Genital chlamydia prevalence in Europe and non-European high income countries: systematic review and meta-analysis

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Abstract

Background: Accurate information about the prevalence of *Chlamydia trachomatis* is needed to assess national prevention and control measures.

Methods: We systematically reviewed population-based cross-sectional studies that estimated chlamydia prevalence in European Union/European Economic Area (EU/EEA) Member States and non-European high income countries from January 1990 to August 2012. We examined results in forest plots, explored heterogeneity using the I^2 statistic, and conducted random effects meta-analysis if appropriate. Meta-regression was used to examine the relationship between study characteristics and chlamydia prevalence estimates.

Results: We included 25 population-based studies from 11 EU/EEA countries and 14 studies from five other high income countries. Four EU/EEA Member States reported on nationally representative surveys of sexually experienced adults aged 18-26 years (response rates 52-71%). In women, chlamydia point prevalence estimates ranged from 3.0-5.3%; the pooled average of these estimates was 3.6% (95% CI 2.4, 4.8, I^2 0%). In men, estimates ranged from 2.4-7.3% (pooled average 3.5%; 95% CI 1.9, 5.2, I^2 27%). Estimates in EU/EEA Member States were statistically consistent with those in other high income countries (I^2 0% for women, 6% for men). There was statistical evidence of an association between survey response rate and estimated chlamydia prevalence; estimates were higher in surveys with lower response rates, (p=0.003 in women, 0.018 in men).

Conclusions: Population-based surveys that estimate chlamydia prevalence are at risk of participation bias owing to low response rates. Estimates obtained in nationally representative samples of the general population of EU/EEA Member States are similar to estimates from other high income countries.

Introduction

Surveys of the population prevalence of *Chlamydia trachomatis* infections (commonly known as chlamydia) can provide information about the need for measures to prevent and control infection. *C. trachomatis* is the most commonly reported sexually transmitted infection (STI) and the most commonly reported of all notifiable infections in Europe and the USA [1,2]. *C. trachomatis* causes infection in the lower genital tract in women and men, which can result in upper genital tract complications and transmission of infection during pregnancy and labour [3,4]. *C. trachomatis* also increases susceptibility to, and infectiousness of, HIV infection [5]. Chlamydia prevalence data for adults aged around 25 years and younger are particularly useful for planning control measures because young adults are affected most [3]. Health authorities in some European and other high income countries recommend screening in this age group to allow both early treatment of asymptomatic infection and the prevention of long term complications [6-9].

National surveillance data report on diagnosed cases of chlamydia infection and reported rates vary widely; from two to 600 per 100,000 population in Europe [1]. These figures cannot be used as estimates of population prevalence, however. Chlamydia infections are mostly asymptomatic and rates of reported infection largely differences in levels of chlamydia testing between countries. Cross-sectional surveys of a representative sample of the general population (population-based surveys) [10] provide less biased estimates of the prevalence of a condition at a particular time than surveys of attenders at health care settings. Participation bias can, however, distort estimates of prevalence in any survey whenever there is incomplete participation [11]. Participation bias is more severe when the prevalence of the condition is low [12] and when participation rates are low, which is likely in surveys of sensitive subjects such as sexual behaviour and STI [12]. In several studies of chlamydia infection participants had higher levels of demographic characteristics or behaviours associated with chlamydia than non-participants [13-15], which would over-estimate prevalence.

National estimates of chlamydia prevalence in cross-sectional population-based surveys vary considerably, even between countries with similar levels of social and economic development [14,16-19]. Differences in chlamydia prevalence between countries could represent real differences in sexual behaviour patterns and chlamydia control efforts, but might also result from variations in study design and participation rates. The primary objective of this study was to systematically review studies reporting chlamydia prevalence in adult women and men in the general population of the European Union and European Economic Area (EU/EEA). A secondary objective was to investigate the association between survey response rate and estimated chlamydia prevalence in both EU/EEA and other high income countries [20].

Methods

We conducted a systematic review using a predefined protocol (Supporting information Text S1) and reported it in accordance with the guidelines on Preferred Items for the Reporting of Systematic Reviews and Meta-Analyses (PRISMA) [21]. The study is part of a project funded by the European Centre for Disease Control and Prevention, for which a technical report describes the results of a group of literature reviews about chlamydia epidemiology and control [22].

Inclusion and exclusion criteria

Eligible studies designs were: cross-sectional surveys that used population-based sampling methods and tested genital specimens from adult women and men for *C. trachomatis*. Studies with the following characteristics were excluded: serological studies and studies sampling only from extra-genital sites; participant age below 13 years; data published in letters, commentaries and editorials. We considered the following specific groups as part of the general population: school students if the sampling frame included all schools in the country or in a sub-national geographic region of a country; and military recruits in countries with compulsory military conscription.

The review focussed on adults in EU/EEA Member States at the time of the first database search. We included the following countries to improve the generalisability of our findings and statistical power of our analyses: non-EU/EEA countries in Europe; high income countries, as defined by the Organisation for Economic Cooperation and Development (OECD) [20].

Data sources and searches

We searched Ovid Medline, Embase, Popline and The Cochrane Library from January 1990 to 17th October 2011 without language restrictions and updated the search on 17th August 2012. Search strategies, adapted for each search engine, included terms for "chlamydia infection" and "prevalence" and individual names of EU/EEA Member States, or "Europe", or the non-European high income countries Australia, Canada, Israel, Japan, Korea, New Zealand and USA [20]. In addition we searched reference lists of potentially eligible studies and asked experts if they were aware of other studies. For countries with no publications identified in the first search we then used only the country name and the free text term "chlamydia" to find further publications. We included additional data from primary studies included in the review even if the additional publications were published after the search deadline. Supporting information Text S1 includes the full search strategy.

Study selection

Two suitably qualified reviewers (SR, KA-K) screened the titles and abstracts of all identified articles independently. The full text of potentially eligible studies was retrieved and two reviewers (SR, KA-

K) independently assessed each against predefined inclusion criteria. Studies were translated where necessary. A third reviewer (NL) resolved differences between reviewers if necessary.

Data extraction and quality assessment

Two reviewers (SR, KA-K, or SW) extracted data independently in duplicate onto standardised piloted forms in EpiData (EpiData Association, Odense, Denmark). If multiple publications were associated with a study, we extracted data from the primary publication first (assigned as the publication with the most detailed description of the survey methods). Data reported in the primary publication were used in the case of inconsistencies. The two reviewers compared the extracted data and resolved differences by discussion. If there was still a discrepancy, a third reviewer (NL) adjudicated. We did not contact authors for additional information.

The following information was extracted: study design; country; study population (sexually experienced only or all participants) and setting (national or sub-national); demographic characteristics; numbers eligible, invited and participating; numbers excluded with reasons; number with *C. trachomatis* detected; diagnostic test method; estimated prevalence and 95% confidence intervals (CI) reported in the study.

We used published guidelines for cross-sectional prevalence surveys to assess the risk of bias related to methodological aspects of included studies [11]. Two reviewers (SR, KA-K, or SW) assessed each study independently. Discrepancies were resolved by discussion or adjudication (NL). The items assessed included: representativeness of the target and source populations; similarity of responders and non-responders; achievement of planned sample size; use of standardised data collection methods; appropriateness of statistical methods; and response rate [11]. We pre-specified criteria to determine whether each feature had been adequately addressed, not adequately addressed, or if there was insufficient information to decide. The guideline defined an adequate response rate as >80% [11]. Few studies attained this level so we also recorded those with response rates of >60% and >70%.

Data synthesis and analysis

We analysed data for women and men separately. First, we estimated chlamydia prevalence using the number of positive chlamydia tests and the number of people tested. Where authors of included studies reported stratified sampling methods we used the published point estimate and 95% CI. Where simple random sampling was done and data were available, we calculated chlamydia prevalence (with binomial 95% CI).

We used forest plots to examine estimates of chlamydia prevalence. The I^2 statistic expressed the percentage of variation between estimates in different studies resulting from factors other than random variation [23]. As a guide, I^2 values above 25%, 50% and 75% are suggested as evidence of mild, moderate and severe between study heterogeneity. Low values of the I^2 statistic suggest that variability

between estimates is compatible with random variation [23]. Where there was evidence of moderate or severe heterogeneity, we explored reasons for this by stratifying studies in pre-defined groups: age ≤25 years; geographic coverage (national or sub-national); and study population analysed (all adults or sexually experienced adults only). Where appropriate, we pooled estimates using random effects meta-analysis to estimate the average of the study estimates and their 95% CI.

We calculated a response rate for each study, using an algorithm to define numerators and denominators consistent with recommendations of the Council of American Survey Research Organisations (CASRO) [24,25]. Where available, the numerator was the number of people providing a sample for chlamydia testing and the denominator was the number of eligible subjects asked to participate, provide a sample, or sent an invitation for testing. If the study report did not include these numbers we used the number of samples tested, followed by the number of test results used in the analysis as the numerator and the number of eligible people as the denominator. We used the published response rate in studies that used complex sampling methods and post-stratification weighting. It was not possible to calculate a response rate in studies in which the group asked to participate is then asked if they have ever had sexual intercourse and chlamydia testing is restricted to those who are sexually experienced. In such studies, the calculated response rate is underestimated.

We used meta-regression to examine the linear association between estimated chlamydia prevalence in ≤25 year old women and men and the calculated response rate. We applied the sex-specific response rate for the whole study to this age group because most study reports did not report age-specific response rates. In these analyses, the I^2 statistic represents the percentage of heterogeneity due to factors other than sampling error after taking into account the association between prevalence and response rate. We also used meta-regression to analyse the association between estimated chlamydia prevalence and the following binary variables: sex (women versus men), age (≤25 years versus >25 years), geographical setting (national versus sub-national) and response rate as reported in the included studies (<60% versus ≥60%). We included a term for the individual study in the model when observations from the same study were not independent. All analyses were done using Stata statistical software (Stata 11, StataCorp, Austin, Texas, USA).

Results

The search strategy gave a total of 1003 hits after de-duplication (Figure 1). We included 25 primary studies (59 publications) in the populations of 11 EU/EEA countries [14,16,17,19,26-46] including Croatia, which became a Member State in July 2013 (Figure 1) and 14 studies (32 publications) in five non-EU/EEA countries: Switzerland [47], Australia [48-51], Canada [52,53], New Zealand [54] and the United States [18,55-59]. We did not find any eligible studies from Israel, Japan or Korea. In the included studies, 121,915 (median 953, interquartile range 471 to 2,350) people in total were tested for chlamydia. Table 1 summarises the characteristics of each study.

Twenty seven studies included women and men [14,16-19,26,29-36,41,43,45,46,48,49,51-54,57-59], six included only women [27,37-39,50,55] and six included only men [28,40,42,44,47,56]. The age group ranged from 15 to 17 years in a nationally representative survey in Germany [31] to 15 to 65 year olds in a single Arctic community in Canada [53]. Included studies ranged from nationally representative general health [18] or sexual lifestyle [14,16,17,58] surveys to studies in localised populations, designed to test the feasibility of chlamydia screening interventions [43,52,54] or to get people tested and treated for chlamydia [42]. All but two studies [38,39] used nucleic acid amplification tests (NAAT) for chlamydia diagnosis (Table 1). Supporting information Table S1 lists the primary publication for each study and its associated publications.

Risk of bias assessment

All included studies were at risk of biases that could affect the estimated chlamydia prevalence (Supporting information Table S2). The target population was assessed as being likely to be representative of the general population in only 8/39 studies; six studies in EU/EEA Member States Croatia [19], France [16], Germany [31], the Netherlands [33], Slovenia [17] and the UK [14] and two studies in the USA [18,58]. Seventeen studies described a comparison between participants and non-participants. More than half of studies (23/39) did not give enough information about the source population to determine whether this was representative of the target population.

Authors of included studies used different denominators and numerators in their reported response rates. We calculated a response rate according to our algorithm for all but 4/39 studies [31,41,47,51]. Amongst studies in EU/EEA countries, no study had a calculated response rate above 80%. The highest response rate (71%) was achieved as part of a national sexual behaviour survey in the UK [14]. Four studies had a response rate between 61% and 70% [27,37-39]. The lowest response rates were in studies where entire populations in large geographic areas were invited by post; 13% in East Anglia, UK [46] and 16% in three regions in the Netherlands [34]. In non-EU countries, the calculated response rate was above 80% in two studies [53,58], between 71% and 80% in two studies [18,57] and between 61% and 70% in one study [55]. As with EU/EEA Member States, the highest response rates were obtained in studies of people who were already taking part in another study [18,53,57,58].

Figure 2 shows the number of people included in the analysis and overall estimate of chlamydia prevalence for each included study. In EU/EEA countries, estimated prevalence in women ranged from 0.2% in sexually experienced 15 to 44 year olds in Barcelona, Spain in a study of human papillomavirus infection [37] to 8.0% in sexually experienced 21 to 23 year olds in Aarhus County, Denmark [29] and 18 to 25 year olds in London and Avon, UK [43], who were invited to take specimens at home in studies examining methods for chlamydia screening (Figure 2). For men point prevalence estimates ranged from 0.4% amongst 16 to 17 year olds taking part in a general health survey in Germany [31] to 6.9% in sexually experienced male military recruits aged 17 to 32 years in

three counties in Denmark [28] (Figure 2). In the two studies that included only teenagers [26,31], estimates were lower in men than in women (2.6% *vs.* 5.0% in Denmark, 0.4% *vs.* 2.1% in Germany). In non-EU/EEA countries, estimated prevalence in women ranged from 0.9% in 18 to 35 year olds in Melbourne, Australia [50] to 13.8% in a Canadian Arctic community aged 18 to 65 years [32] (Figure 2). In men, the lowest estimated prevalences were in 14 to 39 year olds in a general health survey in the USA (1.1% [18]) and military recruits aged 18 to 26 years in the French-speaking region of Switzerland (1.2% [47]). The highest estimate was from 15 to 39 year olds in a remote community in Queensland, Australia (10.6% [48]).

Figure 3 and Figure 4 show chlamydia prevalence estimates from studies conducted in EU/EEA and other high income OECD countries among women and men aged ≤26 years. In nationally representative samples of sexually experienced people in five countries, there was no or only mild heterogeneity. In women, estimates ranged from 3.0% (95% CI 1.7-5.0%) in the UK [14] to 5.3% (95% CI 2.3, 10.2%) in Croatia [19]. The pooled average estimate in all five countries was 4.3% (95% CI 3.6, 5.0%, I^2 0%) (Figure 3) and in the four EU/EEA Member States 3.6% (95% CI 2.4, 4.8%, I^2 0%, not shown in the figure). In men, estimates ranged from 2.4% (95% CI 1.0, 5.7%) in France [16] to 7.3% (95% CI 3.4, 13.4%) in Croatia [19]. The pooled average estimate in all five countries was 3.6% (95% CI 2.8, 4.4%, I^2 6%) (Figure 4) and in the four EU/EEA Member States 3.5% (95% CI 1.9, 5.2%, I^2 27%, not shown in the figure). Heterogeneity was severe (I^2 >75%) in sub-national studies and in nationally representative studies with chlamydia prevalence estimates for the whole study population in both women and men; we did not estimate pooled averages for these groups of studies (Figure 3 and Figure 4).

There was statistical evidence of an association between overall sex-specific survey response rate and estimated chlamydia prevalence in both women and men; estimated chlamydia prevalence was higher in surveys with lower response rates (Figure 5, women, P=0.003; men, P=0.018 from meta-regression). Results were similar if the analysis was restricted to studies that reported age-specific response rates for women and men aged ≤25 years (women, 15 studies, I^2 80.6%, P=0.004; men, 13 studies, I^2 88.6%, P=0.04). When the variable response rate was dichotomised (<60% and ≥60%), the ratio of odds for chlamydia infection was 1.9 times higher in studies with response rates <60% than in studies with response rates ≥60%. After controlling for national or sub-national study coverage, the ratio of odds was 1.7 (95% CI 0.9-3.2, P=0.081). There was no strong evidence of an association between estimated chlamydia prevalence and response rate in surveys of nationally representative population samples in women (P=0.644, Figure 6A) or men (P=0.729, Figure 6B). In sub-national surveys, the meta-regression plot suggests an association between estimated chlamydia prevalence and with response rate (Figure 6A and Figure 6B**).** There was statistical evidence of this association in women (P=0.063) but not men (P=0.267) and there was substantial residual heterogeneity between prevalence estimates (I^2 91% women, 81% men). The regression lines for subnational and national

surveys approached each other at higher levels of response rates. This suggests that at very high response rates, estimated prevalence would be similar in both survey types.

Discussion

Main findings

In this systematic review we found population-based surveys estimating chlamydia prevalence from 11 EU/EEA Member States, one non-EU/EEA European countries and four other high income countries. In nationally representative samples of sexually experienced ≤26 year olds, between study heterogeneity was low in women (five studies, range 3.0%, 95% CI 1.7, 5.0% in UK to 5.3%, 95% CI 2.3, 10.2% in Croatia, pooled estimate 4.3% , 95% CI 3.6, 5.0%, I^2 0%) and men (five studies, range 2.4%, 95% CI 1.0, 5.7% in France to 7.3%, 95% CI 3.4, 13.4% in Croatia, pooled estimate 3.6% ,95% CI 2.8, 4.4%, I^2 6.2%). Chlamydia prevalence estimates from population-based surveys conducted in sub-national population samples were very heterogeneous, ranging from 0.6% to 10.7% in women and 1.1% to 5.9% in men aged ≤25 years. Response rates in most included studies were <60%. There was statistical evidence of an inverse association between survey response rate and chlamydia prevalence estimates in both women (P=0.003) and men (P=0.018).

Strengths and weaknesses of the review

Strengths of this review are the broad and inclusive search strategy and the detailed assessment of study methodology. We think that we are unlikely to have missed any large published articles, but might not have found all unpublished data. Our systematic searches covered studies published until August 2012. Since then, we identified one additional large survey of the UK population in 2010 to 2011 [60], which used methods similar to those of a survey from 1999 to 2000 [14]. Overall response rates and estimates of chlamydia prevalence were similar in both surveys. Another strength is that we only included studies that used population-based sampling methods to obtain estimates of chlamydia prevalence in the general population. Previous systematic reviews have included studies done in health care settings [1,61,62], the results of which cannot be easily extrapolated to the general population because they include people with symptoms and exposures that put them at higher than average risk of chlamydia infection. The inclusion of data from countries outside Europe increased statistical power to examine heterogeneity and allowed us to examine the generalisability of our findings to countries with similar levels of social and economic development. There was some inconsistency in the countries included in the review, however. Bulgaria, Hungary, Romania are EU Member States but not high-income economies; other high-income EU/EEA economies are not OECD members (Cyprus, Latvia, Liechtenstein, Lithuania, Malta). We did not find population-based studies in any of these countries. Two main limitations of the review relate to the small number of studies with comparable data and the completeness of the data reported. First, we could not calculate a consistent response rate for all

studies because of differences between studies in the data reported and differences in study design. We overcame this limitation in part by applying an algorithm to select the numerator and denominator that were closest to the recommended definition [24]. The recommended numerator and denominator cannot be applied, however, in study designs that enrol participants and then restrict chlamydia testing to responders reporting sexual experience. In this case, the calculated response rate underestimates the true response rate and cannot be corrected unless the percentages excluded because they have not had sexual experience are recorded. Second, four countries (Denmark, Netherlands, Sweden, UK) accounted 17/25 included studies from EU/EEA countries. The small number of countries contributing to the review needs to be considered when interpreting the findings.

Interpretation

Estimates of chlamydia prevalence in women and men aged ≤26 years in surveys of nationally representative samples of populations in EU/EEA and other high income countries were statistically consistent and between study variability was compatible with random variation [23]. The pooled estimates for EU/EEA Member States are the average of estimates of chlamydia prevalence from four studies and do not mean that this is the chlamydia prevalence across Europe. The chlamydia prevalence estimates and their precision need to be interpreted in the context of national differences in culture, sexual behaviours and attitudes, health systems and intensity and duration of chlamydia control activities [63,64]. Most of the point estimates of chlamydia prevalence were <5% in both women and men. Participation bias might still affect these estimates because of low response rates and the low estimated prevalence of chlamydia [12]. Over-estimation is more likely than under-estimation because responders have higher levels of factors associated with STI than non-responders [14].

In cross-sectional surveys of chlamydia prevalence, the lower the calculated response rate the higher was the estimated prevalence. The association appeared to be more marked in studies conducted in sub-national regions of a country than in nationally representative population surveys (Figure 6). Differences in the objectives of studies in these groups could help explain this finding. The objectives of sub-national studies were diverse. Studies that assessed the feasibility of chlamydia screening approaches might have specifically encouraged chlamydia testing by people at high risk of infection but have low overall response rates [29,34,45]. Studies designed to measure chlamydia prevalence as a main [50] or subsidiary objective [37] might have enrolled a more representative sample of the target population. In nationally representative surveys, chlamydia testing was done as a small part of studies that were designed to measure a wide range of health-related [58] or sexual health-related behaviours [14,16,17]. These studies tended to have higher overall response rates than sub-national studies. Of note, the national survey with the highest estimate of chlamydia prevalence, in Croatia, also had the lowest response rate [19].

Implications for practice, policy and research

This review highlights several challenges to determining accurate and comparable estimates of chlamydia prevalence between countries. Standard definitions used by survey and market research organisations to define target and study populations and to calculate response rates were rarely adhered to. Reporting standards for prevalence surveys in epidemiological research, perhaps as an extension to existing Standards for the Reporting of Observational Studies in Epidemiology [65] might help to improve consistency in future. The association between estimated chlamydia prevalence and survey response rate suggests that estimates from studies with very low response rates should not be interpreted as estimates of the population chlamydia prevalence, even when sampling has covered a whole defined region of a country. This review does not provide data to specify a threshold response rate below which the value estimated is unreliable, however. Our review shows that population-based chlamydia prevalence has been estimated in a minority of European and other high income countries. Surveys among samples representative of national populations in a wider variety of countries, particularly in non-high income EU Member States, and in other low and middle income countries would be valuable if they use consistent methods and achieve high response rates. Surveys that estimate chlamydia prevalence are at risk of participation bias owing to low response rates; estimates obtained in nationally representative samples of the general population of EU/EEA Member States are similar to estimates from other high income countries.

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Figure legends

Figure 1 Flow diagram of study identification, inclusion and exclusion

Figure 2 Forest plot, overall estimate of chlamydia prevalence in women and men of all ages in EU/EEA and other high-income OECD countries in all included studies. CI, confidence interval. The small filled diamond shows the point estimate, the lines either side are the 95% CI. Each row is a study or group within a study, with separate estimates from women and men, where available. In Denmark 2002, Group 1 received home sampling kits, Group 2 had to request a sampling kit by post. In USA 2012, separate estimates are reported for five survey cycles of the National Health and Nutrition Surveys. In Netherlands 2010, separate estimates were reported separately for Amsterdam and Rotterdam

Figure 3 Forest plot, estimates of chlamydia prevalence in women ≤ 26 years in EU/EEA and other high-income OECD countries. CI, confidence interval. The small filled diamond shows the point estimate, the lines either side are the 95% CI. Each row is a study or group within a study. In Denmark 2002, Group 1 received home sampling kits, Group 2 had to request a sampling kit by post. Estimates are shown separately for sexually experienced participants only or for the overall sample, in either national or sub-national populations

Figure 4 Forest plot, estimates of chlamydia prevalence in men ≤ 26 years in EU/EEA and other high-income OECD countries. CI, confidence interval. The small filled diamond shows the point estimate, the lines either side are the 95% CI. Each row is a study or group within a study. In Denmark 2002, Group 1 received home sampling kits, Group 2 had to request a sampling kit by post. Estimates are shown separately for sexually experienced participants only or for the overall sample, in either national or sub-national populations

Figure 5 Meta-regression analysis of chlamydia prevalence estimates in women and men aged ≤25 years against calculated sex-specific response rate for all women and men in the study, in EU/EEA and other high-income OECD countries. The size of the open circle corresponds to the precision of the prevalence estimate. n= number of studies. For women, n=27, P=0.003, I^2 82.4%; men, n=18, P=0.018, I^2 87.6%.

Figure 6 Meta-regression analysis of chlamydia prevalence estimates in participants of all ages against response rate, by national or sub-national study design. Panel A, women; Panel B, men. The size of the open circle corresponds to the precision of the prevalence estimate. n= number of studies. For women, national studies, n=10, P=0.644, I^2 46.8%; sub-national studies, n=18 studies, P=0.063, I^2 91.23%; for men, national studies, n=10, P=0.729, I^2 57.56%; sub-national studies, n=15 studies, P=0.267, I^2 81.25%.

Table 1 Summary of characteristics of included studies

Study name [ref.]	National or sub-national study	Sex, age in years	Whole study sample, sexually experienced only or both	Sample tested, test used	Number invited for testing (response rate overall for women and men in %)	Study name (acronym), if known; purpose of study, setting and sampling strategy
EU/EEA countries						
Croatia 2011 [19]	National	W&M 18-25	sexually experienced only	urine, NAAT	1005 participants 861 sexually experienced 280 provided urine sample (37.5% women) (27.9% men)	Cross-sectional survey of sexual behaviour and STI prevalence. Nationally representative sample from all 21 counties in Croatia, with multi-stage probability sampling.
Denmark 1998 [26]	Sub-national	W&M mean 18.0 women 18.2 men	sexually experienced only	men first void urine, women urine and vaginal flush sample, NAAT	2603 women 928 eligible (33.3% women) 1733 men 442 eligible (24.8% men)	RCT of home sampling versus usual care. Random sample (half) of all high schools in Aarhus County. All students invited. Eligible if sexually experienced. (Only data from home sampling group included).
Denmark 1999 [27]	Sub-national	W 20-29	whole study sample	cervical swab, NAAT	16345 eligible 11088 in cohort (67.8% women)	Cohort study about risk factors for cervical cancer. Random sample of women born in Denmark, in catchment area of Righospitalet, Copenhagen taking part in a cohort study, who had cervical swab sample taken by gynaecologist.
Denmark 2001 [28]	Sub-national	M 17-32	both	urine, NAAT	2500 (53.8% men)	Cross-sectional survey to estimate chlamydia prevalence. All men in Northern Jutland, Aarhus or Copenhagen counties liable for military service and seen by a medical board.
Denmark 2002 [29]	Sub-national	W&M 21-23	sexually experienced only	men first void urine, women vaginal flush sample, NAAT	4000 women (32.5% women Group 1) (26.3% women Group 2) 5000 men (25.9% men Group 1) (15.4% men Group 2)	RCT on effectiveness of outreach screening strategies. Simple random sample from all residents of Aarhus County in this age group. Group 1 received sampling kit, group 2 had to request kit by post.
Estonia 2008 [30]	Sub-national	W&M 18-35	whole study sample	men urine, women vaginal swab, NAAT	1398 reachable (48% women) (32% men)	Cross-sectional survey to estimate chlamydia prevalence. Stratified random sample of residents of Tartu county.
France 2010 [16]	National	W&M 18-44	sexually experienced only	men urine, women vaginal swab (or urine), NAAT	4957 eligible by age and sexual experience (54.4% women)	Sexual behaviour survey (subsample of Contexte de la Sexualité en France study, NatChla). Random subsample of sexually experienced people from a national population-based survey on sexual behaviour with

					(49.3% men)	two-phase stratified sampling. Urine testing kit only sent to women if no swab returned after 1 month.
Germany 2012[31]	National	W&M 12-17	both	urine, NAAT	5755 in this age group (response rate 63% for ages 14-17)	General health survey (Kinder und Jugendgesundheitsstudie, KiGGS). Two-stage stratified cluster sampling, nationally representative sample of 0-17 year olds. Only tested samples from participants in this age group.
Netherlands 2000 [32]	Sub-national	W&M 15-40	whole study sample	first void urine, NAAT	5714 women (50.8% women) 5791 men (33.0% men)	Cross-sectional survey to estimate chlamydia prevalence and screening feasibility. Simple random sample of patients on the lists of 16 general practices in Amsterdam.
Netherlands 2005 [33]	National	W&M 15-29	both	urine, NAAT	20791 (47.0% women) (33.0% men)	Cross-sectional survey to estimate chlamydia prevalence and screening feasibility (CT PILOT). Stratified probability sample of randomly selected men and women in 4 regions of the Netherlands according to population density. Regions not sampled at random.
Netherlands 2010 [34]	Sub-national	W&M 16-29	sexually experienced only	men urine, women vaginal swab or urine, NAAT	139919 Amsterdam [a] (22.4% women) (10.8% men) 103335 Rotterdam (19.6% women) (10.5% men)	Cluster controlled trial of chlamydia screening effectiveness (Chlamydia Screening Implementation, CSI). All 16-29 year old residents of Amsterdam, Rotterdam, parts of South Limburg. Sexually active people invited to request test kit. South Limburg excluded because eligibility depended on response to questionnaire assessing risk of chlamydia.
Norway 2005 [35]	Sub-national	W&M 18-29	whole study sample	urine, NAAT	646 reached (43.8% women) (25% men)	Cross-sectional survey to estimate chlamydia prevalence. All patients on the list of a group practice in Oslo.
Norway 2012 [36]	Sub-national	W&M 18-25	sexually experienced only	urine, NAAT	10000 invited, 1670 returned sample (18.9% women) (11.9% men)	Cross-sectional survey to estimate chlamydia prevalence. Simple random sample of 10,000 people in this age group living in Rogaland county using unique personal identification number.
Slovenia 2004 [17]	National	W&M 18-49	both	first void urine, NAAT	2616 invited (60.0% women) (50.9% men)	Sexual behaviour study. Stratified two stage probability sample of the general population of Slovenia in this age group. All participants invited to provide specimen for chlamydia testing.
Spain 2007 [37]	Sub-national	W 15-44	sexually experienced only	cervical swab, NAAT	1821 invited 916 reached or accepted (66.1% women)	Cross-sectional multinational HPV prevalence survey. Random age stratified sample of the adult female general population from census list of 4 urban communities in metropolitan Barcelona.
Sweden 1992 [38]	Sub-national	W 15-34	sexually experienced only	cervical and urethral swabs, EIA (± direct IF)	543 reached and were sexually experienced (68.9% women)	Cross-sectional survey to estimate chlamydia prevalence. All women in this age group in a primary health care area in Nättraby invited, only sexually experienced screened.
Sweden 1995 [39]	Sub-national	W 19,21, 23,25	whole study sample	cervical and urethral swabs, culture	816 reached 611 participated (68.3% women)	Cross-sectional survey to estimate chlamydia prevalence. All women of this age living in primary health care area of Ålidhem community centre in Umeå.

Sweden 2003 [40]	Sub-national	M 22	whole study sample	first void urine, NAAT	1074 (35.6% men)	Cross-sectional survey to investigate feasibility of chlamydia screening. All males of this age living in Umeå.
Sweden 2004 [41]	Sub-national	W&M 20-24	whole study sample	first void urine, NAAT	200 (65% women) (45% men)	Cross-sectional survey to estimate chlamydia prevalence and cost-effectiveness of home sampling. Simple random sample of 100 men and 100 women in this age group living in Umeå.
Sweden 2007 [42]	Sub-national	M 19-24	whole study sample	first void urine, NAAT	1936 reached (14.5% men)	Cross-sectional survey to estimate chlamydia prevalence. Sampling method unclear, 1000 men living in Uppsala county (from population register), and 1000 Uppsala university students (from student register database).
United Kingdom 2000a [44]	Sub-national	M 18-35	whole study sample	first pass urine, NAAT	919 invited by post and reachable (45.3% men)	Cross-sectional survey to estimate chlamydia prevalence and screening feasibility. Postal recruitment of all men aged 18-24 and a random sample of men aged 25-35 in 4 general practices in North West London.
United Kingdom 2000b [43]	Sub-national	W&M 18-35	sexually experienced only	men urine, women urine or vulval swab, NAAT	166 women reached (39% women) 175 men reached (46% men)	Pilot study of acceptability of home sampling. Simple random sample of patients on the lists of 3 general practices in North West London and Avon. Urine samples from random 50% of women, vulval swabs from other 50%.
United Kingdom 2001 [14]	National	W&M 18-44	sexually experienced only	urine, NAAT	5026 invited to give urine sample (total 11 161 interviewed) (71.1% women) [b] (68.7% men)	Sexual behaviour study (National Survey of Sexual Attitudes and Lifestyles, Natsal-2). Random sample of sexually experienced people taking part in a stratified probability sample of people aged 16-44 years resident in the United Kingdom.
United Kingdom 2007 [45]	Sub-national	W&M 16-39	whole study sample	men first void urine, women first void urine and vulvo-vaginal swab , NAAT	14382 reached (37.6% women) (27.9% men)	Cross-sectional survey to estimate chlamydia prevalence and screening feasibility (Chlamydia Screening Studies project, ClaSS). Random sample of general population in Birmingham and Bristol areas, selected from 27 general practice lists.
United Kingdom 2012 [46]	Sub-national	W&M 18-24	whole study sample	urine, NAAT	29917 invited (13.2% women) (9.8% men)	Cross-sectional survey investigating feasibility of postal screening invitations. All people in this age group registered with any GP in North East Essex Primary Care Trust.
Non-EU/EEA countries, Europe						
Switzerland 2008 [47]	Sub-national	M 18-26	both	first void urine, NAAT	521 eligible and gave written consent (cannot calculate)	Cross-sectional survey to estimate chlamydia prevalence. All young Swiss men attending obligatory medical board before army recruitment (French speaking region only).
Non-EU/EEA countries, high income OECD						
Australia 2003 [48]	Sub-national	W&M 15-40+	whole study sample	first catch urine, NAAT	6431 eligible 2862 participated (43.8% for women and men)	General health survey. All people living in 26 rural indigenous Australian and Torres Strait Islander communities in northern Queensland taking part in Well Person's Health Check.

Australia 2004 [49]	Sub-national	W&M 15-35	whole study sample	men first void urine, women vaginal swab, NAAT	2703 eligible listed 1219 screened (50.7% women) (39.3% men)	Cross-sectional survey to estimate chlamydia and gonorrhoea prevalence. Indigenous Australian people aged 15-35 living in Alice Springs area
Australia 2006 [50]	Sub-national	W 18-35	both	first void urine, NAAT	1532 eligible households 979 women interviewed 657 gave urine sample (42.9% women)	Cross-sectional survey to estimate chlamydia prevalence. Simple random sample from Melbourne residential telephone directory.
Australia 2008 [51]	Sub-national	W&M 14-40	whole study sample	men first void urine, women low vaginal swabs, NAAT	ca. 1300 in 1996 (cannot calculate)	Cross-sectional survey in STI control programme screening for chlamydia, gonorrhoea and syphilis. All resident indigenous Australians living in the Anangu Pitjantjatjara Yankunytjatjara Lands.
Canada 2002 [52]	Sub-national	W&M 15-39	whole study sample	first catch urine, NAAT	1075 women (29.3% women) 1130 men (16.2% men)	Chlamydia mass screening study. All adults from remote Inuit communities in Nunavik region. All sexually experienced or in this age group especially encouraged to take part.
Canada 2009 [53]	Sub-national	W&M 15-65	whole study sample	urine, NAAT	224 estimated eligible (cannot calculate)181 screened (80.8% for women and men)	Chlamydia and gonorrhoea mass screening study. All men and women in this age group living in a rural Inuit community from Baffin Region, Nunavut.
New Zealand 2002 [54]	Sub-national	W&M 16+	sexually experienced only	urine, NAAT	1582 invited 1136 consented 582 sexually active (cannot calculate)	Cross-sectional survey to estimate chlamydia prevalence. Random sample of 50% of classes in all private and public high schools, Christchurch. Only sexually active had their samples tested.
USA 2001 [55]	Sub-national	W 18-29	sexually experienced only	urine, NAAT	2148 eligible 1439 enrolled 1370 tested 1314 sexually active (61.2% women)	Household survey of risk behaviour and chlamydia prevalence. All English- or Spanish-speaking women in this age group in a random sample of low income housing blocks from the 1990 census (<10th percentile) in 3 counties in California.
USA 2002a [56]	National	M 18-19, 22-26	whole study sample	urine, NAAT	1995 survey: data from 470 aged 18-19, and 995 aged 22-26 who were aged 15-19 in 1988 survey (cannot calculate)	National Surveys of Adolescent Males (NSAM). Sexual health survey. Nationally representative sample of never-married, non-institutionalised men aged 15-19 (1995 survey), and aged 22-26 (aged 15-19 in 1988 survey but re-interviewed in 1995). Oversampling of black and Hispanic youths.

USA 2002b [57]	Sub-national	W&M 18-35	whole study sample	urine, NAAT	1224 adults aged 18-45 reached 728 age-eligible for screening (79.5% women and men)	Cross-sectional survey to estimate chlamydia and gonorrhoea prevalence. Stratified probability sampling of households in Baltimore; urine samples requested from those in study age group.
USA 2004 [58]	National	W&M 18-26	both	first void urine, NAAT	Wave I: 18924 Wave III: 14322 (84% women and men)	Cohort study (US National Longitudinal Study of Adolescent Health, Add Health). Nationally representative sample of young people in the USA.
USA 2011 [59]	Sub-national	W&M 15-35	both	urine, NAAT	4998 eligible (42.7% women and men)	Cross-sectional survey to estimate STI prevalence (Monitoring STI Survey Program). Probability sample of Baltimore residents.
USA 2012 [18]	National	W&M 14-39	whole study sample	urine, NAAT	20836 selected 17190 interviewed (women 80.4%, 2007-2008) [c] (men 74.5%, 2007-2008)	General health survey (US National Health and Nutrition Examination Surveys, NHANES). Stratified multistage probability cluster sampling. Data from five 2-year survey cycles.

Abbreviations: EIA, enzyme immunoassay test; EU/EEA, European Union or European Economic Area Member States; IF, immunofluorescence test; M, men; NAAT, nucleic acid amplification test; OECD, Organization for Economic Cooperation and Development; STI, sexually transmitted infections; W: women.

[a] numbers from van den Broek et al. 2012, 1st invitation; [66]

[b] numbers from technical report Erens et al. 2001; [24]

[c] response rates from online results for 2007-2008 http://www.cdc.gov/nchs/nhanes/response_rates_CPS.ht

Figure 1

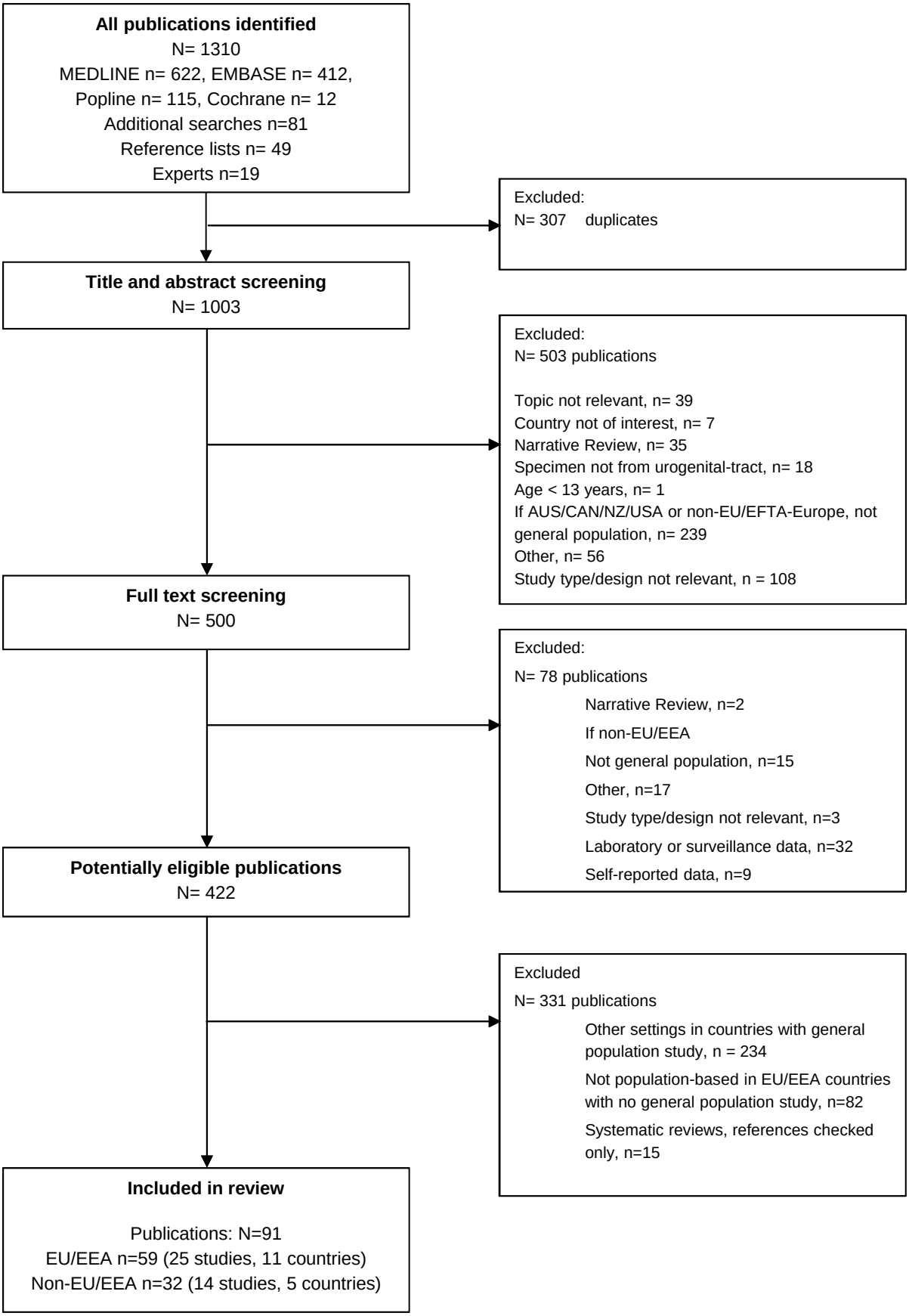

All publications identified
N= 1310
MEDLINE n= 622, EMBASE n= 412,
Popline n= 115, Cochrane n= 12
Additional searches n=81
Reference lists n= 49
Experts n=19
Excluded:
N= 307 duplicates
Title and abstract screening
N= 1003
Excluded:
N= 503 publications
Topic not relevant, n= 39
Country not of interest, n= 7
Narrative Review, n= 35
Specimen not from urogenital-tract, n= 18
Age < 13 years, n= 1
If AUS/CAN/NZ/USA or non-EU/EFTA-Europe, not general population, n= 239
Other, n= 56
Study type/design not relevant, n = 108
Full text screening
N= 500
Excluded:
N= 78 publications
Narrative Review, n=2
If non-EU/EEA
Not general population, n=15
Other, n=17
Study type/design not relevant, n=3
Laboratory or surveillance data, n=32
Self-reported data, n=9
Potentially eligible publications
N= 422
Excluded
N= 331 publications
Other settings in countries with general population study, n = 234
Not population-based in EU/EEA countries with no general population study, n=82
Systematic reviews, references checked only, n=15
Included in review
Publications: N=91
EU/EEA n=59 (25 studies, 11 countries)
Non-EU/EEA n=32 (14 studies, 5 countries)

Figure 2

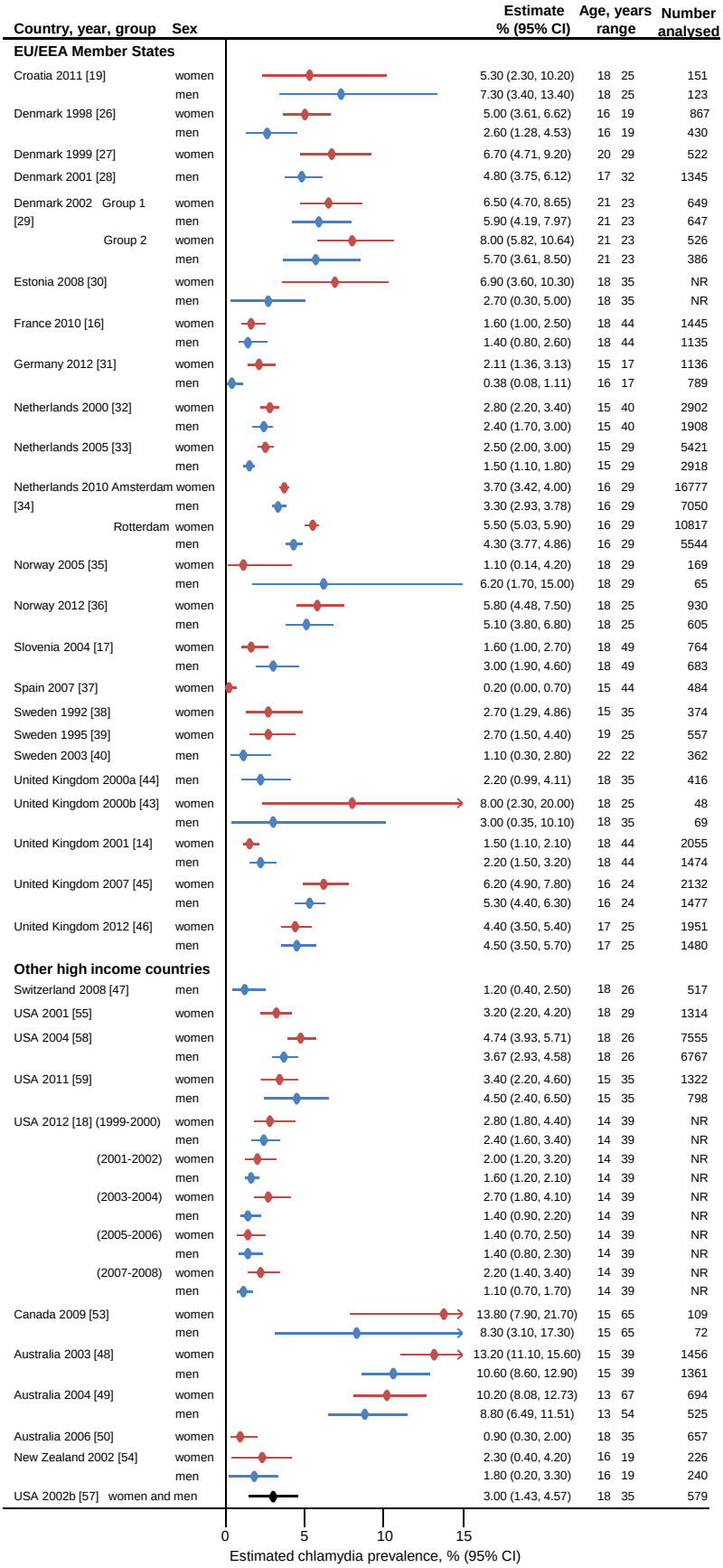

Country, year, group
Sex
Estimate % (95% CI)
Age, years range
Number analysed
EU/EEA Member States
Croatia 2011 [19] women 5.30 (2.30, 10.20) 18 25 151
men 7.30 (3.40, 13.40) 18 25 123
Denmark 1998 [26] women 5.00 (3.61, 6.62) 16 19 867
men 2.60 (1.28, 4.53) 16 19 430
Denmark 1999 [27] women 6.70 (4.71, 9.20) 20 29 522
Denmark 2001 [28] men 4.80 (3.75, 6.12) 17 32 1345
Denmark 2002 [29] Group 1 women 6.50 (4.70, 8.65) 21 23 649
men 5.90 (4.19, 7.97) 21 23 647
Group 2 women 8.00 (5.82, 10.64) 21 23 526
men 5.70 (3.61, 8.50) 21 23 386
Estonia 2008 [30] women 6.90 (3.60, 10.30) 18 35 NR
men 2.70 (0.30, 5.00) 18 35 NR
France 2010 [16] women 1.60 (1.00, 2.50) 18 44 1445
men 1.40 (0.80, 2.60) 18 44 1135
Germany 2012 [31] women 2.11 (1.36, 3.13) 15 17 1136
men 0.38 (0.08, 1.11) 16 17 789
Netherlands 2000 [32] women 2.80 (2.20, 3.40) 15 40 2902
men 2.40 (1.70, 3.00) 15 40 1908
Netherlands 2005 [33] women 2.50 (2.00, 3.00) 15 29 5421
men 1.50 (1.10, 1.80) 15 29 2918
Netherlands 2010 Amsterdam [34] women 3.70 (3.42, 4.00) 16 29 16777
men 3.30 (2.93, 3.78) 16 29 7050
Rotterdam women 5.50 (5.03, 5.90) 16 29 10817
men 4.30 (3.77, 4.86) 16 29 5544
Norway 2005 [35] women 1.10 (0.14, 4.20) 18 29 169
men 6.20 (1.70, 15.00) 18 29 65
Norway 2012 [36] women 5.80 (4.48, 7.50) 18 25 930
men 5.10 (3.80, 6.80) 18 25 605
Slovenia 2004 [17] women 1.60 (1.00, 2.70) 18 49 764
men 3.00 (1.90, 4.60) 18 49 683
Spain 2007 [37] women 0.20 (0.00, 0.70) 15 44 484
Sweden 1992 [38] women 2.70 (1.29, 4.86) 15 35 374
Sweden 1995 [39] women 2.70 (1.50, 4.40) 19 25 557
Sweden 2003 [40] men 1.10 (0.30, 2.80) 22 22 362
United Kingdom 2000a [44] men 2.20 (0.99, 4.11) 18 35 416
United Kingdom 2000b [43] women 8.00 (2.30, 20.00) 18 25 48
men 3.00 (0.35, 10.10) 18 35 69
United Kingdom 2001 [14] women 1.50 (1.10, 2.10) 18 44 2055
men 2.20 (1.50, 3.20) 18 44 1474
United Kingdom 2007 [45] women 6.20 (4.90, 7.80) 16 24 2132
men 5.30 (4.40, 6.30) 16 24 1477
United Kingdom 2012 [46] women 4.40 (3.50, 5.40) 17 25 1951
men 4.50 (3.50, 5.70) 17 25 1480
Other high income countries
Switzerland 2008 [47] men 1.20 (0.40, 2.50) 18 26 517
USA 2001 [55] women 3.20 (2.20, 4.20) 18 29 1314
USA 2004 [58] women 4.74 (3.93, 5.71) 18 26 7555
men 3.67 (2.93, 4.58) 18 26 6767
USA 2011 [59] women 3.40 (2.20, 4.60) 15 35 1322
men 4.50 (2.40, 6.50) 15 35 798
USA 2012 [18] (1999-2000) women 2.80 (1.80, 4.40) 14 39 NR
men 2.40 (1.60, 3.40) 14 39 NR
(2001-2002) women 2.00 (1.20, 3.20) 14 39 NR
men 1.60 (1.20, 2.10) 14 39 NR
(2003-2004) women 2.70 (1.80, 4.10) 14 39 NR
men 1.40 (0.90, 2.20) 14 39 NR
(2005-2006) women 1.40 (0.70, 2.50) 14 39 NR
men 1.40 (0.80, 2.30) 14 39 NR
(2007-2008) women 2.20 (1.40, 3.40) 14 39 NR
men 1.10 (0.70, 1.70) 14 39 NR
Canada 2009 [53] women 13.80 (7.90, 21.70) 15 65 109
men 8.30 (3.10, 17.30) 15 65 72
Australia 2003 [48] women 13.20 (11.10, 15.60) 15 39 1456
men 10.60 (8.60, 12.90) 15 39 1361
Australia 2004 [49] women 10.20 (8.08, 12.73) 13 67 694
men 8.80 (6.49, 11.51) 13 54 525
Australia 2006 [50] women 0.90 (0.30, 2.00) 18 35 657
New Zealand 2002 [54] women 2.30 (0.40, 4.20) 16 19 226
men 1.80 (0.20, 3.30) 16 19 240
USA 2002b [57] women and men 3.00 (1.43, 4.57) 18 35 579
0
5
10
15
Estimated chlamydia prevalence, % (95% CI)

Figure 3

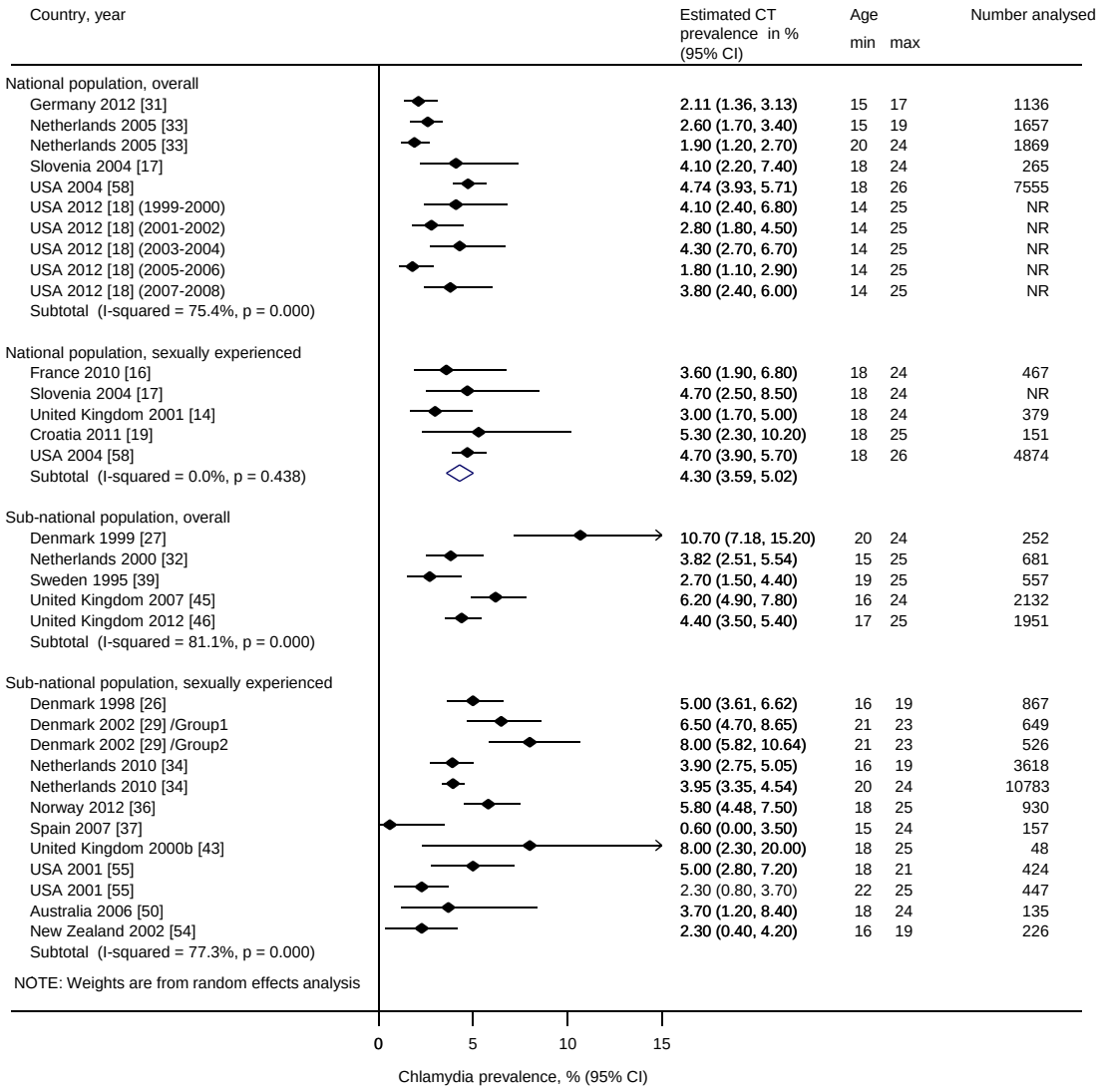

Country, year
Estimated CT prevalence in % (95% CI)
Age
min max
Number analysed
National population, overall
Germany 2012 [31] 2.11 (1.36, 3.13) 15 17 1136
Netherlands 2005 [33] 2.60 (1.70, 3.40) 15 19 1657
Netherlands 2005 [33] 1.90 (1.20, 2.70) 20 24 1869
Slovenia 2004 [17] 4.10 (2.20, 7.40) 18 24 265
USA 2004 [58] 4.74 (3.93, 5.71) 18 26 7555
USA 2012 [18] (1999-2000) 4.10 (2.40, 6.80) 14 25 NR
USA 2012 [18] (2001-2002) 2.80 (1.80, 4.50) 14 25 NR
USA 2012 [18] (2003-2004) 4.30 (2.70, 6.70) 14 25 NR
USA 2012 [18] (2005-2006) 1.80 (1.10, 2.90) 14 25 NR
USA 2012 [18] (2007-2008) 3.80 (2.40, 6.00) 14 25 NR
Subtotal (I-squared = 75.4%, p = 0.000)
National population, sexually experienced
France 2010 [16] 3.60 (1.90, 6.80) 18 24 467
Slovenia 2004 [17] 4.70 (2.50, 8.50) 18 24 NR
United Kingdom 2001 [14] 3.00 (1.70, 5.00) 18 24 379
Croatia 2011 [19] 5.30 (2.30, 10.20) 18 25 151
USA 2004 [58] 4.70 (3.90, 5.70) 18 26 4874
Subtotal (I-squared = 0.0%, p = 0.438) 4.30 (3.59, 5.02)
Sub-national population, overall
Denmark 1999 [27] 10.70 (7.18, 15.20) 20 24 252
Netherlands 2000 [32] 3.82 (2.51, 5.54) 15 25 681
Sweden 1995 [39] 2.70 (1.50, 4.40) 19 25 557
United Kingdom 2007 [45] 6.20 (4.90, 7.80) 16 24 2132
United Kingdom 2012 [46] 4.40 (3.50, 5.40) 17 25 1951
Subtotal (I-squared = 81.1%, p = 0.000)
Sub-national population, sexually experienced
Denmark 1998 [26] 5.00 (3.61, 6.62) 16 19 867
Denmark 2002 [29] /Group1 6.50 (4.70, 8.65) 21 23 649
Denmark 2002 [29] /Group2 8.00 (5.82, 10.64) 21 23 526
Netherlands 2010 [34] 3.90 (2.75, 5.05) 16 19 3618
Netherlands 2010 [34] 3.95 (3.35, 4.54) 20 24 10783
Norway 2012 [36] 5.80 (4.48, 7.50) 18 25 930
Spain 2007 [37] 0.60 (0.00, 3.50) 15 24 157
United Kingdom 2000b [43] 8.00 (2.30, 20.00) 18 25 48
USA 2001 [55] 5.00 (2.80, 7.20) 18 21 424
USA 2001 [55] 2.30 (0.80, 3.70) 22 25 447
Australia 2006 [50] 3.70 (1.20, 8.40) 18 24 135
New Zealand 2002 [54] 2.30 (0.40, 4.20) 16 19 226
Subtotal (I-squared = 77.3%, p = 0.000)
NOTE: Weights are from random effects analysis
0
5
10
15
Chlamydia prevalence, % (95% CI)

Figure 4

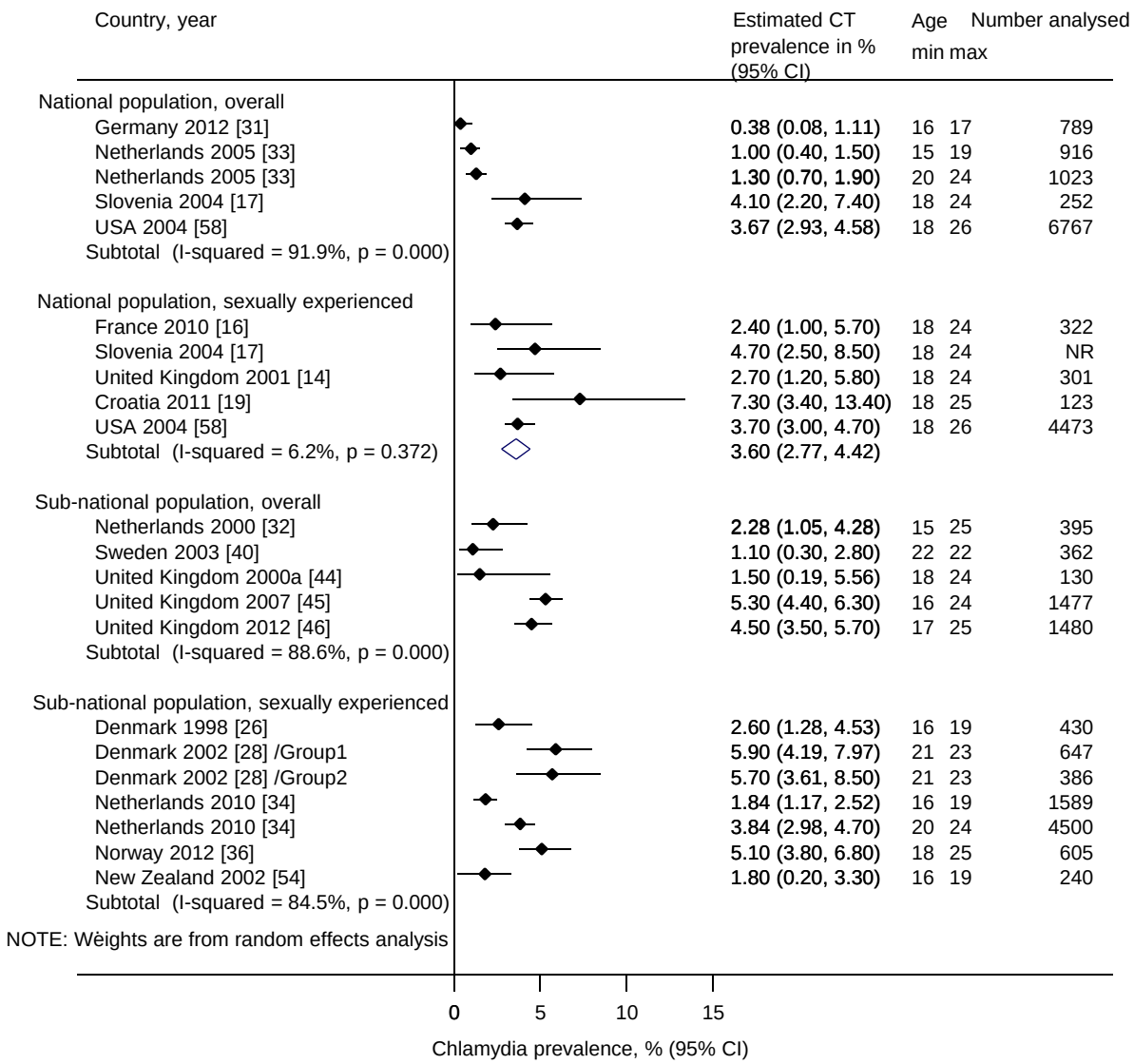

Country, year
Estimated CT prevalence in % (95% CI)
Age min max
Number analysed
National population, overall
Germany 2012 [31] 0.38 (0.08, 1.11) 16 17 789
Netherlands 2005 [33] 1.00 (0.40, 1.50) 15 19 916
Netherlands 2005 [33] 1.30 (0.70, 1.90) 20 24 1023
Slovenia 2004 [17] 4.10 (2.20, 7.40) 18 24 252
USA 2004 [58] 3.67 (2.93, 4.58) 18 26 6767
Subtotal (I-squared = 91.9%, p = 0.000)
National population, sexually experienced
France 2010 [16] 2.40 (1.00, 5.70) 18 24 322
Slovenia 2004 [17] 4.70 (2.50, 8.50) 18 24 NR
United Kingdom 2001 [14] 2.70 (1.20, 5.80) 18 24 301
Croatia 2011 [19] 7.30 (3.40, 13.40) 18 25 123
USA 2004 [58] 3.70 (3.00, 4.70) 18 26 4473
Subtotal (I-squared = 6.2%, p = 0.372) 3.60 (2.77, 4.42)
Sub-national population, overall
Netherlands 2000 [32] 2.28 (1.05, 4.28) 15 25 395
Sweden 2003 [40] 1.10 (0.30, 2.80) 22 22 362
United Kingdom 2000a [44] 1.50 (0.19, 5.56) 18 24 130
United Kingdom 2007 [45] 5.30 (4.40, 6.30) 16 24 1477
United Kingdom 2012 [46] 4.50 (3.50, 5.70) 17 25 1480
Subtotal (I-squared = 88.6%, p = 0.000)
Sub-national population, sexually experienced
Denmark 1998 [26] 2.60 (1.28, 4.53) 16 19 430
Denmark 2002 [28] /Group1 5.90 (4.19, 7.97) 21 23 647
Denmark 2002 [28] /Group2 5.70 (3.61, 8.50) 21 23 386
Netherlands 2010 [34] 1.84 (1.17, 2.52) 16 19 1589
Netherlands 2010 [34] 3.84 (2.98, 4.70) 20 24 4500
Norway 2012 [36] 5.10 (3.80, 6.80) 18 25 605
New Zealand 2002 [54] 1.80 (0.20, 3.30) 16 19 240
Subtotal (I-squared = 84.5%, p = 0.000)
NOTE: Weights are from random effects analysis
0
5
10
15
Chlamydia prevalence, % (95% CI)

Figure 5

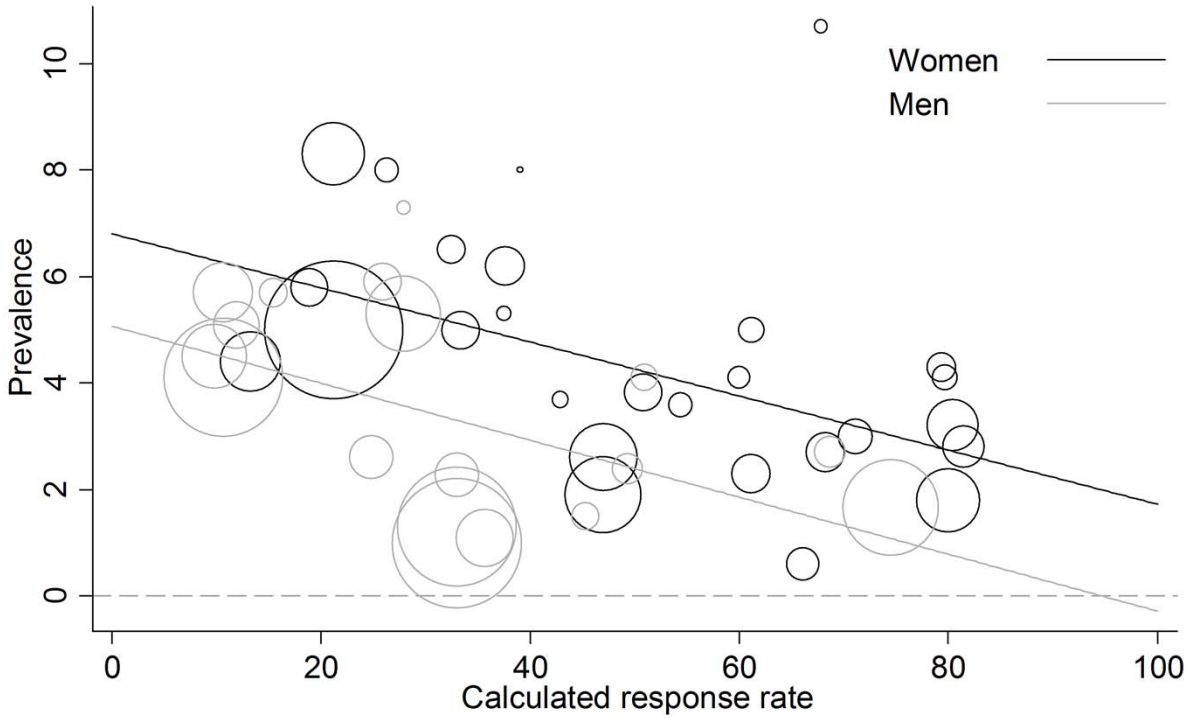
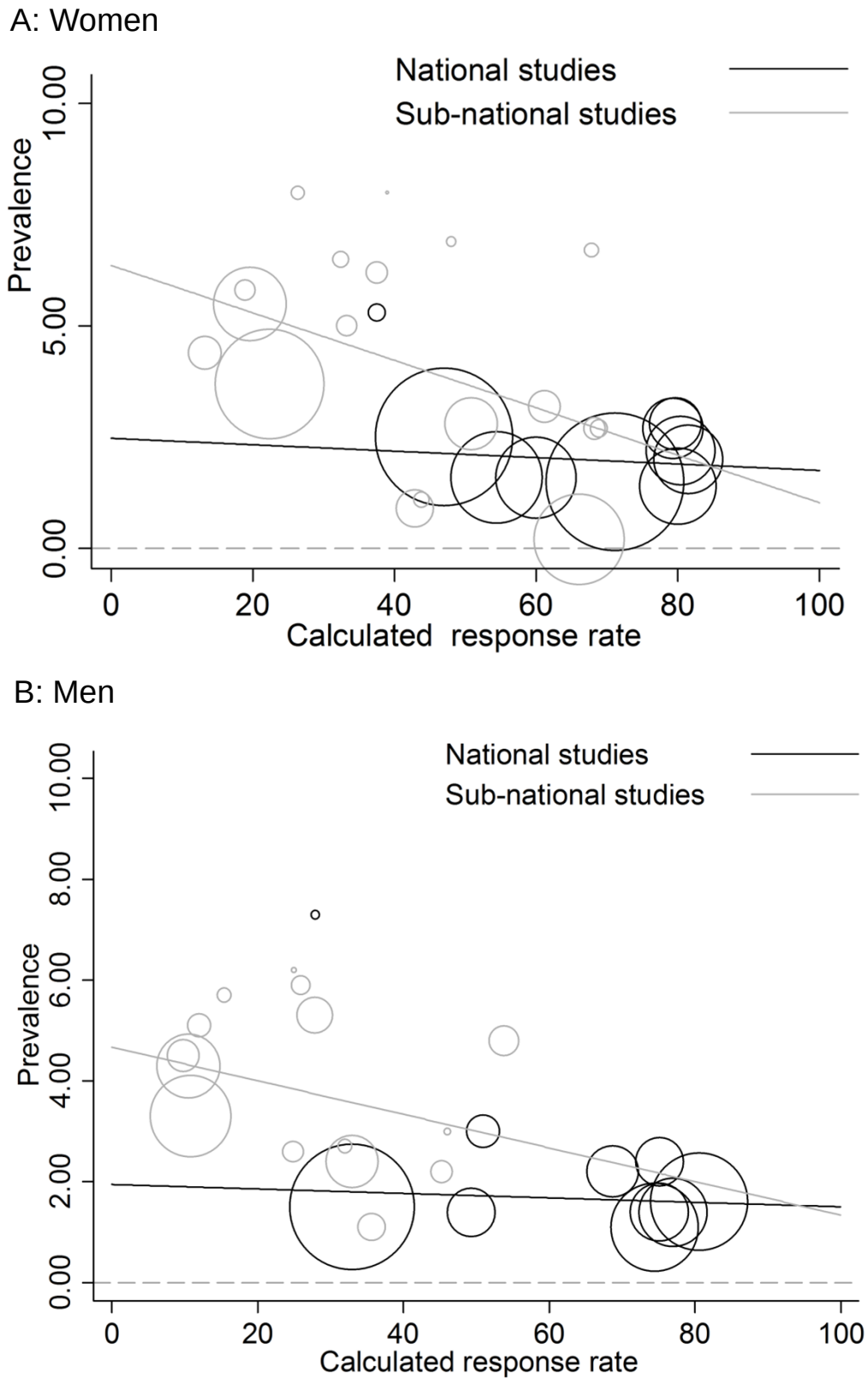

Women
Men
Prevalence
0
2
4
6
8
10
0
20
40
60
80
100
Calculated response rate

Figure 6


A: Women
National studies
Sub-national studies
Prevalence
0.00
5.00
10.00
0
20
40
60
80
100
Calculated response rate
B: Men
National studies
Sub-national studies
Prevalence
0.00
2.00
4.00
6.00
8.00
10.00
0
20
40
60
80
100
Calculated response rate

Supporting information 1

Title: Genital chlamydia prevalence in Europe and non-European high income countries: systematic review and meta-analysis Authors: Shelagh M Redmond, Karin Alexander-Kisslig, Sarah C Woodhall, Ingrid van den Broek, Jan van Bergen, Helen Ward, Anneli Uusküla, Björn Herrmann, Berit Andersen, Hannelore M Götz, Otilia Sfetcu, Nicola Low.

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Protocol

Population prevalence of *Chlamydia trachomatis* infection in the European Union, European Economic Area and other high income countries

A systematic review and meta-analysis

Protocol version 1.1 (September 2011)
Protocol version 2.0 (August 2012, protocol changes highlighted)
Protocol version 2.1 (technical editing 27.12.2013)

1. Background

Chlamydia trachomatis infection is the most commonly reported sexually transmitted infection in Europe [1]. Young adult women and men under the age of 25-30 years are the population group most likely to be infected [2]. In women, the bacteria can ascend from the endocervix, resulting in upper genital tract infection. This can cause pelvic inflammatory disease with potential sequelae of tubal factor infertility, ectopic pregnancy or chronic pelvic pain. *C. trachomatis* has been identified in the placenta of infected pregnant women [3] and infection during pregnancy is associated with prematurity [4]. Infection of the neonate during labour can lead to severe conjunctivitis and pneumonia [2]. In men, ascending chlamydia infection can lead to epididymitis. Additional complications that are more common in men than women include reactive arthritis and Reiter's syndrome. For both sexes, chlamydia infection increases susceptibility and transmission of HIV [5]. Complications of genital tract infection with *C. trachomatis* can impair quality of life in women [6] and result in substantial costs to the healthcare system [7].

Chlamydia infection is preventable and treatable [8].Chlamydia infection can be treated with antibiotics. A single dose of azithromycin or a seven day course of doxycycline is efficacious for short term microbiological cure of *C. trachomatis* in 97-98% of cases [9]. Partner notification and management are essential parts of chlamydia case management for identifying infected cases and preventing re-infection in the index case [10]. Most chlamydia infections are, however, asymptomatic or cause non-specific symptoms, which are often not recognised, particularly in women. Screening of people at high risk of infection is recommended in several European and other high income countries to identify and treat asymptomatic infections and to prevent long term complications [11-14].

Surveys of the population prevalence of *C. trachomatis* infections (chlamydia) can provide information for health policy decision makers about the need for measures to prevent and control infection. The least biased estimates of the prevalence of any condition at a particular time come from cross-sectional surveys of a representative sample of the general population (population-based surveys) [15]. Several large population-based surveys of chlamydia infection have been done in European Union (EU) Member States such as Great Britain [16] and the Netherlands [17] and other countries such as the USA [18]. Estimates of chlamydia prevalence vary between studies, even across countries with similar levels of social and economic development. Differences in estimates between countries could be real (representing differences in sexual behaviour patterns and chlamydia control efforts), but might also result from variations in study design and participation rates. A systematic review of chlamydia prevalence surveys would allow the available data to be collated and differences between studies to be investigated.

This systematic review is part of a project, Chlamydia Control in Europe, initiated, funded and conducted under a framework contract by the European Centre for Disease Prevention and Control (Framework Contract ECDC/2011/031). The main objective of the project was to provide information about Member States of the EU and European Economic Area (EEA). For this review, we will cover other countries in Europe and internationally to examine consistency and increase the generalisability of our findings.

2. Objective

To systematically review surveys estimating the prevalence of *C. trachomatis* infection in the general population of EU/EEA Member States and other high income countries.

3. Methods

3.1. Review questions

1. What is the prevalence of *C. trachomatis* infection in the general population of the EU/EEA Member States and other high income countries?
2. What is the distribution of chlamydia infection in different age, sex and ethnic groups?
3. What methodological features of cross-sectional studies influence estimates of *C. trachomatis* prevalence?

3.2. Inclusion criteria

Using the PICOS (population, intervention, comparison, outcome, study design) framework for defining systematic review questions:

3.2.a. Population

- General population of EU (http://europa.eu/about-eu/countries/member-countries/) and EEA (http://www.efta.int/eea) Member States, as of October 2011: Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and United Kingdom;
- General population of non-EU/EEA European countries, the USA, Canada, Australia, and New Zealand. During the course of the review, before statistical analysis, we decided to include all high income countries, using the definition of the Organisation for Economic Co-operation and Development (OECD, http://www.oecd.org/tad/crc.htm);
- Adults and young people aged 13 years and over;
- Women and men.

3.2.b. Intervention

Not relevant to this review of observational studies

3.2.c. Comparison group

Not relevant to this review of observational studies

3.2.d. Outcome

C. trachomatis infection, defined as a positive result of diagnostic tests used by the study investigators.

3.2.e. Study design

Surveys using methods to obtain a representative sample of the general population or a whole country or sub-national region of a country in one of the following study designs:

- Cross-sectional surveys;
- Baseline survey in randomised controlled trials or cohort studies;
- Systematic review if original data were reported;

- Specimens taken from the urogenital-tract;

3.3. Exclusion criteria

- Countries other than those mentioned above;
- Serological studies and other studies sampling only from extra-genital sites;
- Narrative reviews about *C. trachomatis* that do not contain original data;
- Participant age below 13 years;
- Letters, commentaries and editorials.

3.4. Search strategy

3.4.a. Electronic databases

The following databases will be searched from January 1990 to October 2011. The search will be updated before starting statistical analysis. We will not apply any language restrictions:

- Ovid Medline;
- Embase;
- Popline;
- The Cochrane Library.

3.4.b. Search terms

We will use Medical Subject Headings (MeSH) and explosion search terms for searching Medline and corresponding thesaurus terms for other databases where available, combined using Boolean operators:

- *Chlamydia trachomatis* OR chlamydia infections (NOT *Chlamydophila pneumoniae* OR trachoma) AND
- Names of any eligible individual countries (including historical names from 1990 because 'German Federal Republic', 'German Democratic Republic', Czechoslovakia and Yugoslavia do not appear in the exploded search term) AND
- Prevalence

Search strategies for each database are shown in *Appendix 1*.

3.4.c. Additional searches

- Reference lists: if retrieved publications include source references for potential studies about the prevalence of *C. trachomatis* infections we will retrieve the originals;
- We will contact experts in the field to ask if they know of any additional publications not identified by the search strategy.

3.4.d. De-duplication

We will use Endnote bibliographic software for reference management. The following rules will be used to remove duplicate hits from the database:

1. Compare the title, or various combinations of author, year, secondary title, volume, issue and pages through the 'de-duplication' function;

2. Visually compare the full records of suspected duplicates;

3. Save duplicates in a separate database.

3.5. Selection of eligible studies

Two suitably qualified reviewers will screen titles and abstracts of articles identified by the search strategy independently, using a form to document potential eligibility. Any study selected as being potentially eligible by either reviewer, will be retained for review of the full text. Where no abstract is available electronically, and eligibility cannot be judged from the title alone, the full text of the article will be retrieved and screened. The abstracts of articles identified through additional searches will be reviewed in the same manner as those identified through database searches.

Data will be entered into Epidata (Epidata version 3.1, EpiData Association, Odense, Denmark). The items included in the screening form are listed in *Appendix 2*.

3.5.a. Retrieval of full-text articles

We will obtain the full text of articles or other documents reporting studies identified as being potentially eligible for inclusion. We will make every effort to locate documents through internet downloads, inter-library loans and contacting authors of reviews citing potentially eligible documents. We intend to have articles translated if necessary to confirm or refute eligibility.

3.5.b. Selection of studies for final inclusion

The two independent reviewers will examine full text articles using a more detailed form and compare their lists of studies eligible for inclusion. Studies identified by both reviewers as being eligible for inclusion and having adequate data for extraction will be included in the review. Where there are discrepancies, the reasons for these will be discussed and a decision about inclusion reached by consensus. If there is no agreement, a third independent reviewer will adjudicate to make a final decision about eligibility. The selection of studies is described in a flow chart, and will be included in the publication of the review results. A version of the proposed flowchart is included as *Appendix 3.*

3.5.c. Selecting a population for each country

We aim to identify surveys in each eligible country, carried out in a sample that is representative of the general population. We consider the following groups as part of the general population: school students if the sampling frame included all schools in the country or in a sub-national geographic region of a country; and military recruits in countries with compulsory military conscription.

As part of the overall project, for EU/EEA Member States only, we aim to catalogue surveys estimating levels of chlamydia infection in other settings, such as health-care facilities or outreach studies. We defined categories, according to setting and population (*Appendix 4*).

3.6. Data extraction

Two appropriately qualified reviewers will extract and enter data independently from each included study into Epidata (*Appendix 5*).

Articles in languages other than English will be either translated first and then duplicate data extraction conducted as above or, if there are two reviewers who understand the language of publication, they will extract the data directly.

The two files will be compared using the validation function available in Epidata. Discrepancies in data extraction or data entry will be resolved by consensus. If there is no agreement a third independent reviewer will adjudicate to make a final decision.

Some studies may be excluded at the data entry stage if it became apparent that inclusion criteria are not met or there is not enough information in the documents to extract the required data.

3.6.a. Data extraction forms

The following outcomes will be extracted using Epidata (detailed list of items in *Appendix 2b*):

- Study design;
- Country;
- Population setting: general population of whole country or sub-national population of area;
- Study population: sexually experienced only or all participants;
- Sex, age and ethnic group of participating individuals;
- Social-demographic characteristics, specified if not concerning the general population;
- Numbers eligible, invited, accepting participation, providing samples, samples tested, number of samples included in analysis;
- Numbers excluded, with reasons;
- Diagnostic test method;
- Numbers with positive *C. trachomatis* test result;
- Authors' estimated prevalence and 95% confidence intervals (CI);
- Comparison of responders vs. non-responders, if reported;
- Methodological and reporting quality (Adapted from Boyle, Guidelines for evaluation of prevalence studies) [15] (*Appendix 6*).

3.7. Data analysis

3.7.a. Descriptive analysis

Review questions 1 and 2: C. trachomatis prevalence estimates

We will tabulate estimates of prevalence from each study. Where complex sampling methods had been used we will use the 95% CI presented in published papers. Where simple random sampling has been done and data are available, we will calculate *C. trachomatis* prevalence (with binomial 95% CI) for the available sex, age and ethnic groups.

We will display estimates in forest plots to show the point estimate and confidence intervals for each study.

We will calculate response rates to each survey, based on data provided about the eligible population. Using algorithms defined by the Council of American Survey Research Organizations (CASRO) [19, 20] we will exclude respondents who were ill, away from home or unable to speak English, where possible. We will use authors' reported response rates in complex surveys involving post-stratification weighting.

3.7.b. Statistical analysis

We will use meta-analysis to combine estimates of chlamydia prevalence where appropriate and to examine evidence of between study heterogeneity.

We will use the I^2 statistic to describe the percentage of the variability of results between studies that is due to factors other than random variation [21]. As a guide, I^2 values above 25%, 50% and 75% are suggested as evidence of mild, moderate and severe between study heterogeneity. Where there is evidence of moderate or severe heterogeneity, we will explore reasons for this by stratification or, if enough studies are available, by meta-regression.

Review question 3

We will examine the influence of setting, response rate, and other study characteristics using meta-regression to examine reasons for heterogeneity. We will examine the linear association between estimated chlamydia prevalence and the calculated response rate.

All analyses will be done using Stata statistical software (Stata 11, StataCorp, Austin, Texas, USA).

4. Report writing

Reports will be written following preferred reporting items for reporting of systematic reviews and meta-analyses (PRISMA) guidelines [22].

5. References

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Appendix 1: Search strategies

Ovid Medline

1.	('chlamydia infections' not ('chlamydophila pneumoniae' or trachoma or 'lymphogranuloma venereum')).mp.
2.	prevalence.mp.
3.	europe/ or exp austria/ or exp belgium/ or europe, eastern/ or exp baltic states/ or exp bulgaria/ or exp czech republic/ or exp hungary/ or exp poland/ or exp romania/ or exp slovakia/ or exp slovenia/ or exp yugoslavia/ or exp finland/ or exp france/ or exp germany/ or exp great britain/ or exp greece/ or exp iceland/ or exp ireland/ or exp italy/ or exp liechtenstein/ or exp luxembourg/ or exp mediterranean region/ or exp netherlands/ or exp portugal/ or exp scandinavia/ or exp spain/ or exp switzerland/ or czechoslovakia/ or european union/ canada/ or united states/ or australia/ or new zealand/ japan/ or korea/ or israel/
4.	*prevalence.mp. or mass screening/mt*
5.	*(austria or belgium or estonia or latvia or lithuania or bulgaria or czech republic or hungary or poland or romania or slovakia or slovenia or yugoslavia or finland or france or germany or great Britain or greece or iceland or ireland or italy or liechtenstein or luxembourg or malta or cyprus or netherlands or portugal or norway or sweden or denmark or spain or switzerland or czechoslovakia).mp.*
6.	1 and 2 and 3
7.	1 and 4 and 5
8.	6 and 7
9.	Limit 8 to (humans and yr=”1990 –Current”)

Limits: 1990-current, humans; homepage: http://ovidsp.tx.ovid.com/

Embase

1.	'chlamydiasis'/exp NOT ('lymphogranuloma venereum'/exp OR 'trachoma'/exp) AND [humans]/lim AND [embase]/lim AND [1990-2012]/py
2.	'prevalence'/exp NOT ('human immunodeficiency virus prevalence'/exp OR 'seroprevalence'/exp OR 'parasite prevalence'/exp) AND [humans]/lim AND [embase]/lim AND [1990-2012]/py
3.	'europe'/de OR 'eastern europe'/de OR 'western europe'/de OR 'austria'/exp OR 'baltic states'/exp OR 'belgium'/exp OR 'bulgaria'/exp OR 'cyprus'/exp OR 'czech republic'/exp OR 'czechoslovakia'/exp OR 'france'/exp OR 'germany'/exp OR 'greece'/exp OR 'hungary'/exp OR 'ireland'/exp OR 'italy'/exp OR 'luxembourg'/exp OR 'malta'/exp OR 'netherlands'/exp OR 'poland'/exp OR 'portugal'/exp OR 'romania'/exp OR 'slovakia'/exp OR 'slovenia'/exp OR 'yugoslavia'/exp OR 'scandinavia'/exp OR 'spain'/exp OR 'united kingdom'/exp OR 'switzerland'/exp OR 'iceland'/exp OR 'liechtenstein'/exp OR 'australia'/de OR 'canada'/de OR 'new zealand'/de OR 'united states'/de OR 'japan'/de OR 'korea'/de OR 'israel'/de AND [humans]/lim AND [embase]/lim AND [1990-2013]/py
4.	#1 AND #2 AND #3

Limits: 1990-current, humans, search in Embase only;; Homepage: http://www.embase.com

Popline

	CHLAMYDIA & PREVALENCE & (EUROPE / 'EUROPEAN UNION' / AUSTRIA / BELGIUM / BULGARIA / CYPRUS / 'CZECH REPUBLIC' / CZECHOSLOVAKIA / DENMARK / ESTONIA / FINLAND / FRANCE / GERMANY / 'GERMAN DEMOCRATIC REPUBLIC' / 'FEDERAL REPUBLIC OF GERMANY' / GREECE / HUNGARY / IRELAND / ITALY / LATVIA / LITHUANIA / LUXEMBOURG / MALTA / NETHERLANDS / POLAND / PORTUGAL / ROMANIA / SLOVAKIA / SLOVENIA / SPAIN / SWEDEN / 'UNITED KINGDOM' / YUGOSLAVIA / SWITZERLAND / NORWAY / ICELAND / LIECHTENSTEIN / AUSTRALIA / CANADA / 'NEW ZEALAND' / 'UNITED STATES OF AMERICA'/ JAPAN / KOREA / ISRAEL) NOT TRACHOMA

Limits: search limited to title/keywords; Endnote Import Filter: http://db.jhuccp.org/popinform/basic.html; homepage: http://www.popline.org

The Cochrane Library

1.	MeSH descriptor Chlamydia Infections explode all trees
2.	MeSH descriptor Prevalence explode all trees
3.	MeSH descriptor Europe explode all trees
4.	MeSH descriptor (AUSTRALIA OR CANADA OR NEW ZEALAND OR UNITED STATES OR JAPAN OR KOREA OR ISRAEL)
6.	#1 AND #2 AND #3 OR #4, limit to 1990 – 2012

Homepage: http://onlinelibrary.wiley.com/o/cochrane/cochrane_search_fs.html

Appendix 2: Screening form for study eligibility

Endnote ID: ___

First author: ___

Checklist completed by: __

Inclusion for data extraction?

- Yes;
- Provisional;
- No;
- No, but interesting (retain for discussion or future use)

Study design:

- Cross-sectional study
- Randomised controlled trial
- Cohort study
- Other: ___

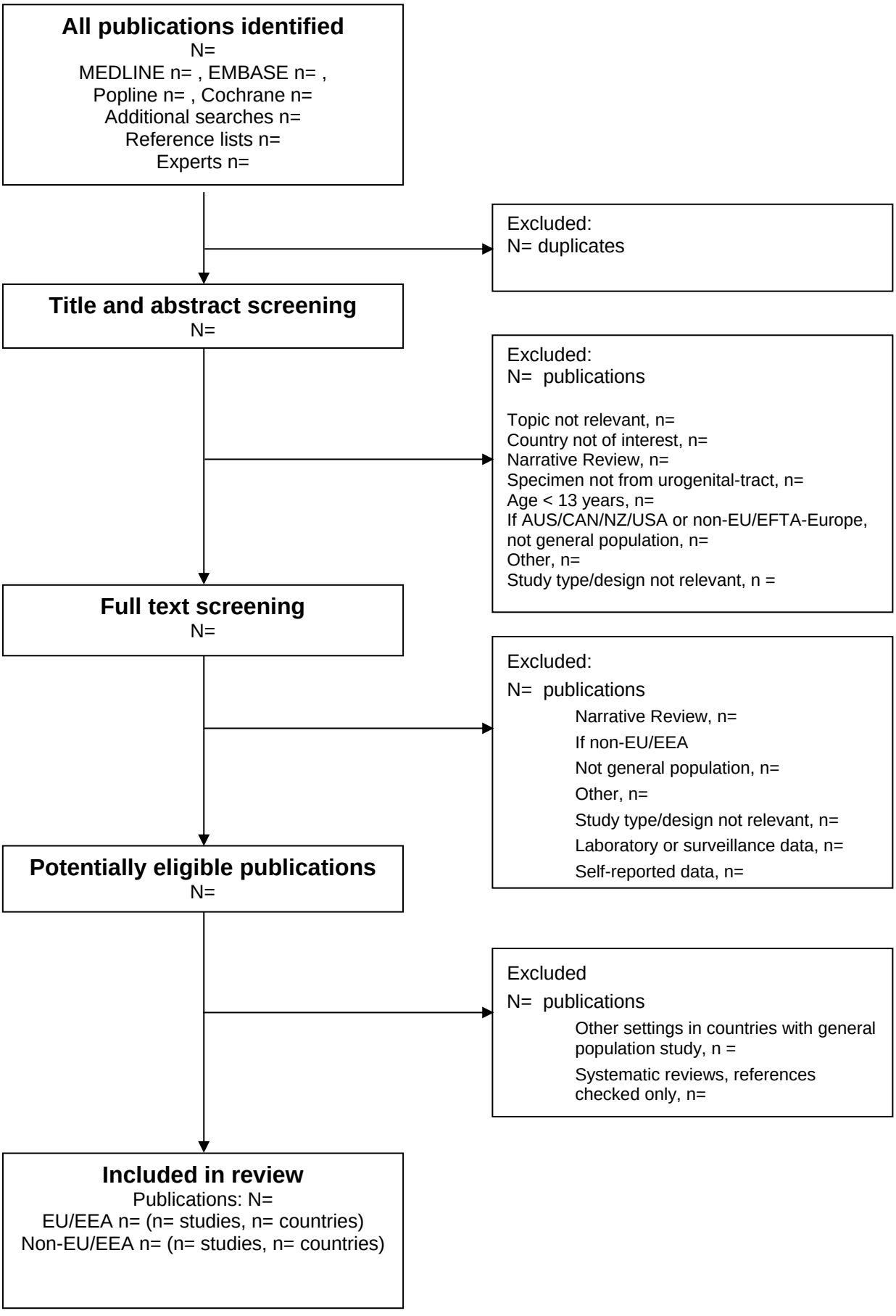
Outcomes described for following population (Used for categories in Appendix 5)

- General population
- General population of a sub-national geographical area
- Population other than in health care settings e.g. schools, institutions, prisons: ___
- Population in health care settings
- Population in genitourinary medicine/sexually transmitted diseases clinic settings
- Population of a specific subgroup e.g. commercial sex worker, men who have sex with men
- People with comorbidity
- Other, describe: ___

Reason for exclusion

- Other than general population if general population are available for this country
- Topic not relevant
- Country not of interest
- Narrative review
- Specimen not from uro-genital tract
- Age under 13 years
- If USA/CAN/AUS/NZ (or other OECD high income countries) not general population
- Study type not relevant
- Other: ___

Appendix 3: Flow chart of the selection process



Appendix 4: Categories of study populations in studies with non-population based sampling methods

- Category 1A: defined random sample of the general population nationally, fulfilling all relevant criteria to minimise risk of bias (Appendix 5)
- Category 1B: defined random sample of the general population nationally, NOT fulfilling all relevant criteria to minimise risk of bias
- Category 2A: defined random sample of the general population of a sub-national geographical region, fulfilling all relevant criteria to minimise risk of bias
- Category 2B: defined random sample of the general population of a a sub-national geographical region, NOT fulfilling all relevant criteria to minimise risk of bias
- Category 3A: random or consecutive sample of a population similar to the general population and not in health care settings, e.g. Schools, Universities, sport-clubs fulfilling all relevant criteria to minimise risk of bias
- Category 3B: random or consecutive sample of a population similar to the general population and not in health care settings, e.g. Schools, Universities, sport-clubs NOT fulfilling all relevant criteria to minimise risk of bias
- Category 4A: random or consecutive sample of attenders at a non-GUM clinic healthcare setting, fulfilling all the relevant criteria to minimise risk of bias
- Category 4B: random or consecutive sample of attenders at a non-GUM clinic healthcare setting, NOT fulfilling all the relevant criteria to minimise risk of bias
- Category 5A: random or consecutive sample from a GUM clinic, fulfilling all the relevant criteria to minimise risk of bias
- Category 5B: data from a GUM-clinic, NOT fulfilling all the relevant criteria to minimise risk of bias
- Category 6A: sample of a specific subgroup at risk e.g. CSW, HIV-positive persons, MSM, fulfilling all the relevant criteria to minimise risk of bias
- Category 6B: sample of a specific subgroup at risk e.g. CSW, HIV-positive persons, MSM, NOT fulfilling all the relevant criteria to minimise risk of bias
- Category 7A: sample of patients with co-morbidity, such as other STD, symptoms of urethritis or PID, infertility, EUG, abortion fulfilling all the relevant criteria to minimise risk of bias
- Category 7B: sample of patients with co-morbidity, such as other STD, symptoms of urethritis or PID, infertility, EUG, abortion NOT fulfilling all the relevant criteria to minimise risk of bias
- Category 8A: other population, such as laboratory reports, specific subgroups which don’t fit into the categories above, fulfilling all the relevant criteria to minimise risk of bias
- Category 8B: other population, such as laboratory reports, specific subgroups which don’t fit into the categories above, NOT fulfilling all the relevant criteria to minimise risk of bias

Appendix 5: Data extraction items

Study design:

- Cross-sectional study
- Randomised controlled trial
- Cohort study
- Other, describe: ___

Inclusion criteria, describe: ___

Exclusion criteria, describe: ___

Select country from the list below:

Austria; Belgium; Bulgaria; Cyprus; Czech Republic; Denmark; Estonia; Finland; France; Great Britain; Germany; Greece; Hungary; Ireland; Italy; Latvia; Lithuania; Luxembourg; Malta; Netherlands; Poland; Portugal; Romania; Slovakia; Slovenia; Spain; Sweden; Iceland; Liechtenstein; Norway; Switzerland; Australia; New Zealand; USA; Canada; other country, describe: ___

Methods

Setting: General population of whole country or general population of a sub-national geographical area

Describe methods and recruitment procedure: ___

Initial approach:

- Mail
- Telephone
- Internet
- Personal contact in household
- Personal contact in health care settings
- Other, describe:

Date of study from ___ until___

Method of *C. trachomatis* detection:

- Nucleic acid amplification test (NAAT) urine;
- NAAT swab
- Enzyme linked immunosorbent assay (ELISA) urine
- ELISA swab
- Immunofluorescence
- Culture
- Other, describe: ___
- Unclear

Is ethical committee approval reported? Yes; No; Not applicable; Unclear

Informed consent; Yes; No; Unclear

Ethnic group:

- White
- Black including Caribbean, African
- Indian, Pakistani and Bangladeshi
- Chinese

- Other Asian
- North African, Arab, Iranian
- Romani
- Not reported/unclear
- Other including unknown, describe: ___

Sampling method:

- Simple random sampling
- Stratified random sampling
- Multistage stratified random sampling
- Consecutive sample
- Convenience sample
- Unclear
- Other
- Describe sampling method: ___

Outcomes reported in the study:

- Prevalence
- Response rate

Outcomes reported for following subgroups (each outcome numbered):

- Age groups combined
- Age groups stratified
- Men and women combined
- Men and women separate
- Men only
- Women only
- Ethnic groups separate
- Certain ethnic group only
- Number of lifetime partners any categorisation
- Not specified
- Others, not covered above: ___

Description of target population: ___

Description of source population: ___

Reported for: Women and men combined; women only; men only

Total number of eligible people__

Total number of people able to participate__

Total number of people asked to participate /sent questionnaire to__

Total number of people agreed to participate/ filled in questionnaire__

Total number of people asked for sample__

Total number of people providing sample__

Total number of samples tested__

Total number of test results included in analysis__

Do these numbers reported above add up logically? Yes; No; Unclear

How were missing data handled? Describe: ___

Age range of participants in overall sample lower limit __; upper limit__

Has any multivariable analysis been done to examine factors associated with Chlamydia? Yes, No; Unclear; If yes describe characteristics analysed: ___

Numerical outcomes

Endnote ID:___

Outcome number

Describe group: ___

Country number for this outcome

Setting

- General population
- General population of a sub-national geographical area
- Describe setting: ___

Sex: Women and men combined; Only women; Only men

Age group: (lower limit to upper limit of age group, write '99' if unknown)

Specimen handed in:

- Urine
- Swab
- Unclear/not reported
- Other, describe:___

Collection method

- Specimen collected by physician
- Self-collected specimen

Ethnic group

- White
- Black, including Caribbean, African
- Indian, Pakistani and Bangladeshi
- Chinese
- Other Asian
- North African, Arab, Iranian
- Romani
- Other, describe: ___
- Not reported/unclear

Raw data, if reported (write 999999 if not reported)

- Number tested positive
- Weighted number tested
- Un-weighted number tested

Outcome (for each reported numbered outcome)

- Prevalence and 95%CI (lower limit, upper limit)
- Response rate and 95%CI (lower limit, upper limit)

Appendix 6: Risk of bias assessment

We will use a list of published items by Boyle for assessing the methodological risk of bias in prevalence surveys [15]. We will use the published criteria to determine whether the risk of bias has been addressed adequately, inadequately, or if there was insufficient information to judge. For some items, we developed our own criteria, reviewers assess methods independently and agree on category by consensus or adjudication.

Items assessed

Item and explanation	Assessment	Criteria
*Is the target population clearly defined? Target population is the population to which the main results of the study will be extrapolated.	Adequate	Target population is defined by shared characteristics, such as age, sex, residency, sexual activity
	Inadequate	Characteristics of target population not described
	Unclear	Characteristics insufficiently defined
Is the source population clearly defined?† Source population is the population from which investigators selected the random sample.	Adequate	Characteristics of the source population are clearly defined, e.g. by age, sex, residency, sexual activity
	Inadequate	Characteristics of source population not described
	Unclear	Characteristics insufficiently defined
*Was probability sampling used to select the sample?	Adequate	Simple, stratified or multistage random sampling methods described
	Inadequate	Convenience sample or other non-random sampling method described
	Unclear	Methods not described in sufficient detail to determine if probability sampling used
Is the source population an adequate sample of the target population? †	Yes	If you can compare data about each and decide that there are no substantial differences, or the authors describe them as being similar
	No	If you or the authors conclude that there are important differences between the source and the target population
	Unclear	No description or unclear if there are important differences
Are the socio-demographic	Adequate	Comparison done and socio-demographic

characteristics of responders and non-responders similar?*		characteristics are described as 'similar' or no important differences observed
	Inadequate	No comparison done, or comparison shows important differences between responders and non-responders
	Unclear	Insufficient information to decide
Sample size calculation described?†	Yes	A sample size calculation is described to show acceptable precision
	No	No sample size calculation
	Unclear	Insufficient information provided
Adequate sample size achieved?†	Yes	Achieved sample size is similar to the sample size calculation
	Unclear, probably yes	No sample size calculation described, but precision of primary outcome judged acceptable
	Unclear, probably no	No sample size calculation described, but precision of primary outcome judged unacceptable
Response rate* Number tested/ Number asked to participate or sent questionnaire to. If other numbers are used to calculate the response rate, do not calculate the response rate.	≥80% 70-79% <70%	Described by Boyle as acceptable [15] Categories defined by reviewers to describe response rates
Valid standardised questionnaire for data collection used?*	Adequate	Authors state that questionnaires for data like age, sex and risk behaviour are valid for all participants
	Inadequate	Authors state that different questionnaires used for different study groups, e.g. by age, sex and risk behaviour, or non-validated
	Unclear	Insufficient information provided
NAAT used for *C. trachomatis* detection?†	Yes	Includes: PCR (including RT-PCR, transcription mediated amplification), branched DNA tests, ligase chain reaction, strand displacement analysis

	No	Other diagnostic test described
	Not described	No information given about test used
Special features of sampling design were accounted by the use of special statistical methods?*	Adequate	Either, special features were accounted for by appropriate statistical methods, or special methods were not needed because simple random sampling used.
Special statistical methods include weighting procedures to adjust for sampling probabilities.	Inadequate	Complex sampling used but not accounted for by appropriate statistical methods
	Unclear	
Confidence intervals included?*	Yes	Reported by authors
	No	Not reported by authors
Data provided to calculate confidence interval?*	Yes	Simple random sampling and raw numbers (positive tests/total number of test results) provided
	No	Simple random sampling but no raw numbers
	Not relevant	Complex sampling method with confidence intervals calculated by authors

***** Items included in assessment tool and criteria for assessment adapted from descriptions by Boyle [15];

† Items added for this systematic review and criteria developed by review team.

Supporting Information Table S1

Bibliography of primary and associated publications, by region and country in alphabetical order

Study name, reference	Main publication	Additional publications
Croatia 2011 [19]	Bozicevic I, Grgic I, Zidovec-Lepej S, Cakalo JI, Belak-Kovacevic S, Stulhofer A et al. (2011) Urine-based testing for Chlamydia trachomatis among young adults in a population-based survey in Croatia: feasibility and prevalence. BMC Public Health 11: 230. 10.1186/1471-2458-11-230 [doi]..	
Denmark 1998 [26]	Ostergaard L, Andersen B, Olesen F, Moller JK (1998) Efficacy of home sampling for screening of Chlamydia trachomatis: randomised study. BMJ 317(7150): 26-27.	Ostergaard L, Andersen B, Moller JK, Olesen F (2000) Home sampling versus conventional swab sampling for screening of chlamydia trachomatis in women: A cluster-randomized 1-year follow-up study. Clin Infect Dis 31(4): 951-957.
Denmark 1999 [27]	Munk C, Morre SA, Kjaer SK, Poll PA, Bock JE, Meijer, CJ et al. (1999) PCR-detected Chlamydia trachomatis infections from the uterine cervix of young women from the general population: prevalence and risk determinants. Sex Transm Dis 26(6): 325-328.	Kjaer SK, van den Brule AJ, Bock JE, Poll PA, Engholm G, Sherman ME et al. (1996) Human papillomavirus--the most significant risk determinant of cervical intraepithelial neoplasia. Int J Cancer 65(5): 601-606.
Denmark 2001 [28]	Bennedsen M, Nygard B, Berthelsen L, Jensen JS, Lind I (2001) [Prevalence of Chlamydia among young men. A screening among men liable for military service and coming before the military board]. Ugeskr Laeger 163(34): 4583-6.	
Denmark 2002 [29]	Andersen B, Olesen F, Moller JK, Ostergaard L (2002) Population-Based Strategies for Outreach Screening of Urogenital Chlamydia trachomatis Infections: A Randomized, Controlled Trial. J Infect Dis 185(2): 252-258.	Moller JK, Andersen B, Olesen F, Lignell T, Ostergaard L (1999) Impact of menstrual cycle on the diagnostic performance of LCR, TMA, and PCE for detection of Chlamydia trachomatis in home obtained and mailed vaginal flush and urine samples. Sex Transm Infect 75(4):228-230. Andersen B, van Valkengoed I, Sokolowski I, Moller JK, Ostergaard L, Olesen F (2011) Impact of intensified testing for urogenital Chlamydia trachomatis infections: a randomised study with 9-year follow-up. Sex Transm Infect 87(2): 156-161.
Estonia 2008 [30]	Uuskula A, Kals M, Denks K, Nurm UK, Kasesalu L, Dehovitz J et al.(2008) The prevalence of chlamydial infection in Estonia: a population-based survey. International Journal of STD AIDS 19(7): 455-458.	Uuskula A, Kals M, McNutt L-A (2011) Assessing non-response to a mailed health survey including self-collection of biological material. European Journal of Public Health 21(4):538-542
France 2010 [16]	Goulet V, de Barbeyrac B, Raherison S, Prudhomme M, Semaille C, Warszawski J (2010) Prevalence of Chlamydia trachomatis: results from the first national population-based survey in France. Sex Transm Infect 86 (4): 263-270.	Bajos N, Bozon M, Beltzer N, Laborde C, Andro A, Ferrand M et al. (2010) Changes in sexual behaviours: from secular trends to public health policies. AIDS 24(8):1185-1191 Goulet, V, De Barbeyrac B, Raherison S, Prudhomme M, Velter A, Semaille C et al. (2011). "National survey on Chlamydia trachomatis infection in France (NatChla Study, CSF 2006 Survey). To whom should screening be proposed? [Enquête nationale de prévalence de l'infection à Chlamydia trachomatis (volet NatChla de l'enquête CSF 2006). À quelles personnes proposer un dépistage ?]." Bulletin épidémiologique hebdomadaire 12(5 avril 2011): 160-164.
Germany 2012	Haar K, (2012) "Prävalenz von urogenitalen Chlamydia trachomatis-	Haar K, Bremer V, Houareau C, Meyer T, Desai S, Thamm M, et al. (2013) Risk factors for Chlamydia trachomatis infection in adolescents: results from a

[31]	Infektionen bei Teilnehmern des bundesweiten Kinder- und Jugendgesunheitssurveys (KiGGS)“Masterarbeit für MPH, Berlin School of Publich Health, Robert Koch Institute, Berlin.	representative population-based survey in Germany, 2003-2006. Euro Surveill. 18 (34): pii=20562 Desai S, Meyer T, Thamm M, Hamouda O, Bermer V (2011). "Prevalence of Chlamydia trachomatis among young German adolescents, 2005-06." Sexual Health 8(1): 120-122. Kurth B-M, Kamtsiuris P, Holling H, Schlaud M, Dolle R, Ellert U et al. (2008). "The challenge of comprehensively mapping children's health in a nation-wide health survey: Design of the German KiGGS-Study." BMC Public Health 8(1): 196. Thierfelder W, Dortschy R, Hintzpeter B, Kahl H, Scheidt-Nave C (2007). "[Biochemical measures in the German Health Interview and Examination Survey for Children and Adolescents (KiGGS)]." Bundesgesundheits-blatt Gesundheitsforschung Gesundheitsschutz 50(5-6): 757-770. Kamtsiuris P, Lange M, Schaffrath RA (2007). "[The German Health Interview and Examinations Survey for Children and Adolescents (KiGGS): Sample design, response and nonresponse analysis]." Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 50(5-6): 547-556.
Netherlands 2000 [32]	van Valkengoed I G, Morre SA, van den Brule AJ, Meijer CJ, Deville W, Bouter LM et al. (2000). "Low diagnostic accuracy of selective screening criteria for asymptomatic Chlamydia trachomatis infections in the general population." Sexually Transmitted Infections 76(5): 375-380.	van Valkengoed IG, Boeke AJ, Morre SA, van den Brule AJ, Meijer CJ, Deville W et al. (2000) Disappointing performance of literature-derived selective screening criteria for asymptomatic Chlamydia trachomatis infection in an inner-city population. Sex Transm Dis 27(9): 504-507. van Valkengoed GM, Boeke AJP, van den Brule AJC, Morre SA, Dekker JH, Meijer CJLM et al. (1999) Systematic screening for asymptomatic Chlamydia trachomatis infections by home obtained mailed urine samples in men and women in general practice. Nederlands Tijdschrift voor Geneeskunde 143(13): 672-676.
Netherlands 2005 [33]	van Bergen J, Gotz HM, Richardus JH, Hoebe CJ, Broer J, Coenen AJ (2005) 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 81(1): 17-23.	van Bergen JEAM, Gotz HM, Richardus JH, Hoebe CJPA, Broer J, Coenen AJJ (2005) Chlamydia trachomatis infection in 4 regions in the Netherlands: Results of a population-based study conducted through municipal health services and implications for screening. Nederlands Tijdschrift voor Geneeskunde 149(39):2167-2174 Veldhuijzen IK, van Bergen JEAM, Gotz HM, Hoebe CJPA, Morre SA, Richardus JH, Pilot Ct Study Group (2005) Reinfections, persistent infections, and new infections after general population screening for Chlamydia trachomatis infection in the Netherlands. Sex Transm Dis 32(10): 599-604. Gotz HM, van Bergen JE, Veldhuijzen IK, Broer J, Hoebe CJ, Steyerberg EW et al. (2005) A prediction rule for selective screening of Chlamydia trachomatis infection. Sex Transm Infect 81(1): 24-30. Gotz HM, Hoebe CJ, van Bergen JE, Veldhuijzen IK, Broer J, de Groot F et al. (2005) Management of Chlamydia cases and their partners: results from a home-based screening program organized by municipal public health services with referral to regular health care. Sex Transm Dis 32(10): 625-629. Gotz HM, Veldhuijzen IK, van Bergen JE, Hoebe CJ de Zwatt O, Richardus JH et al. (2005). "Acceptability and consequences of screening for chlamydia trachomatis by home-based urine testing." Sex Transm Dis 32(9): 557-562. Gotz HM, van Bergen JEAM, Veldhuijzen IK, Hoebe CJPA, Broer J, Coenen AJJ et al. (2006) Lessons learned from a population-based chlamydia screening pilot.

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Non-EU/EEA countries, high income OECD		
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Supporting Information TableS2

Risk of bias in all studies

	Target population representative of country	Target population clearly defined	Source population representative of target	Sample size calculation	Adequate sample size achieved	Probability sampling	Respondents match target population	Response rate 70% limit	Response rate 60% limit	Standardised questionnaire	NAAT used	Appropriate analysis	Confidence intervals
EU/EEA countries													
Denmark 1998	−	?	?	?	?	+	−	−	−	+	+	+	+
Denmark 1999	−	+	−	−	?	+	−	−	−	+	+	+	+
Denmark 2001	?	+	+	?	?	+	−	−	−	+	+	+	+
Denmark 2002	?	?	?	?	?	+	?	−	−	+	+	+	+
Estonia 2008	?	+	+	+	?	+	−	−	−	+	+	+	+
France 2010	+	+	+	+	?	+	?	−	−	+	+	+	+
Germany 2012	+	+	+	+	?	+	+	−	+	+	+	+	+
Netherlands 2000	−	+	?	−	?	+	−	−	−	+	+	+	+
Netherlands 2005	+	+	?	+	+	+	−	−	−	+	+	+	+
Netherlands 2010	?	+	+	+	?	+	−	−	−	+	+	+	+
Norway 2005	−	+	?	?	?	+	−	−	−	+	+	+	+
Norway 2012	?	+	+	−	?	+	−	−	−	+	+	+	+
Slovenia 2004	+	+	+	−	?	+	−	−	+	+	+	+	+
Spain 2007	−	+	?	+	−	+	−	−	−	+	+	+	+
Sweden 1992	−	+	+	−	?	−	?	−	+	+	−	+	+
Sweden 1995	−	+	?	+	?	+	+	+	+	+	−	+	+
Sweden 2003	−	?	?	−	?	−	?	−	−	+	+	+	+
Sweden 2004	−	?	?	−	?	+	?	−	+	+	+	+	−

Sweden 2007	−	?	?	−	?	?	−	−	−	+	+	?	+
United Kingdom 2000a	−	+	?	−	?	+	−	−	−	+	+	+	+
United Kingdom 2000b	−	?	?	−	?	+	−	−	−	+	+	+	+
United Kingdom 2001	+	+	−	−	?	+	−	+	+	+	+	+	+
United Kingdom 2007	?	+	?	+	−	+	−	−	−	+	+	+	+
United Kingdom 2012	?	?	?	−	?	+	−	−	−	+	+	+	+

	Target population representative of country	Target population clearly defined	Source population representative of target	Sample size calculation	Adequate sample size achieved	Probability sampling	Respondents match target population	Response rate 70% limit	Response rate 60% limit	Standardised questionnaire	NAAT used	Appropriate analysis	Confidence intervals
Other European and high-income OECD countries													
Croatia 2011	+	+	?	+	?	+	−	−	−	+	+	+	+
Switzerland 2008	?	+	?	−	?	+	?	?	?	+	+	+	+
USA 2001	−	+	+	+	+	+	−	−	+	+	+	+	+
USA 2002a	?	+	?	−	?	+	+	−	−	+	+	+	−
USA 2002b	−	+	+	−	?	+	+	+	+	+	+	+	+
USA 2004	+	+	+	−	?	+	+	+	+	+	+	+	+
USA 2011	?	+	+	−	?	+	−	−	−	+	+	+	+
USA 2012	+	+	+	−	?	+	−	+	+	+	+	+	+
Canada 2002	−	?	?	−	?	−	?	−	−	+	+	+	−
Canada 2009	−	+	?	−	?	−	−	+	+	+	+	+	−
Australia 2003	−	?	?	−	?	−	+	−	−	+	+	+	+
Australia 2004	−	?	?	?	?	?	?	−	−	?	+	+	−
Australia 2006	?	+	+	+	−	+	−	−	−	+	+	+	+

Australia 2008	−	+	?	−	?	?	+	?	?	?	+	+	−
New Zealand 2002	−	+	?	+	−	+	−	+	+	+	+	+	+

Legend for Supplementary Figure 1

Response rate (defined as number tested/number asked to participate)

+ more than 80% + = 70-80% − less than 70% ? unclear/cannot be calculated (70% limit) OR

+ more than 80% + = 60-80% − less than 60% ? unclear/cannot be calculated (60% limit)

NAAT used and confidence intervals for positivity/prevalence estimates were included or could be calculated.

+ yes − no

All other items + adequate − inadequate ? unclear/not enough information provided

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Online resource 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5-6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Online resource 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Fig 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Fig 3-4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Fig 5-6
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	8
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	8
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	9
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	9-11
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	13

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