− LPS), where LPS = −7.26+0.47×score.

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Table 3 Implications of using the prediction rule for screening for *C trachomatis*

Cut off sum score*	Sensitivity†	Specificity‡	Fraction positive¶	PPV§
⩾0	100.0%	0.0%	100.0%	2.3%
⩾1	100.0%	0.5%	99.5%	2.4%
⩾2	100.0%	2.4%	97.7%	2.4%
⩾3	100.0%	4.6%	95.5%	2.5%
⩾4	99.3%	14.4%	85.9%	2.7%
⩾5	94.4%	23.0%	77.4%	2.9%
⩾6	93.1%	38.3%	62.4%	3.5%
⩾7	86.8%	56.0%	45.0%	4.5%
⩾8	79.2%	68.4%	32.7%	5.7%
⩾9	59.0%	83.2%	17.8%	7.8%
⩾10	41.7%	92.2%	8.6%	11.4%
⩾11	27.8%	96.8%	3.7%	17.5%
⩾12	11.8%	98.9%	1.4%	20.5%
⩾13	4.2%	99.8%	0.3%	31.6%
⩾14	1.4%	99.9%	0.1%	25.0%

*Selection criterion for screening.
†Percentage of detected chlamydial infections among our study participants when screening under the given selection.
‡Percentage of chlamydia negative participants who would not be screened justly.
¶Percentage of the total population that is eligible for screening under the given selection.
§Prevalence in the screened population (predictive value of selection criterion).

were a new contact in the previous two months, and unsafe sex at last contact. This finding is in line with systematic and opportunistic screening programmes in women.[15 25 27 29] Young age at first sex and multiple partners in the previous six months were significant univariable risk factors but did not remain in the model, which can be explained by correlation with lifetime partners.

Methodological considerations

An important objective of this study was to develop a prediction model, based on risk factors that discriminate adequately between those who are infected with *C trachomatis* and those who are not. Logistic regression is the most appropriate statistical technique to achieve this goal. Decisions about selection in screening could also be based on a decision tree type model, but in comparative studies the performance of classification and regression trees was not better than classical regression methods.[30–32] We therefore preferred logistic regression for our statistical analysis.

In the first instance we had constructed separate models for females and males, but because of low numbers the separate male model was not very robust. Also, most risk factors had very similar effects in both sexes (see http://www.stijournal.com/supplemental for tables 4 and 5). To enhance power, we combined males and females in one model. Interaction between sex and all other determinants for chlamydial infection were tested extensively and the only interaction present was between sex and the number of lifetime partners. This effect was included in the combined model, resulting in different scores for this factor for females and males. The strength of the combined model is illustrated for the variable ethnicity. This variable disappeared in the male model because of a lack of power, causing our separate male model to be awkward to work with in practice. In a combined model, effects in males can be influenced by effects in females, but as the ratio of females to males is approximately 2:1, we consider the balance between the sexes in our combined model to be acceptable.

Performance of screening criteria in a study population is often too optimistic, and is seldom evaluated in another population. This is illustrated by the disappointing performance of selective screening criteria for asymptomatic chlamydial infection in an inner city population[33] and in different clinics.[12 13 15] Whereas those studies used one part of their data as the development sample and another part to validate their screening criteria, we used bootstrap resampling, which is statistically more efficient.[20] Bootstrapping may help to improve the calibration of predictions, and give an impression of the discriminative ability in similar populations. In our test for generalisability (external validation), the model showed acceptable performance for the various MHS regions when using the three other MHS regions for developing the model. The lower AUCs at external validation can be explained to some extent by the sampling method, which was designed to obtain a representative sample for the Netherlands. Not all AAD categories were present in the respective MHS samples. Although our internal and external validation procedures showed satisfactory results in general, further validation is necessary before the prediction rule can be applied reliably in practice. Validation could be done on existing datasets that used similar definition of the predictor variables and for presence of chlamydial infection.

A limitation of our data is that we asked for details of sexual behaviour only in people who had been sexually active in the previous six months—as this had consequences for partner tracing. Therefore, multivariable analysis could only be done for 90% (6303) of all sexually active participants and the derived score can be applied only to those who have been sexually active in the previous six months. The prevalence among those ever sexually active, but not in the previous six months, was 1% (7/681). Assuming no recent partner change and condom use at last contact (both score zero), allowed us to estimate the sum score with the available data. We then predicted chlamydial infection among those ever sexually active (through the formula in table 2). The AUC of the prediction in all ever sexually active participants was 0.80 (0.76–0.83) compared with the AUC of 0.81 (0.77–0.84) in the participants who were sexually active recently. This result provides an argument that in practice the prediction rule can be applied to all sexually active people. Another possible limitation of our study is the fact that the relatively low response rate, especially among men, non-Dutch, and those with intermediate education might affect our results due to selection bias.[16]

Application of the prediction rule for screening

Our sum score allows for prediction of chlamydial infection in individuals as well as applications for cut off values for decisions in screening programmes at population level. Usually a fixed choice of risk factors is used as selection criterion for screening. Instead, our sum score consists of varying combinations of risk factors, mirroring the probability of infection. Not every person has to fulfil a fixed combination of criteria for screening. The sum score can (potentially) guide individuals in their decision to accept the screening test. As we have shown, the predictive value of the screening criterion based on a selection of a score ⩾8 would be 5.7%. Hence 94.3% of the eligible population screened would not have chlamydia. However, the absolute number of people screened unnecessarily is lower than when screening without selection. The issue of the most efficient cut off level depends on both costs and priorities—either finding most cases or minimising unnecessarily screened people. In population based screening—whether in a specified age group in the whole population or in a restricted geographic area—a prediction rule can be applied to motivate people with a score above a certain level to participate. For instance, an invitation letter for screening could include a simple questionnaire for calculating a personal score, together with a request form for a test kit, or a referral to a website. In

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Key messages

- Risk factors for chlamydia can be used for targeted screening and thus may improve the efficiency of screening in population based programmes.
- Regression modelling including a validation process can be used to derive a score, which can be applied at an individual level to determine whether screening should be offered.
- In a population based study in the Netherlands, prevalence of *C trachomatis* was 2.6% in women and 2.0% in men. Predictors for chlamydial infection were high urbanisation, young age, ethnicity, low or intermediate education, multiple lifetime partners, a new contact in the previous two months, no condom use at last sexual contact, and complaints of (post)coital bleeding in women and frequent urination in men.
- In the population studied, the prediction score had adequate discriminative ability, but because such a score developed for one population tends to perform less well in other populations, it should be subject to external validation.

opportunistic screening, the clinician can inquire about the predictive criteria.

In conclusion, this study found demographic, geographic, and behavioural characteristics as well as urogenital symptoms as indicators for chlamydial infections in 15–29 year old women and men in a population based study. Our study indicates that one could consider screening all young women and/or men universally, whether systematic or opportunistic, in regions or settings with high prevalence, or apply the predictive score in regions or settings with lower prevalence. The prediction rule for chlamydial infection opens new avenues for risk assessment in population based screening and possibly in opportunistic screening as well.

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CONTRIBUTORS

HG wrote the first draft and finalised the report. JVB was project leader of PILOT CT. HG, JVB, IV, JB, CH, JR, AC, FDG, DVS, and MV have contributed to the study design and protocol, collected and interpreted data, critically reviewed the draft, and were all involved in the final report. Statistical analysis was performed by IV, HG, JR, and ES.

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REFERENCES

1 **Stamm W**. Chlamydia trachomatis infections of the adult. In: *Sexually transmitted diseases*, In: Holmes K, Sparling P, Mardh PA, eds. New York: McGraw-Hill, 1999:407–23.
2 **Gotz H**, Lindback J, Ripa T, *et al*. Is the increase in notifications of Chlamydia trachomatis infections in Sweden the result of changes in prevalence, sampling frequency or diagnostic methods? *Scand J Infect Dis* 2002;**34**:28–34.
3 **van de Laar MJW**, van Veen MG, Coenen AJJ. Registration of STI and HIV consultations at Regional Community Health Services in the Netherlands: Annual Report 2002. RIVM report 441500015/2003. Bilthoven, 2003 (in Dutch).
4 **van der Snoek EM**, Götz HM, Mulder PG, *et al*. Prevalence of STD and HIV infections among attenders of the Erasmus MC STD clinic, Rotterdam, the Netherlands, during the years 1996 to 2000. *Int J STD AIDS* 2003;**14**:119–24.
5 **Wilson J S**, Honey E, Templeton A, *et al*. A systematic review of the prevalence of Chlamydia trachomatis among European women. *Hum Reprod Update* 2002;**8**:385–94.
6 **Egger M**, Low N, Smith GD, *et al*. Screening for chlamydial infections and the risk of ectopic pregnancy in a county in Sweden: ecological analysis. *BMJ* 1998;**316**:1776–80.
7 **Scholes D**, Stergachis A, Heidrich FE, *et al*. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *N Engl J Med* 1996;**334**:1362–6.
8 **Andersen B**, Ostergaard L, Moller JK, *et al*. Home sampling versus conventional contact tracing for detecting Chlamydia trachomatis infection in male partners of infected women: randomised study. *BMJ* 1998;**316**:350–1.
9 **Morre SA**, van Valkengoed IG, de Jong A, *et al*. Mailed, home-obtained urine specimens: a reliable screening approach for detecting asymptomatic Chlamydia trachomatis infections. *J Clin Microbiol* 1999;**37**:976–80.
10 **Morre SA**, Van Valkengoed IG, Moes RM, *et al*. Determination of Chlamydia trachomatis prevalence in an asymptomatic screening population: performances of the LCx and COBAS Amplicor tests with urine specimens. *J Clin Microbiol* 1999;**37**:3092–6.
11 **Ostergaard L**, Andersen B, Olesen F, *et al*. Efficacy of home sampling for screening of Chlamydia trachomatis: randomised study. *BMJ* 1998;**317**:26–7.
12 **Marrazzo JM**, Fine D, Celum CL, *et al*. Selective screening for chlamydial infection in women: a comparison of three sets of criteria. *Fam Plann Perspect* 1997;**29**:158–62.
13 **Miller WC**, Hoffman IF, Owen-O'Dowd J, *et al*. Selective screening for chlamydial infection: which criteria to use? *Am J Prev Med* 2000;**18**:115–22.
14 **Andersen B**, van Valkengoed I, Olesen F, *et al*. Value of self-reportable screening criteria to identify asymptomatic individuals in the general population for urogential Chlamydia trachomatis infection screening. *Clin Infect Dis* 2003;**36**:837–44.
15 **van Valkengoed IG**, Morre SA, van den Brule AJ, *et al*. Low diagnostic accuracy of selective screening criteria for asymptomatic Chlamydia trachomatis infections in the general population. *Sex Transm Infect* 2000;**76**:375–80.
16 **Van Bergen JEAM**, Gotz HM, Richardus JH, *et al*. Prevalence of urogenital *Chlamydia trachomatis* increases significantly with level of urbanisation and suggests targeted screening approaches: results from the first national population-based study in the Netherlands. *Sex Transm Infect* 2005;**81**:17–23.
17 **Hosmer D**, Lemeshow S. Assessing the fit of the model. In: *Applied logistic regression*. Wiley J. New York: 1999;(11):135–75.
18 **Harrell FE**, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med* 1996;**15**:361–87.
19 **Steyerberg EW**, Bleeker SE, Moll HA, *et al*. Internal and external validation of predictive models: a simulation study of bias and precision in small samples. *J Clin Epidemiol* 2003;**56**:441–7.
20 **Steyerberg EW**, Harrell FE, Borsboom GJ, *et al*. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. *J Clin Epidemiol* 2001;**54**:774–81.
21 **Harrell F**. Regression coefficients and scoring rules. *J Clin Epidemiol* 1996;**49**:819.
22 **Van Houwelingen JC**, Le Cessie S. Predictive value of statistical models. *Stat Med* 1990;**9**:1303–25.
23 **Moons KG**, Harrell FE, Steyerberg EW. Should scoring rules be based on odds ratios or regression coefficients? *J Clin Epidemiol* 2002;**55**:1054–5.
24 **Krijnen P**, van Jaarsveld BC, Steyerberg EW, *et al*. A clinical prediction rule for renal artery stenosis. *Ann Intern Med* 1998;**129**:705–11.
25 **Fenton KA**, Korovessis C, Johnson AM, *et al*. Sexual behaviour in Britain: reported sexually transmitted infections and prevalent genital Chlamydia trachomatis infection. *Lancet* 2001;**358**:1851–4.

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26 **van den Hoek JA**, Mulder-Folkerts DK, Coutinho RA, *et al*. Opportunistische screening op genitale infecties met Chlamydia trachomatis onder de seksueel actieve bevolking in Amsterdam. I. Meer dan 90% deelname en bijna 5% prevalentie. *Ned Tijdschr Geneeskd* 1999;**143**:668–72.
27 **Verhoeven V**, Avonts D, Meheus A, *et al*. Chlamydial infection: an accurate model for opportunistic screening in general practice. *Sex Transm Infect* 2003;**79**:313–17.
28 **Miller WC**. Screening for chlamydial infection. A model program based on prevalence. *Sex Transm Dis* 1998;**25**:201–10.
29 **Paukku M**, Kilpikari R, Puolakkainen M, *et al*. Criteria for selective screening for Chlamydia trachomatis. *Sex Transm Dis* 2003;**30**:120–3.
30 **Ennis M**, Hinton G, Naylor D, *et al*. A comparison of statistical learning methods on the Gusto database. *Stat Med* 1998;**17**:2501–8.
31 **Marshall RJ**. The use of classification and regression trees in clinical epidemiology. *J Clin Epidemiol* 2001;**54**:603–9.
32 **van Dijk MR**, Steyerberg EW, Stenning SP, *et al*. Survival of patients with nonseminomatous germ cell cancer: a review of the IGCC classification by Cox regression and recursive partitioning. *Br J Cancer* 2004;**90**:1176–83.
33 **van Valkengoed IG**, Boeke AJ, Morre SA, *et al*. Disappointing performance of literature-derived selective screening criteria for asymptomatic Chlamydia trachomatis infection in an inner-city population. *Sex Transm Dis* 2000;**27**:504–7.

CHESTER CHRONICLES

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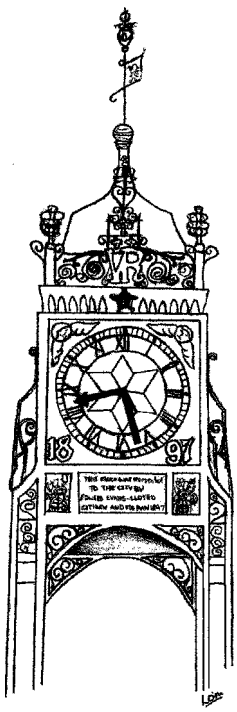
Art attack



EASTGATE CLOCK, CHESTER

"Whoa! Where's my pictures gone?" I stare dumfounded at dusty blank areas on the wall of the corridor into the Sexual Health Clinic—somebody's nicked my pictures. I remembered painfully carrying them one by one from the car park from the boot of my own car with great difficulty. They were at least 4'0"×4'0" heavy pine frames, and now some scurrilous scally has made off with them. It was now 7.30 on a Tuesday evening and none of the other staff who had left earlier had noticed anything missing. I told Security, who simply said to phone the police in the morning and report it as an incident. This wasn't good enough. I wanted justice. The next morning, I took the extreme liberty of abusing the hospital email system by sending an email to all Countess of Chester Hospital staff. This has often been done in the past by people saying "car lights left on," etc, etc, so I felt justified under these extenuating circumstances in sending out the following email:

"Some low life made off with two large 4'0"×4'0" pictures from the corridor of Genito-Urinary Medicine yesterday evening at about 6–6.30 pm. Surely, somebody must have seen something. I hope the individual concerned develops an incurable STD—any info to Security or Dr O'Mahony."

Within minutes I was emailed back with perfect information regarding the description of the individual and the timing of the theft, allowing a specific check of security cameras to locate the event! See, I knew those Morse videos were educational.

The Cheshire Constabulary also duly arrived and I proudly expounded on the investigative acumen of Detective Inspector C O'Mahony who was now within an ace of recovery of the goods and catching the culprit. However, the officer was appalled when reading my email to come across the injudicious wish of an incurable STD. Not since my last appraisal have I been so thoroughly ridiculed and chastised, as he pointed out to me that any documentation in a case must be supplied to the defence also, and they would have taken me to the cleaners over such an ill advised comment. Imagine the local newspaper (the real "Chester Chronicle") with a headline from court "Leading Hospital Consultant Threatens Incurable STD on Innocent…"

Luckily, the police didn't have to take the matter further, as the Hospital Security Staff interviewed a patient who led them to where the pictures had been stashed for later collection and disposal. Suffice it to say, my pictures are back, my rashness is reprimanded, and the case is closed.

Incidentally, a third picture was also found in the stash and no one has the faintest idea where it's from. It's a weird, ugly picture, and looks to be by some guy called Edward or Edvard? Munch and there are some Belgian Museum markings on the frame. If no one claims it soon, we'll just have to chuck it out, as I couldn't possibly contemplate putting it up in the clinic. Any takers?

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PostScript

LETTERS

A case of a false positive result on a home HIV test kit obtained on the internet

There are two major reasons to diagnose asymptomatic HIV infection: to facilitate timely initiation of antiretroviral therapy, and to reduce the chance of onward transmission. A negative test offers an opportunity for preventive health promotion. All these aspects of testing require follow up by suitably trained personnel. We describe a case illustrating the hazards of self testing for HIV.

A 31 year old British heterosexual man attended the genitourinary medicine clinic requesting an HIV test. His last sexual contact was 3 weeks earlier with a female partner of 3 months. He had recently learnt that she had had a previous male partner who had had African sexual partners and therefore may be at higher risk of having HIV infection. He obtained a home HIV test kit (''Discreet'' HIV Home Test Kit, Seville Marketing Ltd) from a Canadian based internet site and this result was positive. On further inquiry he gave a history of sore throat and swollen cervical lymph nodes 2 months previously, although these symptoms had largely resolved. He had never tested for HIV before and had no other significant risk factors.

We requested an HIV test on the patient; the result was negative. We repeated the test after 3 months and again it was negative, confirming that the patient was not infected at the time he performed the home HIV test. The current HIV screening test used by our centre uses both HIV antibody and p24 antigen detection and is known to detect HIV infection 3–12 weeks after infection. Given that he was now symptom free with negative syphilis serology and at low risk for acquiring HIV, no further investigations were undertaken.

The patient had disposed of the test kit and it was not available for inspection. Unlike oral fluid kits recently licensed in the United States,[1] this kit required a fingerprick and a drop of blood to be applied to a reagent strip. The company claimed ''99.4% accuracy'' for the kit's results. From discussion with the patient it seemed that the result displayed by the testing kit evolved over time and had to be read between 3 minutes and 8 minutes after applying the drop of blood. The time dependency of the reaction made the kit liable to be misread.

We performed an internet search and found that websites selling the kit were no longer active. Furthermore, a US Federal Trade Commission restraining order had been placed on the kit 2 days before the patient presented to our clinic. As well as finding the company to be in breach of US law by selling the kit in the United States, the Centers for Disease Control and Prevention had tested the accuracy of the kit. ''Results of the testing, based on the package instructions, 'changed dramatically' during the 15 minutes that the results were reported. After 3 minutes, 15.4% of the kits gave erroneous readings; after 8 minutes, 29.6% registered inaccurate results; after 15 minutes, 59.3% of the kits gave inaccurate results. Moreover, the kits showed both inaccurate HIV positive results and inaccurate HIV negative results.''[2]

This case is important because the use of the internet to obtain HIV test kits is likely to increase. One study in California found fairly high levels of interest in instant home HIV tests[3] and it is not difficult to locate kits for HIV testing and other diagnostic services on the internet. A home HIV test kit using oral fluid has been licensed in the United States and a home blood collection and telemedicine system is also available,[4 5] but these are not available legally in the United Kingdom or Europe. All healthcare professionals involved in counselling and testing patients for HIV should be aware that self taken HIV tests may be inaccurate and confirmatory testing in an appropriate laboratory should be performed before making a diagnosis of HIV infection.

Although access problems to sexual health services have rightly engendered innovative approaches to diagnosis and management, there should be a note of caution on using new HIV technologies of rapid testing in non-healthcare settings and legalisation of home and over the counter HIV testing kits.[6] It is imperative that clinical governance issues are addressed. Medicolegal consequences are important, but of greater significance is the distress to individuals and their partners who are wrongly diagnosed or inappropriately reassured through the use of poorly performing kits.

Contributors

LH saw the patient before and after testing and wrote the case report; AR suggested the case be reported and reviewed/redrafted the manuscript.

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Jane Sudlow counselled the patient and commented on the case. Julian Tang provided advice on HIV testing and confirmation.

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Ethics: A signed statement of consent to publish was obtained from the patient.

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References

1 **Schramm W**, Angula GB, Torres PC, *et al*. A simple saliva-based test for detecting antibodies to human immunodeficiency virus. *Clin Diagn Lab Immunol* 1999;**6**:577–80.
2 **Federal Trade Commission, USA**. FTC halts US sales of defective ''discreet'' HIV home test kits (www.ftc.gov/opa/2004/06/seville.htm, accessed 9 June 2004).
3 **Phillips KA**, Chen JL. Willingness to use instant home HIV tests: data from the California Behavioral Risk Factor Surveillance Survey. *Am J Prev Med* 2003;**24**:340–8.
4 **Frank AP**, Wandell MG, Headings MD, *et al*. Anonymous HIV testing using home collection and telemedicine counseling. *Arch Intern Med* 1997;**157**:309–14.
5 **Stryker J**. Center for AIDS Prevention Studies at the University of California San Francisco. What is the role of HIV testing at home? (www.caps.ucsf.edu/hometestrev.html, accessed 9 July 2004).
6 **Terence Higgins Trust**. *Blueprint for the future. Developing sexual health and HIV services*. London: Terence Higgins Trust, April, 2004:14.

Primary HIV infection masquerading as Munchausen's syndrome

Since 1986 there have been several case reports describing factitious HIV infection.[1] We have seen two acute presentations where the patients claimed to have chronic HIV infection, were found to be HIV antibody negative but on closer evaluation were found to be seroconverting with primary HIV infection (PHI). We believe that the patients were motivated by the psychological need to assume the sick role, fulfilling the principal feature of a factitious disorder, rather than malingering.

Case 1

A 40 year old homosexual man presented to HIV services with an acute diarrhoeal illness, claiming to have been diagnosed as HIV positive at another hospital 2 years previously. A third generation HIV test, Abbott AxSYM HIV 1/2 gO (antibody only), was negative. He returned 1 month later, still denying any sexual risk, and requested a repeat HIV test, which was again antibody negative but reactive with the fourth generation assay, Abbott HIV Ag/Ab Combo (antibody and p24 antigen combined).

Case 2

A 39 year old homosexual man presented to the accident and emergency department with fever, ulcerative gingivitis, and maculopapular rash, claiming to have been diagnosed HIV positive 4 years previously. He reported safer sex with 30 casual male partners in the previous 3 months and stated that his regular male partner was HIV negative. He was found to have had four negative HIV tests in the previous 2 years at this hospital and numerous negative HIV tests at other hospitals. The third generation HIV test was negative. The following day, however, a fourth generation test was reactive.

Comment

The ability to diagnose PHI has always required a high index of suspicion and a keenly taken history, and if missed the next opportunity for testing may not be until years later when the patient presents in ill health, with symptomatic HIV or even AIDS.[2] Clearly, a missed diagnosis of PHI may have a deleterious effect on the individual's prognosis, but there may also be significant public health consequences, as early infection is a core factor in the propagation of an epidemic[3 4] because of high viral burden and de facto risk taking sexual behaviour. Indeed, early detection of PHI probably represents the

single most important method of slowing the spread of HIV within populations, with mathematical modelling indicating that eliminating high infectivity in early infection has more effect than at any other disease stage.[5]

Thus, the diagnosis of PHI in at-risk individuals has considerable advantages in both individual and public heath terms. These two cases demonstrate how easy it can be to disregard such patients as having factitious HIV infection and are a gentle reminder that a negative antibody test does not necessarily exclude PHI. Healthcare professionals must continue to be alert to the less common clinical manifestations of PHI, be aware of the particular assays used in their own laboratory, and because no combination of symptoms is 100% sensitive or specific, diagnostic procedure must be broad and inclusive.[6]

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References

1 **Churchill DR**, De Cock KM, Miller RF. Feigned HIV infection/AIDS: malingering and Munchausen's syndrome. *Genitourin Med* 1994;**70**:314–16.
2 **Castilla J**, Sobrino P, De La Fuente L, *et al*. Late diagnosis of HIV infection in the era of highly active antiretroviral therapy: consequences for AIDS incidence. *AIDS*, 2002;16, 1945–51.
3 **Vernazza PL**, Eron JJ, Fiscus SA, *et al*. Sexual transmission of HIV: infectiousness and prevention. *AIDS* 1999;**13**:155–66.
4 **Leynaert B**, Downs AM, de Vincenzi I. Heterosexual transmission of human immunodeficiency virus: variability of infectivity throughout the course of infection. European Study Group on Heterosexual Transmission of HIV. *Am J Epidemiol* 1998;**148**:88–96.
5 **Koopman JS**, Jacquez JA, Welch GW, *et al*. Role of the Primary Infection in epidemics of HIV infection in gay cohorts. *J Acquir Immune Defic Syndr* 1994;**7**:1169–8.
6 **Kahn JO**, Walker BD. Acute human immunodeficiency virus type 1 infection. *N Engl J Med* 1998;**339**:33–9.

Complementary therapy and genital warts

Complementary therapy (CT) is now the second biggest growth industry in Europe (after IT). Up to 20% of the UK population visit a complementary therapist each year and as much as £5 billion is spent annually on such therapies.[1] In the United States this figure is $30 billion. The National Institutes of Health in the United States are keen to fund good scientific studies showing efficacy of CT, in order to ''disseminate authoritative information to the public and professionals''.[2] Objective data gathering is all the more important as a large majority of physicians view CT very negatively.[3]

Five years ago we were approached by a group of Reiki therapists to undertake a study showing the efficacy of Reiki healing on STIs. Reiki healing (RH) is a hands-on healing method that may be undertaken as distance healing.[4] There is a precedent for CT therapies being used in the form of yoga for patients with infection—in particular a well designed randomised trial showing efficacy in tuberculosis.[5] In view of this we undertook a study of the effect of RH at a distance on genital warts. The study had local ethics committee approval.

Patients with anogenital warts who were awaiting surgical treatment initially had their wart size and number assessed by a nurse using standard techniques.[6] Waiting time from this point to surgical removal of the warts averaged 6 weeks (plus or minus 1 week). Another nurse, who was blind to the initial wart visualisation, photographed the back of patient's head and then allocated each patient to a treatment (RH) or no treatment group according to a random code .Twelve Reiki healers were then each sent the photographs and undertook RH on them at a distance on a daily basis for about 10 minutes. Thus, half the patients received RH and the other half did not. Just before surgical removal of the warts the size and number of the warts was again assessed by the original nurse.

Considering a difference between a 35% reduction in wart volume for the Reiki treated group and a 10% reduction for the placebo (90% power 0.05) it was considered that 130 patients would be needed (65 in each arm); in fact, only 27 patients were enrolled into the study. Ten were lost to follow up .Of the 17 who completed the study nine received RH and eight did not. Two patients who received RH and one who did not totally cleared their warts. Seven who received RH and two who did not had an increase in wart mass/number. No patient who received RH and five who did not showed some degree of decrease in wart mass/number. These rates of regression are similar to those described in the placebo arms of recent double blind trials.[7 8]

Although this is a small study, we believe it was well designed but we failed to enrol large enough numbers. We also think it failed to show any efficacy for RH. Undertaking well designed trials of CT in the STI arena is important—not least because a majority of patients attending STI clinics may already be using them, and open discussion about them can help patients to make informed decisions as well as avoid drug interactions.[9]

In terms of common skin warts, efficacy of Reiki healing has not been shown to be effective.[10]

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References

1 **What Medicine**. CAM on the up as more people look for an alternative (www.whatmedicine.co.uk/articlesCompMed.htm).
2 **Anonymous**. About the National Center for Complementary and Alternative Medicine. (/nccam.nih.gov/aboutnccam/index.htm).
3 **Risberg T**, Kolsta A, Bremmes Y, Knowledge of and attitudes toward complementary and alternative therapies ; a national multicentre study of oncology professionals in Norway, *et al*. *Eur J Cancer* 2004;**40**:529–35.
4 **Mansour AA**, Beuche M, Laing G, *et al*. A study to test the effectiveness of placebo Reiki standardised procedures developed for a planned Reiki efficacy study. *J Altern Complement Med* 1999;**5**:153–64.
5 **Visweswaraiah NK**, Telles S. Randomised trial of yoga as a complementary therapy for pulmonary tuberculosis. *Respirology* 2004;**9**:96–101.
6 **Lacey CJN**, Goodall R, Tennvall GT, *et al*. Randomised controlled trial and economic evaluation of podophyllotoxin solution, podophyllotoxin cream, and podophyllin in the treatment of genital warts. *Sex Transm Infect* 2003;**79**:270–5.
7 **Tyring S**, Edwards L, Cherry K, *et al*. Safety and efficacy of 0.5% podofilox gel in the treatment of anogenital warts. *Arch Dermatol* 1998;**134**:33–8.
8 **Edwards L**, Ferenczy A, Eron L, *et al*. Self-administered topical 5% imiquimod cream for external anogenital warts. *Arch Dermatol* 1998;**134**:25–30.
9 **Trutnovsky G**, Law C, Simpson JM, *et al*. Use of complementary therapies in a sexual health clinic setting. *Int J STD AIDS* 2001;**12**:307–9.
10 **Harkness EF**, Abbot NC, Ernst E. A randomised trial of distant healing for skin warts. *Am J Med* 2000;**108**:507–8.

Chlamydia trachomatis PCR positivity and inflammatory changes on cervical cytology

The presence of genital infection does not increase the likelihood of an inadequate Papanicolaou (Pap) test.[1] Conversely, testing for *Chlamydia trachomatis* at the time of routine cytological screening presents an opportunity to detect asymptomatic genital tract infection.[2] The PreservCyt fixative fluid (Cytyc Corporation, Boxborough. MA, USA) used for the ThinPrep Pap test (Cytyc Corporation) can be used for detection by the polymerase chain reaction (PCR) of *C trachomatis*.[3 4] This presents an opportunity to study the correlation between the chlamydia result and the Pap test finding.

We retrospectively reviewed all routine requests for chlamydia PCR on ThinPrep samples sent to our laboratory over a year. Data were collected on the woman's age, chlamydia PCR result, result of genital tract cultures if performed on the same date, and Pap test result. Data on the Pap test result included presence or absence of an epithelial cell abnormality either high grade (HGEA) or low grade (LGEA), whether the Pap was inflammatory and the presence or absence of recognisable pathogens. Cervical specimens collected in PreservCyt transport medium were processed for *C trachomatis* using the automated Cobas Amplicor (Roche Diagnostic Systems) and the method by Bianchi *et al*.[3]

Over the study period, 733 samples were received, of which 23 (3.1%) had *C trachomatis* DNA detected by PCR. Comparison of the women with chlamydia infection, with those without chlamydia infection is shown in table 1. There was no statistical difference in the presence of high or low grade epithelial abnormalities, recognition of other pathogens, or age of the women; however, 26% of women with chlamydia had an inflammatory Pap test compared to 9% of women without chlamydia ($p<0.01$).

Table 1 Comparison of women with and without chlamydia infection

	Positive *C trachomatis* PCR	Negative *C trachomatis* PCR	p Value
Median age	24 (range 19–40)	28 (range 15–68)	0.182
LGEA/HGEA	5 (22%)	106 (15%)	0.37
Other pathogens	1 (17%)	12 (18%)	NS
Inflammation on Pap test	6 (26%)	65 (9%)	<0.01

LGEA, low grade epithelial abnormalities; HGEA, high grade epithelial abnormalities.

The association of inflammation on Pap testing and chlamydial infection has been previously examined with variable methodologies and findings.[5] We utilised the same sample (ThinPrep) for determining both the presence of inflammatory changes on Pap test and chlamydia infection and found a positive association between the two despite a low prevalence population. Our study confirms the feasibility of performing chlamydia PCR from liquid based cytology samples in a routine diagnostic setting. Testing for chlamydia should be considered in women with inflammatory Pap tests for which there is no other explanation.

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References

1 **Edwards S**, Sonnex C. Influence of genital infection on cervical cytology. *Sex Transm Infect* 1998;**74**:271–3.
2 **Hopwood J**, Mallinson H, Hodgson E, *et al*. Liquid based cytology: examination of its potential in a chlamydia screening programme. *Sex Transm Infect* 2004;**80**:371–3.
3 **Bianchi A**, Moret F, Desrues JM, *et al*. PreservCyt transport medium used for the ThinPrep Pap Test is a suitable medium for detection of Chlamydia trachomatis by the Cobas Amplicor CT/NG test: results of a preliminary study and future implications. *J Clin Microbiol* 2002;**40**:1749–54.
4 **Koumans EH**, Black CM, Markowitz LE, *et al*. Comparison of methods for detection of Chlamydia trachomatis and Neisseria gonorrhoeae using commercially available nucleic acid amplification tests and a liquid Pap smear medium. *J Clin Microbiol* 2003;**41**:1507–11.
5 **Paler RJ**, Simpson DR, Kaye AM, *et al*. The relationship of inflammation in the papanicolaou smear to Chlamydia trachomatis infection in a high-risk population. *Contraception* 2000;**61**:231–4.

Cardiovascular syphilis in HIV infection: a case-control study at the Institute of Sexually Transmitted Diseases, Chennai, India

It is known that HIV co-infection with syphilis may accelerate the onset of gummata and neurosyphilis and increase their severity. However, this has only been reported for cardiovascular syphilis in two previous cases.[1 2]

This case-control study deals with a total of 14 HIV seropositive and 100 HIV 1 and 2 seronegative individuals with syphilis, who were seen in our clinic between June 2000 and May 2001. Of the 14 HIV seropositive individuals, 12 were reactive for VDRL (venereal diseases reference laboratory) and TPHA (*Treponema pallidum* haemagglutination assay) and two had primary syphilis confirmed by dark field examination for *T pallidum*. Of the 100 HIV seronegative individuals, 85 had reactive VDRL and TPHA and 15 had primary syphilis confirmed by dark field examination. The prevalence of cardiovascular syphilis in the HIV seropositive and seronegative groups was 14.3% and 2%, respectively (OR 8.2; 95% CI 1.1 to 61.5).

Two HIV seropositive individuals with cardiovascular syphilis had aortic root dilatation while the two HIV seronegative individuals had aortic aneurysm. The HIV seropositive individuals were asymptomatic with regard to cardiac status but one HIV seronegative individual had chest pain and the other was asymptomatic. None in the HIV seronegative group had aortic root dilatation ($p<0.01$). There was a theoretical possibility that aortic root dilatation could be a manifestation of HIV or opportunistic infections involving the heart. A parallel study done on cardiovascular involvement in HIV seropositive individuals from the same institute during the same time interval had revealed that none of the 61 non-syphilitic HIV seropositive individuals had aortic root dilatation, compared with 2 out of 14 with syphilis ($p<0.01$; paper in preparation).

The mean duration of diagnosing cardiovascular syphilis from the time of acquiring syphilis was 40 months (27 and 53) in the HIV seropositive group and 102 months (84 and 120) in the HIV seronegative group. The mean age of the HIV seropositive individuals who had cardiovascular syphilis was 31.5 years (29 and 34) and that of HIV seronegative individuals was 45.5 years (44 and 47).

The shorter duration for diagnosing cardio vascular syphilis from the time of acquiring syphilis for the HIV seropositive group (40 months) compared with the HIV seronegative group (102 months) ($p<0.003$) could be explained by the fact that HIV hastens the progression to late syphilis,[3] which might be due to an alteration to the immune system. It could also be possible that HIV infected individuals seek medical attention because of opportunistic infections, which might have led to the earlier diagnosis of cardiac lesions because the two individuals with aortic root dilatation were asymptomatic with regard to cardiac status. The difference in the clinical manifestation of cardiovascular syphilis between these two groups could not be explained at this point of time.

Contributions

MM designed the study, collected the data, interpreted the results, and analysed the results and statistics; SKG contributed to collecting data, interpretation of results and laboratory collaboration.

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References

1 **Chetty R**, Batitag S, Nair R. Large artery vasculopathy in HIV-positive patients: another vasculitic enigma. *Hum Pathol* 2000;**31**:374–9.
2 **Olmos JM**, Fernandez-Ayala M, Gutierrez JA, *et al*. Superior vena cava syndrome secondary to syphilitic aneurysm of the ascending aorta in a human immunodeficiency virus-infected patient. *Clin Infect Dis* 1998;**27**:1331–2.
3 **Gregory N**, Sanchez M, Buchness MR. The spectrum of syphilis in patients with human immunodeficiency virus infection. *J Am Acad Dermatol* 1990;**22**:1061–7.

Antiretroviral therapy—alternative uses

Recently, while speaking to a patient from Nigeria I was very concerned to discover that she had been taking combivir for breast enhancement. On closer questioning it appears that she had accessed this drug, passed to her in individual sachets with no information insert etc, via a friend. Her friend, knowing that my patient wished for larger breasts, had passed her the combivir to use on an as required basis for breast enhancement. My patient claims that the drug did work to enlarge her breasts.

The drugs were apparently prescribed by a doctor in Nigeria at the cost of about US$250 for six sachets and the pharmacist dispensing them had been asking why the girls were taking them. Apparently the sachets did not come with any leaflets or drug information inserts.

My patient and her friends appeared to be totally unaware of the fact that the combivir was for use in HIV therapy and were unaware of any potential side effects from the drug. It was only when my patient was surfing the web that she found out about the licensed use for combivir.

My patient, sadly, acquired HIV from a blood transfusion in Africa and on primary resistance testing showed very broad nucleoside reverse transcriptase inhibitor resistance and apparent full sensitivity to protease inhibitors and non-nucleoside reverse transcriptase inhibitors (NNRTIs). Resistance to

NNRTIs was only confirmed after weeks of unsuccessful therapy by further resistance testing.

My patient has alerted all her friends in Nigeria as to the real nature of combivir and advised them to stop using it for breast enhancement. She has also told me that she believes the doctor in Nigeria who prescribed these drugs may have had this activity terminated.

Because no one I have spoken to has come across this particular misuse of antiretroviral therapy I felt it was worth highlighting to a wider audience in the hope that such practises may be addressed.

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This patient has agreed to publish details of her case to help prevent recurrent misuse of this drug.

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CORRECTION

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The order of the authors of the paper by Götz *et al* on page 24 of the February 2005 issue (HM Götz *et al*. A prediction rule for selective screening of Chlamydia trachomatis infection. *Sex Transm Infect* 2005;**81**:24–30) were wrong. The order should have been as follows: HM Götz, JEAM van Bergen, IK Veldhuijzen, J Broer, CJPA Hoebe, EW Steyerberg, AJJ Coenen, F de Groot, MJC Verhooren, DT van Schaik, and JH Richardus.