

Opportunistic testing for urogenital infection with *Chlamydia trachomatis* in south-western Switzerland, 2012: a feasibility study

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The feasibility of opportunistic screening of urogenital infections with *Chlamydia trachomatis* was assessed in a cross-sectional study in 2012, in two cantons of south-western Switzerland: Vaud and Valais. Sexually active persons younger than 30 years, not tested for *C. trachomatis* in the last three months, were invited for free *C. trachomatis* testing by PCR in urine or self-applied vaginal swabs. Of 2,461 consenting participants, 1,899 (77%) were women and all but six (0.3%) submitted a sample. Forty-seven per cent of female and 25% of male participants were younger than 20 years. Overall, 134 (5.5%) of 2,455 tested participants had a positive result and were followed up. Seven per cent of all candidates for screening were not invited, 10% of invited candidates were not eligible, 15% of the eligible candidates declined participation, 5% of tested participants testing positive were not treated, 29% of those treated were not retested after six months and 9% of those retested were positive for *C. trachomatis*. Opportunistic *C. trachomatis* testing proved technically feasible and acceptable, at least if free of charge. Men and peripheral rural regions were more difficult to reach. Efforts to increase testing and decrease dropout at all stages of the screening procedure are necessary.

Introduction

Chlamydia trachomatis is a frequent cause of sexually transmitted urogenital infections [1]. Carriers with asymptomatic infection are a difficult to reach reservoir promoting transmission to their sexual partners [2]. Complications, although rarely life threatening, can be substantial, especially for women. They include pelvic inflammatory disease, chronic abdominal pain, ectopic pregnancy, tubal sterility [2] and possibly a higher risk for adverse pregnancy outcomes [3,4].

Rates of *Chlamydia*-related complications in a given population correlate with the prevalence of chlamydial infection [5]. Treatment of urogenital infections caused by *C. trachomatis* can prevent complications, at least in the short term [6,7]. The pooled risk ratio for all-cause pelvic inflammatory disease after one year of follow-up in women invited to have *C. trachomatis* screening in four randomised controlled trials was 0.64 (95% confidence interval (CI): 0.45–0.90) [2]. Complications may occur despite regular screening at fixed intervals because of infection after treatment or during screening intervals [8,9]. It has also been hypothesised that early treatment may impede development of immunity and favour future re-infection [10,11].

Following a decline in the late 1980s and early 1990s, laboratory notifications of infections with *C. trachomatis* in Switzerland have more than quadrupled since 2000 [1,12]. In 2003, most infections were diagnosed by gynaecologists, hospital services and primary healthcare physicians [13]. One study, published in 1989, found a positive culture rate of 18% in 600 women aged 18 to 55 years at a sexual health centre in Lausanne [14]. Half of these women (49%) were symptomatic. More recent studies in Switzerland using PCR testing found lower rates: In 1998, 1% of 817 pregnant women and 2.8% of 772 other sexually active women were found to be PCR-positive for *Chlamydia* by their gynaecologist [15]. In 2006 and 2007, 1.2% of 517 male Swiss military recruits with a mean age of 20 years were found by PCR to be infected [16], as were 7.3% of 386 healthy pregnant women in the period from 2006 to 2009 [4].

The European Centre for Disease Prevention and Control (ECDC) recommends implementation of *C. trachomatis*

control using a strategy of four levels: primary prevention, case management, opportunistic testing and systematic screening [2,17]. In Switzerland, a national programme for primary prevention of human immunodeficiency virus (HIV) infection was started in 1987, and subsequently widened in 2011 to all sexually transmitted infections (STI) [18]. A national guideline for case management of STI including *C. trachomatis* was published in 2011 [19], but no recommendations exist for testing. A *C. trachomatis* test with administration fees costs CHF 119 (EUR 111), not including any medical consultation fees. These costs are reimbursed by basic insurance when the yearly medical costs exceed CHF 300 (EUR 281). The young and healthy without other health expenses therefore pay screening costs directly.

This study explores the feasibility of opportunistic testing for *C. trachomatis* control, the third level in the ECDC recommendations. From a public health perspective, feasibility should be examined at all stages of programme implementation, from societal to individual level. These may be conceptualised as political acceptance, provider compliance, target population acceptance, and user compliance. We report on feasibility at all of these levels.

Methods

The study was conducted in two cantons with a combined population of 1 million, situated in the south-western part of Switzerland: Valais and Vaud. The capital cities of Vaud and Valais, Lausanne and Sion, have 142,000 and 42,000 inhabitants, respectively. Both cantons have rural districts, some of them extending into partially remote alpine valleys. Most districts are French speaking; German is spoken in the eastern districts of Valais (about one in twelve of the total study population).

Free *C. trachomatis* testing in first-void urine or, for women according to personal preference, self-applied vaginal swabs, was offered from February to August 2012 to all persons younger than 30 years in public health services representative of the whole territory. These included all centres of two public cantonal sexual health networks (eight in Vaud, including seven with an on-site physician; five in Valais, none with on-site physicians) and, for comparison, two infectious disease (ID) outpatient clinics (Sion and Visp, Valais). As the number of available tests was restricted by the allocated study budget, the recruitment period was shortened in centres with high testing activity in order to allow testing in centres with lower throughput. Every candidate, defined as a female or male person visiting a screening centre or clinic, was given an invitation (invited candidates) for screening together with an information sheet about *C. trachomatis*. Individuals who had never had sexual intercourse or who had been screened for urogenital *C. trachomatis* infection less than three months previously were excluded. Participation was confirmed by written consent. Consenting participants (Figure 1) were given a questionnaire on demographics and

sexual behaviour and a self-sampling kit with illustrated instructions on how to sample urine and, for women, how to take a vaginal swab.

The urine and vaginal swab samples of tested participants were collected at the screening centre and centrally analysed by PCR. In Valais, a commercial kit (Roche Diagnostics, Switzerland) was used by the Central Institute laboratory for molecular biology, Sion (Institut Central Hôpital du Valais; ICHV). In Vaud, a validated in-house *C. trachomatis* PCR [20] was used by the Institute of Microbiology of the University of Lausanne (IMUL).

According to the participant's choice, treatment for *Chlamydia* was organised with their primary care physician or gynaecologist, at the screening centre or at the nearest centre with an on-site physician. Partner notification was recorded for each infection. Screening for other STI and preventive counselling were left to the discretion of the treating physician. A control visit, involving a second free test for *C. trachomatis*, was scheduled for cases with documented infection six months after treatment. Each screening centre had to document for each candidate all the steps up to either a negative screening result or, in the case of a positive result, the negative control test result six months after treatment. The first step not fulfilled was noted as the point of drop-out.

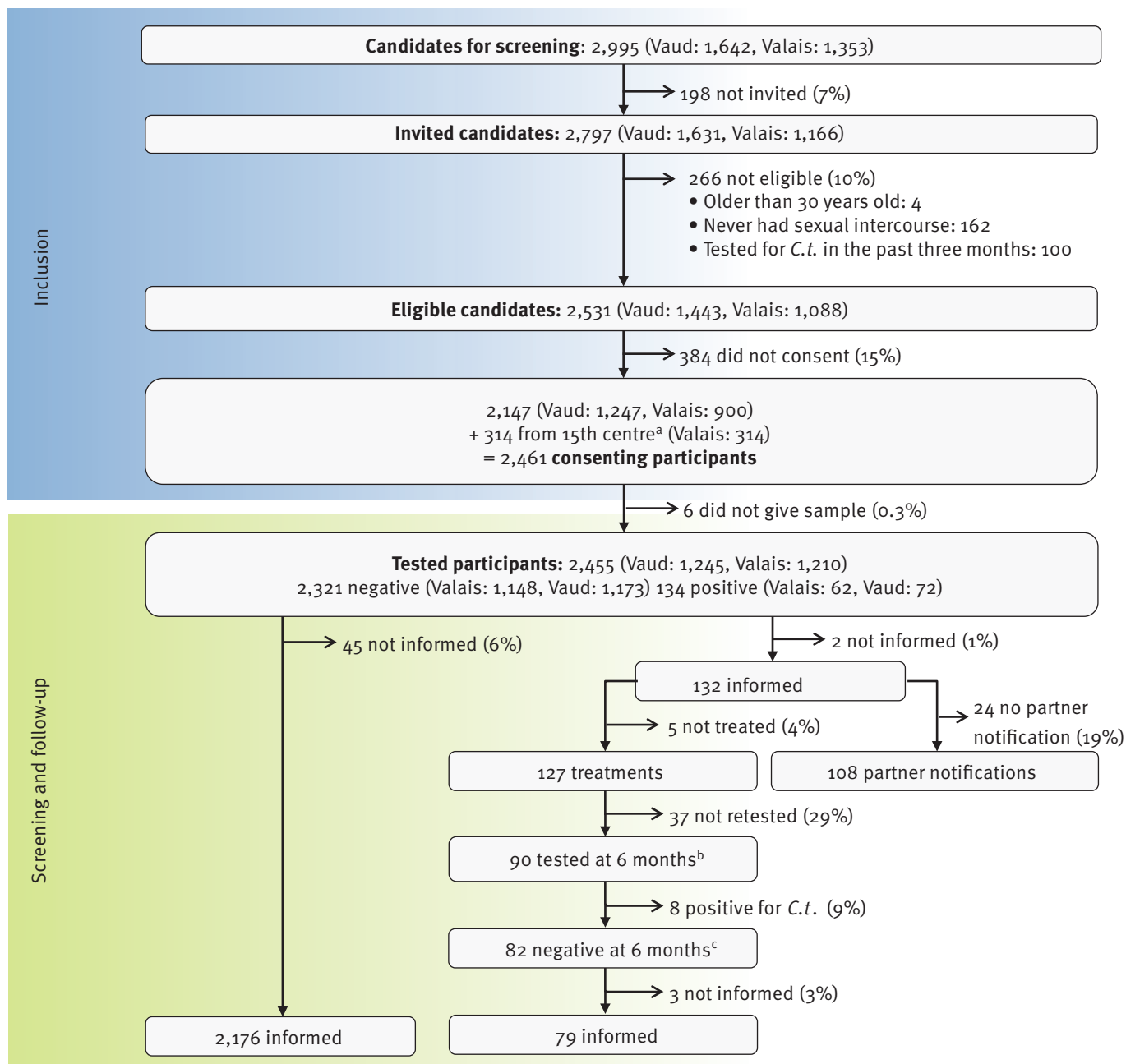
The study protocol was submitted and accepted by the ethical committee in each participating canton (Valais: no. CCVEM 023/11; Vaud: no. 281/11). The study was supervised by a committee of representatives of the participating screening centres, the public health authorities and the testing laboratories. It also included a research specialist from the University Institute of Social and Preventive Medicine, Lausanne.

Descriptive statistics and comparisons (Fisher's exact test for 2x2 tables (proportions), chi-square test for other tables and Kruskal-Wallis test for continuous variables) and other calculations were produced with open source R, version 3.0.3 [21]. Confidence intervals for proportions were calculated with the asymptotic definition for confidence limits on a single proportion using the Central Limit Theorem (binom.test function in package binom).

Results

Results regarding each successive level of the study flow are summarised in Figure 1.

Provider compliance, assessed by rates of screening invitations, and target population acceptance, assessed by rates of participation, could be monitored in 14 of the 15 screening centres, totalling 2,995 candidates between February and December 2012. One centre did not consistently distinguish between non-invitation and non-participation and was therefore excluded from this part of the analysis. This centre was

FIGURE 1Study flowchart, *Chlamydia trachomatis* screening, Switzerland, 2012 (n = 2,995)

C.t.: Chlamydia trachomatis.

^a One of 15 centres did not consistently distinguish between non-invitation and non-participation and was excluded from the inclusion part of analysis. This centre provided an additional 314 consenting participants included in screening and follow up.

^b Control test by PCR at 6 months after treatment.

^c Negative control test by PCR at six months after treatment.

TABLE 1

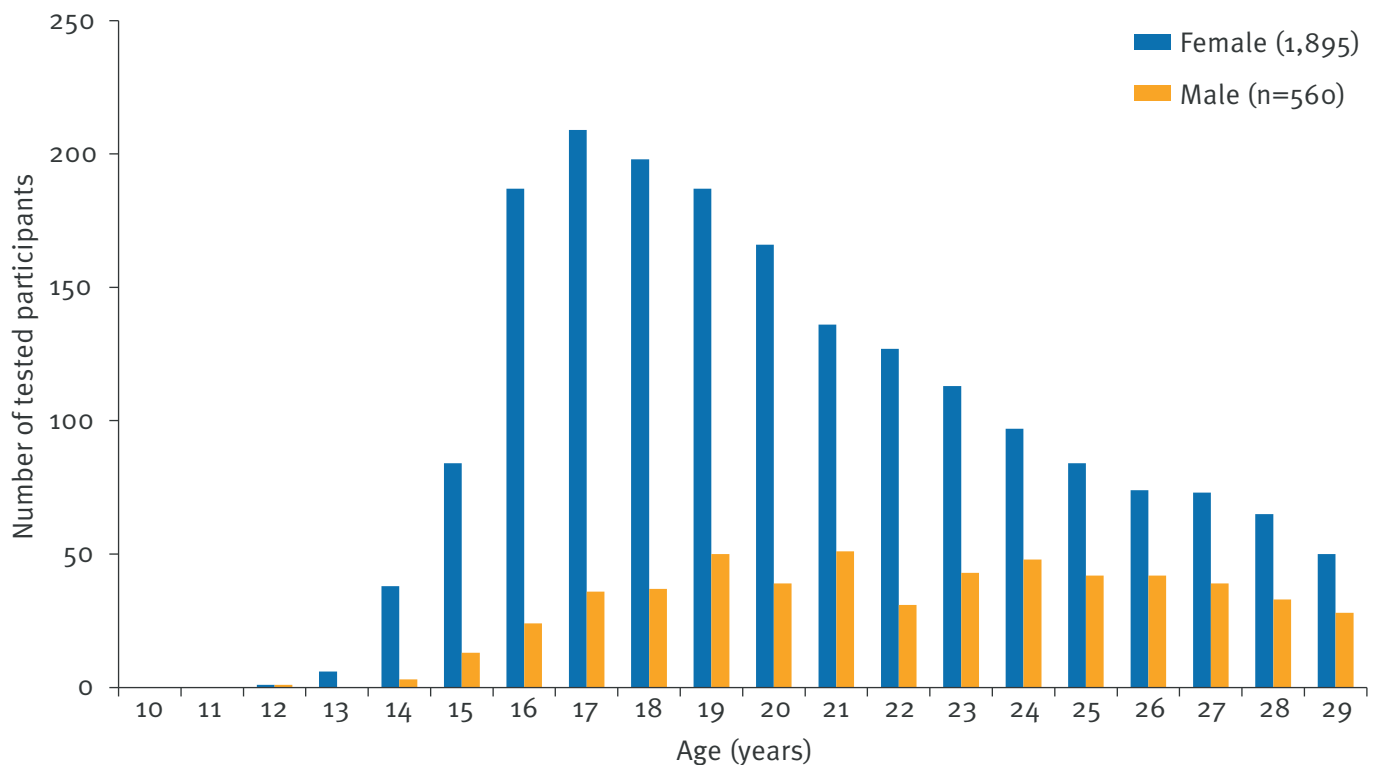
Reasons given for declining *Chlamydia trachomatis* screening by 269 of 384 persons invited in 14 of 15 screening centres, Switzerland, 2012 (n = 269)

Reason	Vaud	Valais	All
Not interested / not in the mood	46 (30%)	34 (30%)	80 (30%)
No time	11 (7.1%)	37 (32%)	48 (18%)
Believes to be at too low risk to justify screening	14 (9.1%)	10 (8.7%)	24 (8.9%)
Long-term stable relationship	16 (10%)	2 (1.7%)	18 (6.7%)
Believes not to be at risk (always protected sexual intercourse or mutual first partners)	9 (5.8%)	6 (5.2%)	15 (5.6%)
<i>C. trachomatis</i> screening already done before study	3 (1.9%)	5 (4.3%)	8 (3.0%)
Doesn't speak the language (French or German)	4 (2.6%)	2 (1.7%)	6 (2.2%)
Cannot urinate	5 (3.2%)	2 (1.7%)	7 (2.6%)
Wishes parental advice first	5 (3.2%)	0 (0%)	5 (1.9%)
Wants to go somewhere else for screening	3 (1.9%)	2 (1.7%)	5 (1.9%)
Other reasons	38 (25%)	15 (13%)	53 (20%)
Total	154 (100%)	115 (100%)	269 (100%)
No reason given			115
Total of declined invitations			384

The invited persons declining screening were encouraged to write down their reasons not to participate. These reasons in free text were grouped together.

FIGURE 2

Age distribution of tested participants, *Chlamydia trachomatis* screening, Switzerland, 2012 (n = 2,455)



910 (48%) of all female tested participants were younger than 20 years, 129 (6.8%) younger than 16 years.

164 (29%) of all male tested participants were younger than 20 years, 17 (3.0%) younger than 16 years.

TABLE 2

Characteristics of tested participants and questionnaire answers, *Chlamydia trachomatis* screening, Switzerland, 2012 (n = 2,455)

Number of answers (total)	Vaud		Valais		p value	All	
	1,245		1,210			2,455	
	Proportion of positive answers	Positive/total answers	Proportion of positive answers	Positive/total answers		Proportion of positive answers	Positive/total answers
Demographic information							
Female sex	88%	1,091/1,245	66%	804/1,210	<0.0001	77%	1,895/2,455
Women: pregnant	3.0%	33/1,085	4.8%	38/790	0.051	3.8%	71/1,875
Mean age (years)	21.2	n = 1,245	21.6	n = 1,210	0.047	21.4	n = 2,455
Median age (years)	20.6	n = 1,245	21	n = 1,210	0.047	21.4	n = 2,455
≤ 16 years-old	5.9%	73/1,245	6%	73/1,210	>0.1	5.9%	146/2,455
≤ 20 years-old	45%	559/1,245	43%	515/1,210	>0.1	44%	1,074/2,455
Motive for consultation							
Sexual health	67%	819/1,228	32%	380/1,203	<0.0001	49%	1,199/2,431
STI screening	23%	285/1,228	38%	462/1,203	<0.0001	31%	747/2,431
Pregnancy	1.5%	18/1,228	5.1%	61/1,203	<0.0001	3.3%	79/2,431
Pregnancy interruption	1.1%	14/1,228	1.2%	14/1,203	>0.1	1.2%	28/2,431
Symptoms of active STI	4.4%	54/1,228	1.2%	15/1,203	<0.0001	2.8%	69/2,431
Travel ^a	NA	NA	15%	177/1,203	<0.0001	7.3%	177/2,431
No link to sexual health ^b	0.41%	5/1,228	4.4%	53/1,203	<0.0001	2.4%	58/2,431
Other	2.7%	33/1,228	3.4%	41/1,203	>0.1	3%	74/2,431
Questionnaire							
Heard of <i>C. trachomatis</i>	49%	605/1,243	34%	407/1,207	<0.0001	41%	1,012/2,450
Subjective symptoms of STI present	6.4%	79/1,236	5.1%	61/1,201	>0.1	5.7%	140/2,437
Tested for <i>C. trachomatis</i>	22%	267/1,241	3.9%	47/1,202	<0.0001	13%	314/2,443
Born in Switzerland vs other	73%	908/1,243	81%	975/1,208	<0.0001	77%	1,883/2,451
Resident in a commune < 10,000 inhabitants	52%	628/1,210	64%	756/1,183	<0.0001	58%	1,384/2,393
Mean age at first sexual intercourse (years)	16.4	n = 1,240	16.4	n = 1,196	>0.1	16.4	n = 2,436
Median age at first sexual intercourse (years)	16	n = 1,240	16	n = 1,196	>0.1	16.4	n = 2,436
Having had heterosexual intercourse	99%	1,210/1,228	97%	1,153/1,185	0.044	98%	2,363/2,413
Having had homosexual intercourse	5.3%	65/1,222	6.4%	75/1,175	>0.1	5.8%	140/2,397
Mean number of sexual partners in the past 6 months	1.8	n = 1,238	1.7	n = 1,200	>0.1	1.7	n = 2,438
Median number of sexual partners in the past 6 months	1	n = 1,238	1	n = 1,200	>0.1	1.7	n = 2,438

NA: not applicable; STI: sexually transmitted infection.

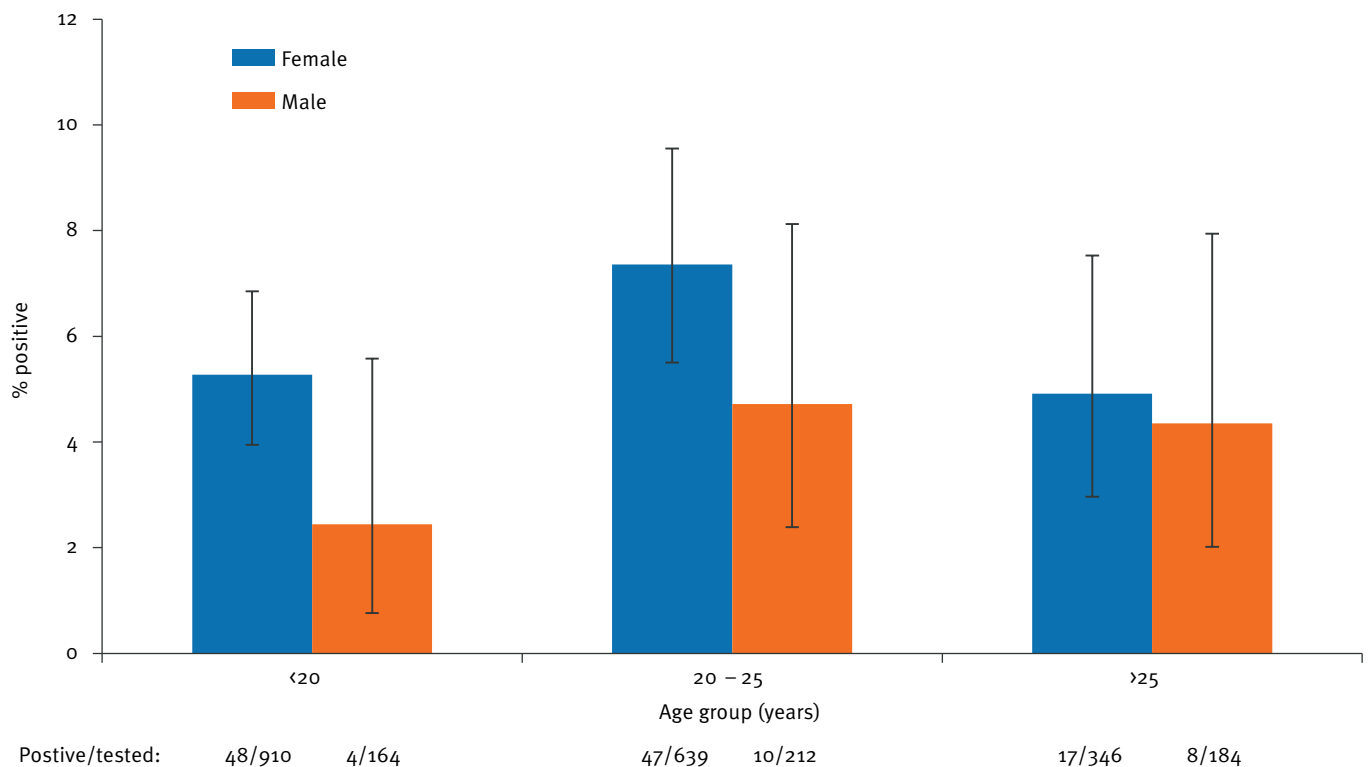
Statistic tests (comparisons between the two cantons): for proportions (2x2): Fisher's exact test; for continuous data: Kruskal-Wallis. p values are not corrected for multiple testing. Totals can be lower than those in the column header because of missing answers or counts in subpopulations.

^a Valais: travellers coming for vaccination (infectious disease clinic in Sion).

^b Valais: mostly patients treated for other infectious diseases such as HIV and hepatitis C (infectious disease clinic in Sion).

organised as a walk-in clinic and was overwhelmed by candidates. Its recruitment rate was only 314 participants for 1,522 candidates (21%), compared with 2,147 of 2,995 (72%) for the 14 other centres combined ($p < 0.001$). In these 14 centres, 2,797 of the 2,995 candidates (93%) were invited for screening; the individual centres' invitation rates ranged from 78% to 100%. Of the 2,797 invited candidates, 2,531 (90%) were eligible and 2,147 of those (85%) accepted screening. Acceptance rates were the same (85%) for both sexes (with seven (0.3%) missing answers) and differed little by age group (< 20 years: 920/1,069 (86%); 20 to < 25 years: 748/844 (89%); 25 to 29 years: 478/553 (86%);

missing answers: 65 (2.6%); $p > 0.05$). Acceptance rates were highest in those primarily consulting for STI screening or diagnosis, with or without symptoms of STI, or for other reasons related to sexual health, with rates of 659 of 704 (94%) and 1,165 of 1,318 (88%), respectively. Of 383 persons consulting for reasons unrelated to sexual health, 300 (78%) accepted screening ($p < 0.001$). 126 answers (5%) were missing, more frequently in those declining screening (27%) than in those accepting (1%). Acceptance rates per screening centre ranged from 58% to 91% and were higher in French-speaking centres than in German-speaking ones (2,083/2,432 (86%) vs 64/99 (65%); $p < 0.001$). Of

FIGURE 3*Chlamydia trachomatis* infection rate by age group, Switzerland, 2012 (n = 2,455)

Bars show 95% confidence intervals.

the 384 persons declining screening, 269 gave a reason. These were grouped into categories, as shown in Table 1.

Including data from all 15 centres, there were a total of 2,461 consenting participants (Vaud: n = 1,247, Valais: n = 1,214). Of these, 2,455 (99.8%) provided a test sample and a questionnaire. Of the tested participants, 1,895 (77%) were women (Vaud: 1,091 (88%), Valais: 804 (66%)), of whom 358 (19%; Vaud: 299 (28%), Valais: 59 (7.3%)) chose to supply a vaginal swab and 1,537 (81%) chose to supply first-void urine. Age distribution, demographic data, reason for consultation and other information in the questionnaire are provided in Figure 2 and Table 2.

A mean of 149 consenting participants (125 women, 24 men) were tested per week when all centres were open. Extrapolated over 52 weeks, assuming access to testing under the same conditions and 82% of the population sexually active (personal communication: Locicero S, Spencer B, July 2014), 3.7% (6.7% of women, 1.2% of men) of the sexually active population aged between 12 and 29 years in 2012 in the study region [22] would have been tested.

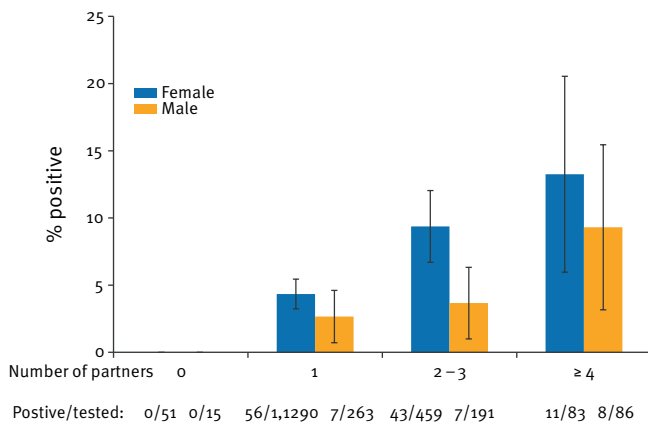
A PCR test result was available for all 2,455 samples (Figure 1). 134 samples (5.5%, 95% CI: 4.6–6.4; Vaud 5.8%, Valais 5.1%) proved to be positive for *C. trachomatis*: 112 of 1,895 women (5.9%, 95% CI: 4.8–7.0) and 22 of 560 men (3.9%, 95% CI: 2.3–5.5). The median age and youngest age with a positive screening result were 20.6 and 14.0 years, respectively, for female participants and 23.5 and 17.0 years, respectively, for male participants. Infection rates in women were significantly higher at age 19 to 22 years compared with those younger or older (Figure 3) and peaked in the age group 20 to 22 years (9.9%, 95% CI: 6.6–13.3). Twelve infections were found in 88 women (14%, 95% CI: 6.4–20.8) who were 13 years-old or younger at their first sexual intercourse. Lower numbers preclude a similar analysis for male participants.

A treatment consultation was arranged for 127 of 134 participants with documented infection (95%). Of these, 90 (71%) were retested after six months, with 82 (91%) negative results. Some 108 partners of 134 participants with infection (81%) were notified, 94 (87%) by the participants themselves and 14 (13%) by the screening centre.

Infection rates were similar for different educational levels, districts of residence, sizes of population of

FIGURE 4

Chlamydia trachomatis infection rate by number of sex partners in the six months before screening, Switzerland, 2012 (n=2,438; 17 missing answers)



Bars show 95% confidence intervals.

the town of residence ($\geq 10,000$ vs $<10,000$ inhabitants) and country of birth (Switzerland vs other). No infection was found in 66 female participants indicating no sexual partner in the last six months. The four districts with only one, seven, 13 and 39 tested participants reported zero infections. Infection rates were higher for sexual health patients (including general counselling, gynaecology checks, pregnancy, STI screening) than for patients in travel clinics and other sources, with infection rates of 127 of 2,122 (6.0%, 95% CI 5.0%–7.0%), two of 177 (1.1%, 95% CI 0–2.7%) and five of 156 (3.2%, 95% CI 0.4–6.0%), respectively. Patients in travel clinics were older than sexual health patients at screening (median age: 24.8 vs 20.6 years, $p < 0.0001$) and at their first sexual intercourse (median age: 17 vs 16 years, $p < 0.01$). Of all 134 infections, 63 (47%) were found in participants indicating one sexual partner in the last six months. For both sexes, the infection rate increased with an increasing number of sexual partners in the six months before screening (Figure 4), with 19 infections in 169 participants (11%, 95% CI: 6.5–16.0) indicating more than three sexual partners in the last six months. Of 140 (5.7%) participants reporting symptoms of STI, 16 (11%) had a positive screening test.

In 2012, 974 *Chlamydia* infections were notified by laboratories in the study region (not including those found in this study). Extrapolating the study experience over one year, 375 infections in women (infection rate 5.9%) and 47 in men (infection rate 3.9%) could have been diagnosed by the study test centres, increasing the study region's total number of diagnosed infections by 422 infections (43%).

Discussion

Independently of the on-site presence of a physician, testing for urogenital infection with *C. trachomatis* in sexually active adults younger than 30 years using self-applied urine samples, or, for women, vaginal swabs, proved technically feasible in the two Swiss cantons under study. When offered at no cost, *C. trachomatis* testing proved acceptable overall, despite the fact that almost half of participants had never previously heard of *C. trachomatis* infection (Table 2). Only 31% of all participants were consulting for HIV/STI-screening, mostly anonymous HIV-screening. *C. trachomatis* screening can be proposed successfully in situations other than STI screening, particularly those related to sexual health, but also in those a priori unrelated to sexual health such as travel counselling, with acceptance rates that were not much lower (78%), independently of factors such as age and sex. The German-speaking region, a more secluded and rural mountain community, had not only a lower acceptance rate, but significantly less consultation activity. This may be best explained by cultural factors resulting in less demand and geographical factors impeding easy access to testing facilities. With the exception of one walk-in facility, it was possible to integrate *Chlamydia* screening into the centres' daily workload without adjustment in the workforce or increased consultation times. The information sheet and illustrated instructions for sampling proved helpful. *C. trachomatis* PCRs exhibit similar positivity rates in urine and vaginal swabs, but urine sampling was preferred over vaginal swabs by ca 80% of women.

In this study, infection rates varied between 1% and 11%, depending on already known risk factors, and were not substantially different from infection rates reported in Switzerland and Europe [4,15,16]. Population-based studies in European Union Member States report infection rates between $<1\%$ and 10% for women and between $<1\%$ and 6% for men, depending on country and characteristics of the study population [2]. The National *Chlamydia* Screening Programme (NCSP) in the United Kingdom (UK) reported an infection rate of 7.7% in 2012 [23] and a Dutch pilot study (2008–2011) a rate of 4.3% [23,24]. Infection rates for men at similar risk are consistently lower than for women of the same age and level of risk [2,23,24]. Our study did not find different infection rates in individuals born in Switzerland vs those born elsewhere.

Nearly half of the female participants were younger than 20 years and the study participants had a profile of low to medium risk, with a median of one sex partner in the six months before screening. Half of all infections were therefore diagnosed in low-risk participants with only one sexual partner in the past six months. Although the questionnaire identified factors representing a relatively higher risk, such as presence of symptoms (11% positivity rate), being female and in the peak age group (10%) or having more than three sex partners in the six months before screening (11%),

the only characteristic specific to individuals with no risk of infection was having had no sex partner in the past six months (having been sexually active before). Risk-based selection algorithms aiming at improved cost effectiveness [25] may therefore miss a substantial number of infections occurring in parts of the population associated with lower risk.

Limitations and challenges

Despite *C. trachomatis* screening proving to be technically feasible and reliable and treatment being simple and affordable, important obstacles remain. Despite near universal insurance coverage, access to screening for *C. trachomatis* in Switzerland is limited owing to a mandatory minimal yearly participation of CHF 300 (EUR 280). The high cost of a *C. trachomatis* test needs to be reviewed in order to allow affordable access, especially for adolescents. Men proved to be more difficult to reach in this context, constituting only 23% of the sample. Male participants were older than female participants and the proportion younger than 20 years was significantly lower. In the NCSP, men were more likely to order self-applied tests on the Internet than to visit a clinic for testing, and the number of tests ordered in this way increased from <1% to 6% of all tests between 2006 and 2010 [26]. A screening programme in 13 schools in New Orleans, United States, in 1995 to 2005 showed up to 49% repeated testing in male students (with parental consent) [27]. Of men aged 18 to 35 years in a survey in the UK, 75% had seen their family doctor in the last year, without relevant differences between different age groups among the 18 to 35-year-olds, providing general practitioners with occasions for opportunistic STI screening [28]. In the NCSP, 9% of male 15 to 24 years-olds were tested by their general practitioner. Extrapolated over one year, the centres in our study alone would have tested a small proportion, ca 4%, of the 12 to 29 years-olds in the study region [1]. Such testing activity would thus have little impact on *Chlamydia* transmission or its prevalence on a population level. In Switzerland, gynaecologists, hospitals services and primary care physicians notified most of all notified *C. trachomatis* infections in 2003 [13], but those healthcare providers were not included in this study. School-initiated home testing in post-obligatory schools (age 16 years and upwards) was initially intended. The school authorities in one canton declined participation, which shows a limitation on political grounds.

Nineteen per cent of all partners of tested participants with a positive result could be notified. Most partner notifications were only documented by asking the study participants. Whether sex partners actually received treatment was not assessed. Ascertaining if all partners are treated is a difficult challenge [29] and would also have been difficult in this study.

Conclusions

C. trachomatis notifications in Switzerland have increased from 2,123 in 1999 to 9,701 in 2014. It remains

unknown if this trend corresponds to an increasing incidence or other factors such as increased screening or an increased notification rate. Based on our results four main statements can be made to inform the public health authorities of Valais and Vaud regarding preventive measures for urogenital *C. trachomatis* infection and its complications. Firstly, *C. trachomatis* is present in the study region and therefore screening and efficient treatment would be desirable to prevent complications, no less than in other countries with similar infection rates. Secondly, as this study shows that *C. trachomatis* screening in existing sexual health centres in south-western Switzerland is technically feasible, these screening services can also be used for epidemiological investigation. Thirdly, *C. trachomatis* testing at low and affordable cost could promote use by those at risk. Finally, more screening opportunities need to be created, especially for difficult to reach populations such as men or people living in regions with difficult access for geographical reasons, and drop-outs during the screening and follow-up process need to be decreased.

Acknowledgements

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Study organisation: Mandate Valais: the Service des maladies infectieuses, Institut Central (Hôpital du Valais – ICHV), was mandated by the Service de la santé publique de l'Etat du Valais. Vaud: the Fondation Profa, Consultations de santé sexuelle, was mandated by the Service de la santé publique de l'Etat de Vaud.

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Conflict of interest

None declared.

Authors' contributions

Frank Bally: Study preparation, writing of the study protocol, protocol submission (Valais and Vaud), study implementation (Valais), data administration and analysis, writing of report and manuscript, revisions, member of study committee. Adeline Quach: Study implementation (Vaud), protocol submission (Vaud), study preparation, protocol, revision of report and article, member of study committee. Gilbert Greub: Study preparation, protocol, revision of the article, member of study committee. Katia Jaton: Study preparation, protocol, organisation of laboratory tests (Vaud), revision of report and article, member of study committee. Christiane Petignat: Study preparation, protocol, revision of report and article, member of study committee. Christian Ambord: Member of study committee, acknowledgement of report and article. Jacqueline Fellay: Organisation of one testing site (Sion, Valais), member of study committee, acknowledgement of report and article. Eric Masserey: Study preparation, protocol, acknowledgement of report and article, member of study committee. Brenda Spencer: Methodological supervision, study preparation, protocol, revision of report and article, member of study committee.

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