

## ORIGINAL ARTICLE

## Chlamydial infection: an accurate model for opportunistic screening in general practice

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**Objectives:** To estimate the prevalence of *Chlamydia trachomatis* in women in general practice and to assess risk factors associated with infection.

**Methods:** The study was carried out in 2001–2 in different general practices in Antwerp, Belgium. Sexually active women, visiting their general practitioner for routine gynaecological care (mostly pill prescription or PAP smear), were offered opportunistic screening for chlamydia. 787 participants aged 15–40 delivered a self taken vaginal sample and filled in a questionnaire which included questions on demographic variables, urogenital symptoms, sexual history, and sexual behaviour. Samples were tested for presence of chlamydial DNA by means of a ligase chain reaction (LCR) assay, and positives were confirmed by two other amplification assays (PCR and SDA).

**Results:** Overall prevalence was 5.0% (95% CI: 3.5 to 6.5). Determinants of infection in logistic regression analysis were age 18–27 years, >1 partner in the past year, no use of contraceptives, frequent postcoital bleeding, having a symptomatic partner, painful micturition, and living in the inner city. The area under the ROC curve in the full model was 0.88. Selective screening based on a combination of the five first determinants detects 92.3% of infections in this sample; 37.5% of the population would need to be screened.

**Conclusion:** Targeted screening for chlamydial infection is possible, even in a heterogeneous group of general practice attendants. Implementing this model would require considerable communication skills from healthcare providers.

In spite of raised public awareness, improved detecting methods, and effective single dose treatment, urogenital *Chlamydia trachomatis* (CT) infection continues to be a major public health problem. Although the precise burden of illness of chlamydial infection remains unclear,<sup>1</sup> CT is a major cause of pelvic inflammatory disease (PID), ectopic pregnancy, and infertility. The economic and human costs of managing these complications are considerable. High prevalence rates of CT are found in various settings in Europe, including in general practice attendants.<sup>2</sup>

Recently, an increase in sexual risk behaviours among young people<sup>3</sup> and a subsequent increase in CT prevalence rates<sup>4</sup> have been reported.

The asymptomatic and persistent nature of the chlamydial infection extends the reservoir of infection which can only be controlled through screening. However, there are still some gaps in the evidence which limit support for large scale routine screening.<sup>5</sup> These include aspects of screening intervals, relapse/reinfection issues, natural history of DNA amplification detected infections,<sup>6</sup> effects of screening on prevalence, etc. On the other hand, there is good evidence that selective screening of women reduces the incidence of PID.<sup>7</sup>

Opportunistic screening will detect a relatively small number of infections, but optimises cost effectiveness<sup>8</sup> and offers the opportunity to limit possible adverse effects of screening by carefully selecting and counselling eligible candidates. Success of screening programmes in the general population is compromised by the lack of valid selective screening criteria. Risk markers observed in selected high risk groups are not necessarily useful for screening in the general population.<sup>9</sup>

In this study we develop a strategy for selective, opportunistic screening of women in general practice.

## METHODS

## Population and specimen collection

The study was carried out in 32 general practices in Antwerp, Belgium. Forty six general practitioners (GPs) participated for variable periods of time between February 2001 and June 2002. They offered opportunistic screening for *Chlamydia* to their female patients, who attended for routine gynaecological care (mostly contraceptive pill prescription or PAP smear). Women were eligible for participation if they were under 40 years old and if they had been sexually active in the past year. Women in whom chlamydial infection or PID was clinically suspected were not eligible, and were diagnosed according to usual clinical practice. Test results of patients in the study were available 2–3 weeks after the sample was sent to the laboratory.

Participants received a package containing a polyurethane tipped swab (Culturette EZ, Becton Dickinson), an instruction form, a standardised questionnaire, and a post-free addressed envelope. The 47 item questionnaire included questions on demographic variables, urogenital symptoms, sexual history, and sexual behaviour and was available in Dutch, French, English, and Turkish.

Patients collected their own vaginal samples at home by inserting the swab into the low vagina to a distance of about 2–3 cm. The simple procedure was explained by the GP and illustrated in the instruction form. Vaginal self sampling has shown to be a sensitive and acceptable method for diagnosing chlamydial infection.<sup>10–11</sup> Testing materials were coded, so anonymous participation was possible. The swab and the questionnaire were returned to the university laboratory by mail. The diagnostic efficacy of samples obtained by women at home and mailed to the laboratory is as good as for samples obtained by a GP and delivered to the laboratory.<sup>12</sup>

The study has been approved by the medical ethics committee of Antwerp University.

**Table 1** Univariate determinants of CT infection, selected for multivariate analysis

Determinant	No*	% CT +	Pearson $\chi^2$
Age			0.249
14–17	50	2.0	
18–22	226	6.6	
23–27	256	5.9	
28–40	244	3.3	
Situation of living			0.036
With parents	231	2.2	
With partner	320	5.3	
Without partner	168	8.9	
Other	20	10.0	
Activities, occupation			0.096
"Stable": school/work/housewife	652	4.4	
"Unstable": unemployed, combinations of jobs and school	125	8.0	
Location of practice			0.005
Inner city	566	6.4	
Suburban, rural	211	1.4	
Partner having urinary complaints			0.000
No	738	4.2	
Yes	39	20.5	
Intermenstrual bleeding in past 3 months			0.023
No	568	4.1	
Yes	195	8.2	
Postcoital bleeding in past 3 months			0.000
No/sometimes	755	4.8	
Frequently	9	33.3	
Vaginal discharge			0.171
No	598	4.5	
Yes	168	7.1	
Painful or frequent micturition			0.003
No	642	4.1	
Yes	124	10.5	
Age at first coitus			0.008
≤15	150	10.0	
16–18	395	4.1	
≥19	232	3.5	
Number of partners in the past year			0.000
1	532	2.4	
2	140	8.6	
3–5	70	12.9	
≥6	28	17.9	
Start of last relationship			0.037
>6 months	499	3.8	
<6 months	185	8.7	
No relationship now	85	4.7	
Partner having another partner in the past 3 months			0.052
No	555	4.5	
Yes/don't know	149	8.7	
I have no partner right now	60	1.7	
Oral contraception (OAC) use			0.001
Yes	534	3.2	
No	243	9.1	
Contraception			0.000
Any	644	3.1	
None or coitus interruptus	133	14.3	
Condom use			0.028
Never	306	3.6	
Sometimes/regularly	411	6.8	
Always	58	0.0	
Use of MAP (emergency contraception)			0.004
Never	599	3.8	
Ever	174	9.2	
Ever been pregnant unintendedly			0.110
No	663	4.5	
Yes	111	8.1	
Marital status†			0.950
Single	504	5.4	
Married	113	4.4	
Cohabiting	133	4.5	
Separated/divorced	26	3.9	
Ethnicity†			0.375
Autochthonous Belgian	640	5.0	
Allochthonous Belgian (Turkish/Moroccan parents)	30	3.3	
West European	37	2.7	
Eastern European	19	15.8	
African	19	0.0	
Asian	13	7.7	
Other	16	6.3	
Education†			0.918
Secondary school	257	5.5	
Technical secondary school/professional training/art education	159	5.0	
Higher education (short studies)	157	3.8	
High school/university	174	5.8	
Various	30	3.3	

\*The sum of the categories for each determinant varies slightly because of missing data.  
†Non-significant determinant; added in multivariate analysis as possible confounder.

## Diagnosics

Methods of sample preparation and processing in the laboratory have been described and validated previously.<sup>13</sup> Specimens were tested for the presence of chlamydial DNA by means of a ligase chain reaction (LCR) assay (LCx, Abbott Laboratories), and positives were confirmed by two other amplification assays (Roche PCR and Becton Dickinson SDA). Specimens were considered true positive for *C trachomatis* if they were positive by at least two amplification assays. The results were communicated to the GPs who counselled and treated infected patients and their partners.

## Statistics

Analyses were performed with the SPSS package version 10.0.

Univariate analysis ( $\chi^2$ ) was used to identify candidate variables for multivariate modelling. Variables showing an influence on presence/absence of infection at a significance level of  $p < 0.3$  were selected for further analysis. Possible confounders which showed no univariate association were also included (for example, ethnicity, marital status, and education level).

In the next stage, logistic regression<sup>14</sup> was performed to derive a multivariate model. Backward variable selection was used, with the likelihood ratio test to select variables for removal. Calibration of the model was assessed by the Hosmer-Lemeshow goodness of fit statistic. We assessed discrimination of the model with receiver operating characteristic (ROC) curve analysis.

## RESULTS

Less than 1% of approached women refused to accept the screening package from their GP; 75% of all distributed packages were returned by the patients.

We received packages from 825 patients, of which 787 were eligible for the study; 38 patients did not meet the inclusion criteria—they were not sexually active during the past year (17), males (two), age  $> 40$  (six), missing questionnaire (six), controls of treated infections (six), wrong type of swab (one). Women who had taken azithromycin or doxycycline in the month before entering the study ( $n = 11$ ) were counted for the prevalence, but were not considered in risk factor modelling.

### Patient characteristics

Age of participants varied from 14–40 years with a mean age of 25.2 years. In all, 64.9% of the women lived with their parents or without a partner; 31.7% were married or cohabitating and 3.4% were separated, divorced, or widowed; 33.1% were in general secondary school or had a secondary school degree; 20.5% followed technical secondary school classes, or had a technical secondary school degree; 20.2% had attended or were attending higher education courses (apart from high school); 22.4% had a high school or university qualification or were getting one; and 3.9% had no qualifications or followed evening classes.

Overall prevalence of *Chlamydia trachomatis* was 5.0% (95% CI: 3.5 to 6.5). Prevalence according to age was 2.0% (1/50) for women aged 14–17, 6.6% (15/227) for women aged 18–22, 5.8% (15/260) for women aged 23–27, 3.6% (8/220) for women aged 28–35, and 0.0% (0/30) for women aged 36–40.

At least five infected patients (12.8%) had symptoms which could be related to complicated chlamydial disease: unexplained lower abdominal pain (two) or difficulties in becoming pregnant (three). One patient was diagnosed with fulminant PID, 1 week after participating in the screening. All patients returned for treatment. Notification of partners was voluntary and contact tracing was performed by most GPs through patient referral.

Table 1 shows determinants of infection in univariate analysis, which were selected for multivariate modelling

**Table 2** Determinants of chlamydial infection: logistic regression model

Determinant	Coefficient (SE)	Adjusted odds ratio (95% CI)	p Value
Age			
14–17	–0.634 (1.184)	0.530 (0.052 to 5.397)	0.592
18–22	1.422 (0.537)	4.145 (1.446 to 11.879)	0.008
23–27	1.284 (0.526)	3.612 (1.289 to 10.119)	0.015
28–40		1	
Number of partners last year			
1		1	
2	1.794 (0.499)	6.013 (2.263 to 15.974)	0.000
3–5	2.178 (0.552)	8.832 (2.991 to 26.074)	0.000
$\geq 6$	2.277 (0.642)	9.748 (2.771 to 34.296)	0.000
Contraception			
Any		1	
None	2.438 (0.441)	11.452 (4.823 to 27.192)	0.000
Dysuria/frequent urination			
No		1	
Yes	0.883 (0.429)	2.418 (1.043 to 5.605)	0.040
Partner having urinary complaints			
No		1	
Yes	2.050 (0.534)	7.765 (2.726 to 22.119)	0.000
Postcoital bleeding			
No		1	
Seldom	0.214 (0.494)	1.238 (0.470 to 3.262)	0.666
Frequently	3.048 (0.984)	21.080 (3.066 to 144.951)	0.002
Location of practice			
Inner city		1	
Suburban/rural	–1.135 (0.649)	0.321 (0.090 to 1.147)	0.080
Constant	–1.979 (7.355)	0.138	0.788

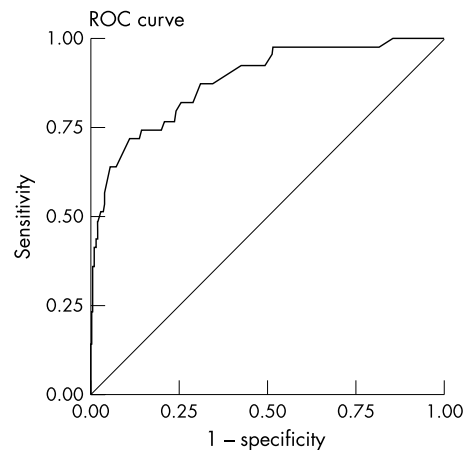
( $p < 0.3$ ). In general, behavioural factors and urogenital complaints were more significant than sociodemographic characteristics.

Variables not selected for multivariate analysis were parity, sexual inclination, menarche, lower abdominal pain, vaginal douching, vaginal itching, dyspareunia, previous STI diagnosis, being sterilised, and irregular intake of contraceptive pill.

Table 2 shows determinants of chlamydial infection in a multivariate logistic regression analysis. The resulting model was not altered by introducing different combinations of non-significant variables as possible confounders. Interaction terms were taken into consideration, but were not included as they did not significantly improve the model.

In figure 1, accuracy of the regression model—that is, the ability of the model to correctly classify women with and without infection, is visualised in a receiver operating characteristic (ROC) curve. The area under the curve is 0.88, indicating excellent accuracy.

From this model, a simplified screening algorithm was derived, which is applicable in clinical practice. To evaluate the



**Figure 1** Discriminative power of the regression model visualised in a receiver operating characteristic (ROC) curve. Area under the curve is 0.88.

**Table 3** Usefulness of determinants of infection for screening purposes

Determinant	Sensitivity (%)	Percentage of population	Prevalence in population with determinant (%) (positive predictive value)
Age 18–27	76.9	62.0	6.2
>1 partner in the past year	66.6	30.6	10.9
No contraception	48.7	17.1	14.3
Dysuria/frequent urination	33.3	16.0	10.5
Partner having urinary complaints (dysuria/discharge)	20.5	5.0	20.5
Frequent postcoital bleeding	7.6	1.2	33.3
Location of practice (inner city)	92.3	72.8	6.4

usefulness of each determinant for screening, the magnitude of the odds ratio was considered by function of the prevalence of the determinant. For example, postcoital bleeding is a strong determinant of infection, but is rare, thus usefulness for screening is limited. Table 3 shows the relevance of each variable for screening purposes.

From this analysis we derived the following screening model:

- To screen all women under 35 with >1 partner in the past year

and

- To screen all women with two of the following characteristics: age 18–27 years, frequent postcoital bleeding, no contraception, a partner with urinary complaints.

In this model 92.3% of infections are detected and 37.5% of the population is screened.

Prevalence in the screened population is 12.4% in this model.

## DISCUSSION

The significant burden of undiagnosed CT infection observed in this study indicates that screening should be considered.

Our data show that targeted screening on the basis of a simple, evidence based algorithm is possible, even in a heterogeneous group of general practice attendants.

In our study, not all consecutive eligible women were offered screening, mostly because of the high additional workload for the GPs. Some selection bias, because of unintended selection of patients, cannot be excluded. Furthermore, although participation rate is satisfactory and is considerably higher than in community based screening programmes,<sup>15,16</sup> the dropout of 25% non-participants can affect the results. However, the sociodemographic structure of our study population (as shown in table 1) reflects quite well the constitution of the general practice population in Antwerp in this age category. Behavioural characteristics are comparable to those in the recent British national survey of sexual attitudes and lifestyles (NATSAL 2000)<sup>3,17</sup>: mean age of first sexual intercourse was 17.5 years, versus 17 years; 8.6% (versus 12.6%) was ever diagnosed with an STI; 14.1% of women with one partner in the past year and 28.7% of women with more than one partner reported consistent condom use in the past year (*v* 16.8% and 24.1% of women who reported consistent condom use in the past 4 weeks in the NATSAL survey).

If the sample examined was not representative of the general population, it surely is a clinically relevant sample, representing a population that is accessible by healthcare providers and is willing to undergo screening.

A strong association between infection and very young age, as observed in the United States and in high risk populations (STD, family planning, abortion clinics) in Europe, was not found in this study. Low prevalence in the relatively small sample of participants aged 14–17 is confirmed by a recent

study in secondary schools in the same area.<sup>18</sup> A substantial prevalence is still found in women in their late 20s. STI surveillance data in Belgium reveal that half of diagnosed chlamydial infections are in women >25 years.<sup>19</sup> Similar data have been reported in other European studies in general practice, in which young age was not<sup>15</sup> or only slightly<sup>20</sup> associated with an increase in infection risk. Others reported higher prevalences in women under 25 than in those over 25, but the absolute number of diagnosed infections in the older group was equally high<sup>21</sup> or even higher<sup>17</sup> than in the younger group. This finding is important, because screening programmes traditionally focus on women under 25,<sup>3,22</sup> passing over a substantial group of accessible women at risk, who often have not started to form a family and become pregnant. Extending the target group would yield more health gain, not only for these women, but also on the population level, resulting in greater decline of prevalence rates.<sup>23</sup>

Likewise, in high risk groups, chlamydial infection was found to be linked to various sociodemographic characteristics, such as low education, nulliparity, or single status; these associations are far less significant in the general population and tend to incorrectly classify too many women at risk of chlamydial infection, thus reducing effectiveness of screening.

Urogenital symptoms are strong but infrequent determinants of CT infection. A pill check or routine gynaecology consultation is an ideal opportunity to establish whether any suggestive symptoms are present—often too mild to be mentioned spontaneously.

In this study, behavioural factors are the best determinants of infection. These are reasonably the most direct risk indicators and are probably the most constant predictors in changing times and social structures.

The performance of the model presented (measured as percentage of detected infections/screened population), which is not based on age but on the number of partners in the past year as the primary determinant for screening, is better than earlier reported models in general practice settings. The validity of the model has to be assessed. If successfully implemented, this model could be an important public health intervention for the control of STI in the general population. However, large scale implementation of this strategy will demand sustained efforts from healthcare providers, as it is far more easy for a physician to assess his female patient's age or education level than to specifically and actively ask some questions related to her sexual activities. The latter is labour intensive and requires considerable communication skills, especially since STI issues have to be raised with asymptomatic patients.<sup>24</sup> It is well documented that STI counselling in primary care is rarely performed and often inadequate.<sup>25,26</sup> However, the specific general practice setting offers unique opportunities, not only to estimate STI risk, but also to discuss sexual health in a broader context. Therefore, in order that primary care based CT control programmes have a chance to succeed, educating physicians is a preliminary condition.

## CONTRIBUTORS

VV is guarantor for the study and contributed to study design, data analysis and interpretation, and drafting the manuscript; DA and PVR contributed to study conception, data analysis, and interpretation; MI, HG, SC, and CL contributed to diagnostic and organisational aspects of the study; AM contributed to data interpretation and drafting the article. All co-authors approved the final manuscript.

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