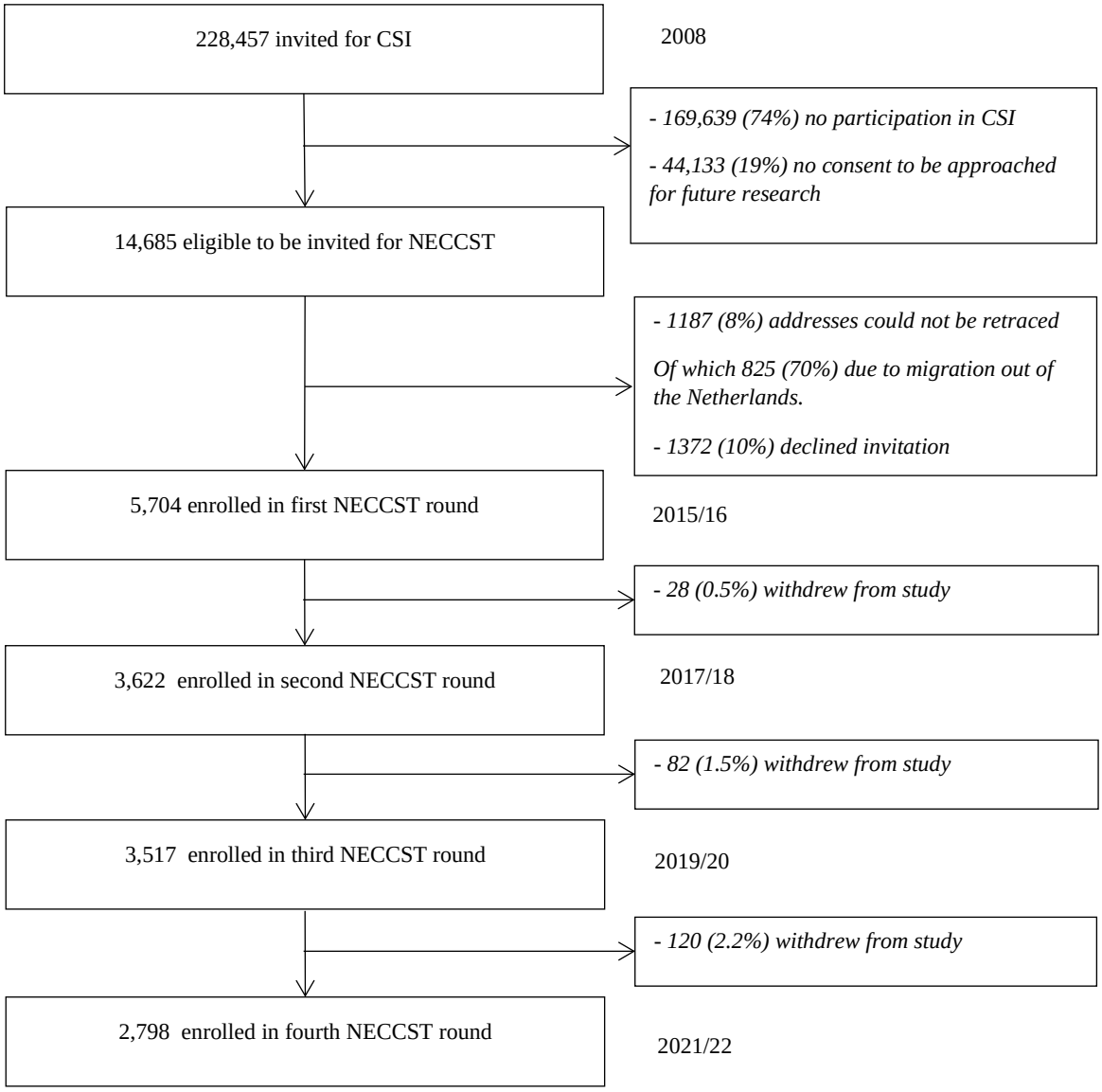
Supplementary materials - Table of contents

Figure S1 - Study inclusion flowchart

Details are described in Box S1.



CSI = Chlamydia Screening Implementation. NECCST = Netherlands Chlamydia Cohort Study.

Figure S2 - Retention of participants

In first round, second round, third round and fourth round of NECCST cohort. Grey boxes indicate (partial) loss to follow up. Details are described in Box S1.

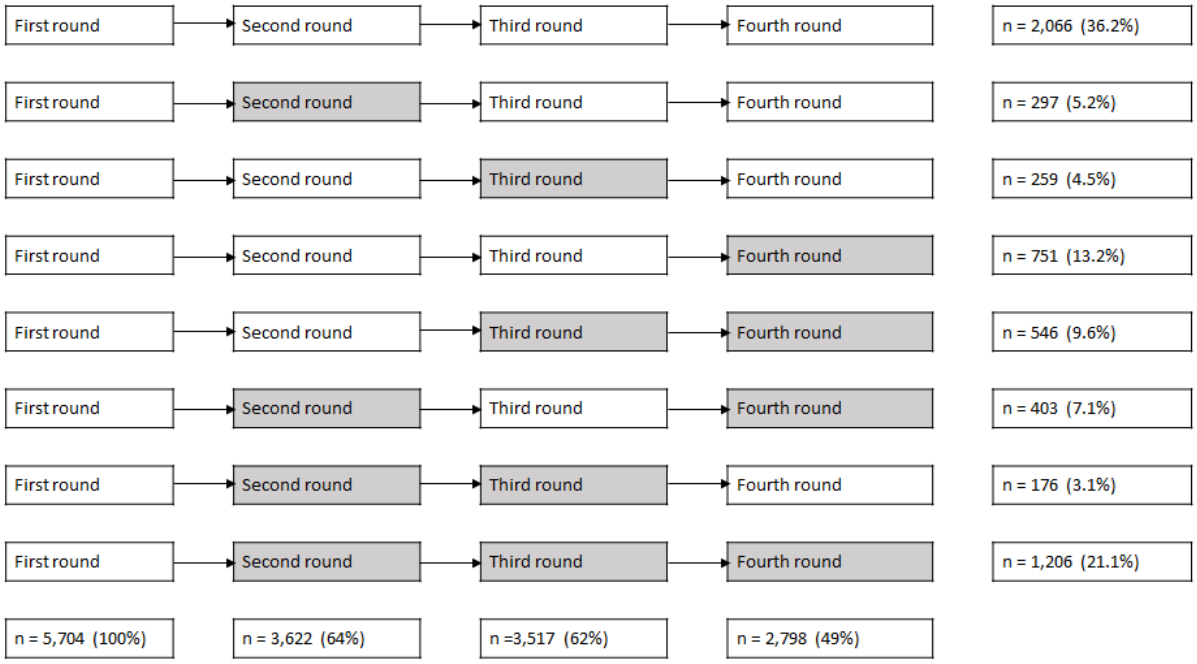
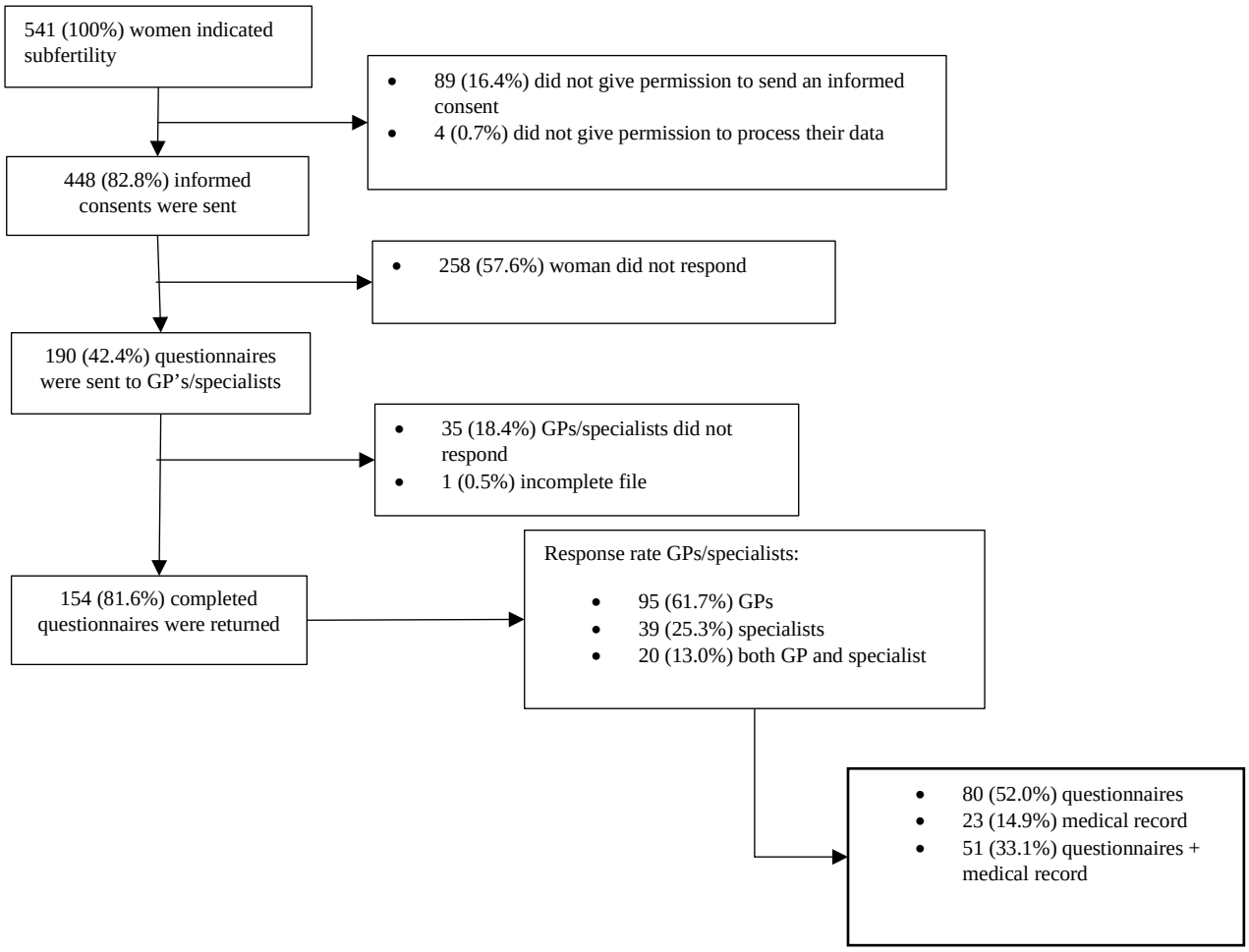


Figure S3 - Flowchart medical registry check

Details are described in Box S2.



Box S1 - Details of response and loss-to-follow up

All women, whether chlamydia-positive or chlamydia-negative, who were invited to participate in NECCST were from the same population. Of the total women from the general population sample invited for CSI (n=228,457), 26% (n=58,818) engaged in the CSI at least once. Women that were enrolled in CSI compared to the general population were more often of Non-Western migration background and had more often a theoretical education background. Behavioral factors associated with participation were having no long-standing relationship and reported history or symptoms of sexually transmitted infections (1).

From the female CSI participants, 14,685 (6%) granted consent to be considered for future STI research, making them eligible for NECCST (figure S1). Within NECCST, 5704 women (38.8%) participated, as depicted in Figure S1. The NECCST cohort, totaling 5704 women, encompassed both those with and without prior chlamydia infections. Women that were enrolled in NECCST compared to non-respondents more often had a theoretical education, were more often Dutch and had less lifetime or recent sex partners.

NECCST comprised four data-collection rounds. All women who participated in the first round were invited to join the second, third, and fourth rounds, regardless of their participation in previous rounds. Participation rates were 63.5% (3,622 women) in the second round, 61.7% (3,517 women) in the third round, and 49.1% (2,798 women) in the final round (see Figure S1).

A total of 2,066 women (36.2%) participated in all four rounds, while 1,206 women (21.1%) participated only in the first round. Approximately 23% (n=1,307) of women participated in three rounds, and 19.7% (n=1,125) participated in two rounds (see Figure S2). Determinants associated with study retention included younger age, higher education, Western migration background, absence of previous chlamydia infections, fewer lifetime partners, and a greater number of previous chlamydia tests (regardless of outcome). Across all subsequent NECCST rounds after the initial round, women without chlamydia infection at baseline were significantly more likely to participate compared to the first round alone: first round 65.9%, second round 72.0%, third round 72.8%, and fourth round 72.5%, respectively.

Box S2 – Details of medical register validation

An accurate TFI diagnosis needs invasive medical examinations. All women who self-reported subfertility were asked which fertility examinations had been conducted, i.e. chlamydia antibody testing (CAT), hysterosalpingography (HSG), contrast ultrasonography, laparoscopy or 'none of the above'. Furthermore they were asked about the cause of subfertility i.e. tubal pathology, endometriosis, ovulatory dysfunction, surgery/removal of ovaries, fallopian tubes and/or uterus, unexplained or other. Those who reported subfertility due to only male factor were not asked further questions about examinations and causes.

To test the validity of a self-reported TFI diagnosis, we asked all women that reported in the questionnaire to be sub fertile if we could verify this in their medical record at either the GP or medical (fertility) specialist. In total, 541 (9.5%) women reported to be sub fertile and were asked if we could contact them for informed consent for medical registry insight. Eventually 448 (82.8%) informed consent files including information letters were sent. Forty-two percent signed the informed consent forms for the medical record request. Eventually, 154 (34.4%) files were used to validate self-reported answers in medical records (Figure S3). Healthcare providers could either provide the information in a questionnaire or send relevant parts of the electronic patient record.

In this study the validity between self-reported causes of subfertility and medical records data was assessed from all four rounds of NECCST. The validity of overall subfertility was high as 86.4% was validated from medical record data. A substantial level of agreement (kappa = 0.72) was found in our study for tubal subfertility (Table S1**)**. This was comparable with results from a cohort study by de Boer et al. that assessed the validity of self-reported data on causes of subfertility (2). They found a kappa value of 0.79 for tubal subfertility, which they classified as 'excellent agreement'.

There was possible under-reporting of TFI cases due to misclassification of participants in our study. Of the self-reported TFI cases that we could not validate in the medical record, 33.3% had "removal of the ovaries or fallopian tubes" as cause of subfertility in the medical record. A possible reason for removal of fallopian tubes could be hydrosalpinx or extra-uterine gravidity. In this case, participants did not end up in the medical record TFI group, but may belong to it. But we can also not exclude these cases are unrelated to TFI. Especially for removal of the ovaries which is more often related to endometriosis, cysts or (increased risk of) ovarian cancer.

Under-reporting of TFI was also found for participants that had TFI as cause of subfertility in the medical record, but did not self-reported it. Of these participants, 40.0% reported "removal of the ovaries or fallopian tubes" in the online questionnaire. It could be that participants were not aware of anatomical differences between for example ovaries or fallopian tubes. In this case participants did not end up in the self-reported TFI group, but probably did belong to it. Considering this, we regard 0.72 to be an acceptable agreement.

References

1. Op de Coul EL, Gotz HM, van Bergen JE, Fennema JS, Hoebe CJ, Koekenbier RH, et al. Demographic and behavioral correlates of participation and positivity in the Dutch Chlamydia screening: Who participates? Sex Transm Dis. 2012;39(2):97-103.

2. de Boer EJ, den Tonkelaar I, Burger CW, van Leeuwen FE, Group OP. Self-reported causes of subfertility: Validity assessment. Am J Epidemiol. 2005;161(10):978-86.

Table S1 - Medical registry check outcomes
Comparison for subfertility and its causes between self-reported data and medical data from GPs or specialists for women for whom the medical record could be retrieved (n=154). For each women each cause of subfertility was analyzed independently and therefore combinations were not taken into account.

Self-reported (+) indicating that specific cause was self-reported, self-reported (-) indicating that specific cause was not self-reported. Medical record (+) indicating that specific cause was documented in medical records, medical record (-) indicating that specific cause was not documented in medical records. # only women with at least one self-reported cause of subfertility were included in the analysis.

	Subfertility cause Self-reported (+)		**Subfertility cause Self-reported (-)**		**Validity**			**Reliability**	
	Medical record (+)	Medical record (-)	Medical record (+)	Medical record (-)	Positive predictive value (%)	Sensitivity (%)	Specificity (%)	Agreement (%)	Kappa value
Subfertility	133	21	-[#]	-[#]	86.4	-	-	-	-
Causes									
Tubal pathology	12	3	5	134	80.0	70.6	97.8	94.8	0.72
Endometriosis	5	3	8	138	62.5	38.5	97.9	92.9	0.44
Ovulatory dysfunction	71	45	11	27	61.2	86.6	37.5	63.6	0.25
Surgery/Removal of ovaries, fallopian tubes	2	11	3	138	15.4	40.0	92.6	90.9	0.18
	6	34	10	104	15.0	37.5	75.4	71.4	0.08
Other	3	-	25	126	100	10.7	100	83.7	0.16
Unexplained									

Table S2 – Potential confounders

Overview of variables collected from NECCST participants assessed as potential confounders

variable	timing	data source	definition	class	categories
gonorrhea diagnosis	time-varying	self-reported	recorded by calender year	categorical	yes/no
IUD insertion	time-varying	self-reported	recorded by calender year	categorical	yes/no
age	sexual debut	self-reported	at sexual debut	continious	
condom use with casual partner	NECCST study inclusion	self-reported	last 12 months	categorical	always, mostly/ sometimes/ never or not often/ no casual partners
smoking	NECCST study inclusion	self-reported	lifetime	categorical	daily/ yes, but not continuously/ never
BMI	NECCST study inclusion	self-reported		categorical	<25/ 25-30/ >30
number of chlamydia tests	NECCST study inclusion	self-reported	lifetime	categorical	1-2/ 3-5/ ≥6
number of sex partners	NECCST study inclusion	self-reported	lifetime	categorical	<6/ 6-12/ >12
education level	NECCST study inclusion	self-reported	highest completed	categorical	theoretical (higher professional education, university level education)/ practical (all other education)
migration background	NECCST study inclusion	population registries	based on country of birth of both parents	categorical	Western (Dutch, Western Non-Dutch (incl. West European countries, Australia, North America, Indonesia and Japan))/ non-Western (Marocco and Turkey, SAN, other Non-western countries)

IUD = intratuterine device, SAN = SAN: Suriname, Aruba and the former Dutch Antilles

Table S3 - Characteristics of the study population by chlamydia status

Overall and stratified by chlamydia status at last data collection

	Overall, N = 5,704[1]	Chlamydia-negative, N = 3,691[1]	Chlamydia-positive, N = 2,013[1]	p-value[2]
Age (years) mean (SD)[#]	35.28 (4.45)	35.46 (4.42)	34.95 (4.50)	<0.001
Chlamydia status[#]				
CT negative	3,691 (65%)	3,691 (100%)	0 (0%)	
Self-reported + screening-PCR	230 (4.0%)	0 (0%)	230 (11%)	
Self-reported + screening-PCR + CT-IgG	112 (2.0%)	0 (0%)	112 (5.6%)	
Self-reported + CT-IgG	350 (6.1%)	0 (0%)	350 (17%)	
Self-reported only	868 (15%)	0 (0%)	868 (43%)	
Screening-PCR + CT-IgG	1 (<0.1%)	0 (0%)	1 (<0.1%)	
Screening-PCR only	3 (<0.1%)	0 (0%)	3 (0.1%)	
CT-IgG only	449 (7.9%)	0 (0%)	449 (22%)	
Migration background				<0.001
Non-western	869 (15%)	410 (11%)	459 (23%)	
Western	4,565 (80%)	3,121 (85%)	1,444 (72%)	
Unknown	270 (4.7%)	160 (4.3%)	110 (5.5%)	
Educational level[$]				<0.001
Practical	1,163 (20%)	603 (16%)	560 (28%)	
Theoretical	4,539 (80%)	3,088 (84%)	1,451 (72%)	
Unknown	2 (<0.1%)	0 (0%)	2 (<0.1%)	
Smoking (lifetime)				<0.001
Daily	525 (9.2%)	267 (7.2%)	258 (13%)	
Yes, but not continuously	2,919 (51%)	1,819 (49%)	1,100 (55%)	
Never	2,260 (40%)	1,605 (43%)	655 (33%)	
BMI				0.002
<25	4,322 (76%)	2,849 (77%)	1,473 (73%)	
25-30	939 (16%)	587 (16%)	352 (17%)	
>30	431 (7.6%)	249 (6.7%)	182 (9.0%)	
Unknown	12 (0.2%)	6 (0.2%)	6 (0.3%)	
Age at sexual debut mean (SD)	16.94 (2.35)	17.15 (2.38)	16.55 (2.24)	<0.001
Lifetime sex partners				<0.001
<6	718 (13%)	526 (14%)	192 (9.5%)	
6-12	1,989 (35%)	1,457 (39%)	532 (26%)	
>12	2,997 (53%)	1,708 (46%)	1,289 (64%)	

	Overall, N = 5,704[1]	Chlamydia-negative, N = 3,691[1]	Chlamydia-positive, N = 2,013[1]	p-value[2]
Condom use with casual partners (last 12 months)				
Always, mostly	2,610 (46%)	1,745 (47%)	865 (43%)	<0.001
Sometimes	1,807 (32%)	1,012 (27%)	795 (39%)	
Never/not often	340 (6.0%)	204 (5.5%)	136 (6.8%)	
No casual partners	936 (16%)	721 (20%)	215 (11%)	
Unknown	11 (0.2%)	9 (0.2%)	2 (<0.1%)	
Gonorrhea positivity (n%)[#]	120 (2.1%)	30 (0.8%)	90 (4.5%)	<0.001
Use of IUD[#]				0.3
Never	3,160 (55%)	2,064 (56%)	1,096 (54%)	
At least once	2,544 (45%)	1,627 (44%)	917 (46%)	
Pregnancy[#]				0.4
Never pregnant nor tried	1,765 (31%)	1,157 (31%)	608 (30%)	
Tried or trying and failed to become pregnant	247 (4.3%)	152 (4.1%)	95 (4.7%)	
Ever pregnant	3,692 (65%)	2,382 (65%)	1,310 (65%)	
Planned (at least once)	2,989 (52%)	2,039 (55%)	950 (47%)	<0.001
Age at first pregnancy (years) mean (SD)[#]	29.25 (5.35)	29.83 (4.83)	28.20 (6.04)	<0.001
Number of chlamydia tests (lifetime)				<0.001
1-2	2,581 (45%)	1,999 (54%)	582 (29%)	
3-5	2,700 (47%)	1,563 (42%)	1,137 (56%)	
6 or more	423 (7.4%)	129 (3.5%)	294 (15%)	
Chlamydia specific variables				
Chlamydia diagnosis[#]				
No infection	3,691 (65%)	3,691 (100%)	0 (0%)	
Asymptomatic	767 (13%)	0 (0%)	767 (38%)	
Symptomatic	797 (14%)	0 (0%)	797 (40%)	
Serology+ only	449 (7.9%)	0 (0%)	449 (22%)	
Repeat chlamydia infections[#]				
No infection	3,691 (65%)	3,691 (100%)	0 (0%)	
Single	1,138 (20%)	0 (0%)	1,138 (56%)	
Multiple	426 (7.5%)	0 (0%)	426 (21%)	
Serology+ only	449 (7.9%)	0 (0%)	449 (22%)	
Age at first chlamydia infection[#]				

	Overall, N = 5,704[1]	Chlamydia-negative, N = 3,691[1]	Chlamydia-positive, N = 2,013[1]	p-value[2]
13-22	706 (45%)	0 (0%)	706 (45%)	
23-31	775 (50%)	0 (0%)	775 (50%)	
32-41	73 (4.7%)	0 (0%)	73 (4.7%)	
No infection / Serology+ only	4,149	3,690	459	
Chlamydia antibodies (serology)[#]				
Negative	2,749 (48%)	2,271 (62%)	478 (24%)	
Positive	912 (16%)	0 (0%)	912 (45%)	
Unknown[^]	2,043 (36%)	1,420 (38%)	623 (31%)	

Chlamydia-positive was defined as a positive screening-PCR outcome in the CSI study (screening-PCR), and/or the presence of chlamydia IgG antibodies (serology) and/or a self-reported chlamydia infection (self-reported). Variables were assessed using data from baseline unless marked as assessed by the most recent data collection indicated with [#]. Lifetime variables were based on data from sexual debut until baseline questionnaire. If ≥5% was missing in one of the subgroups an extra category `unknown` was included. [$]Educational level: theoretical (higher professional education, university level education) vs practical (all other educations). + migration background classified as 'Western' if both parents had a Western country of birth i.e. a country from Europe [excluding Turkey], North America, Oceania, Indonesia and Japan, 'non-Western' if at least one parent had a non-Western country of birth, and 'unknown' if one parent was Western while the country of birth of the other parent was unknown or when the country of birth of both parents was unknown. [^]No serum sample submitted or not sufficient amount of serum to be tested. [1]Mean (SD) n (%); [2]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test; * = statistically significant, $p<0.05$. SD = standard deviation. CSI = chlamydia screening implementation. CT = *Chlamydia trachomatis*. IUD = Intrauterine Device. IgG= Immunoglobulin G. BMI = Body mass index.

Table S4 - Characteristics of the study population by imputation status

Among those for which year of chlamydia infection was imputed versus not imputed.

	Overall, N = 2,013[1]	Not imputed, N = 1,554[1]	Imputed, N = 459[1]	p-value[2]
Age (years) mean (SD)	34.95 (4.50)	34.63 (4.49)	36.05 (4.36)	<0.001
Chlamydia status[#]				
Self-reported + screening-PCR	230 (11%)	230 (15%)	0 (0%)	
Self-reported + screening-PCR + CT-IgG	112 (5.6%)	112 (7.2%)	0 (0%)	
Self-reported + CT-IgG	350 (17%)	349 (22%)	1 (0.2%)	
Self-reported only	868 (43%)	863 (56%)	5 (1.1%)	
Screening-PCR + CT-IgG	1 (<0.1%)	0 (0%)	1 (0.2%)	
Screening-PCR only	3 (0.1%)	0 (0%)	3 (0.7%)	
CT-IgG only	449 (22%)	0 (0%)	449 (98%)	
Migration background				<0.001
Non-western	459 (23%)	384 (25%)	75 (16%)	
Western	1,444 (72%)	1,085 (70%)	359 (78%)	
Unknown	110 (5.5%)	85 (5.5%)	25 (5.4%)	
Educational level[$]				<0.001
Practical	560 (28%)	471 (30%)	89 (19%)	
Theoretical	1,451 (72%)	1,082 (70%)	369 (80%)	
Unknown	2 (<0.1%)	1 (<0.1%)	1 (0.2%)	
Smoking (lifetime)				0.005
Every day	258 (13%)	216 (14%)	42 (9.2%)	
Yes, but not continuously	1,100 (55%)	854 (55%)	246 (54%)	
Never	655 (33%)	484 (31%)	171 (37%)	
BMI				0.8
<25	1,473 (73%)	1,133 (73%)	340 (74%)	
25-30	352 (17%)	273 (18%)	79 (17%)	
>30	182 (9.0%)	144 (9.3%)	38 (8.3%)	
Unknown	6 (0.3%)	4 (0.3%)	2 (0.4%)	
Age at sexual debut mean (SD)	16.55 (2.24)	16.40 (2.13)	17.05 (2.53)	<0.001
Lifetime sex partners				<0.001
<6	192 (9.5%)	131 (8.4%)	61 (13%)	
6-12	532 (26%)	380 (24%)	152 (33%)	
>=12	1,289 (64%)	1,043 (67%)	246 (54%)	

	Overall, N = 2,013[1]	Not imputed, N = 1,554[1]	Imputed, N = 459[1]	p-value[2]
Condom use with casual partners (last 12 months)				<0.001
Always, mostly	865 (43%)	651 (42%)	214 (47%)	
Sometimes	795 (39%)	669 (43%)	126 (27%)	
Never/not often	136 (6.8%)	101 (6.5%)	35 (7.6%)	
No casual partners	215 (11%)	132 (8.5%)	83 (18%)	
Unknown	2 (<0.1%)	1 (<0.1%)	1 (0.2%)	
Gonorrhea positivity (n%)[#]	90 (4.5%)	82 (5.3%)	8 (1.7%)	0.001
Use of IUD[#]				0.7
Never	1,096 (54%)	850 (55%)	246 (54%)	
At least once	917 (46%)	704 (45%)	213 (46%)	
Pregnancy[#]				0.047
Ever pregnant	1,310 (65%)	997 (64%)	313 (68%)	
Never pregnant nor tried	611 (30%)	477 (31%)	134 (29%)	
Tried or trying and failed to become pregnant	92 (4.6%)	80 (5.1%)	12 (2.6%)	
Planned (at least once)[#]				<0.001
Not planned (at least once)	1,089 (54%)	883 (57%)	206 (45%)	
Planned (at least once)	924 (46%)	671 (43%)	253 (55%)	
Age at first pregnancy (years) mean (SD)[#]	28.20 (6.04)	27.80 (6.14)	29.48 (5.51)	<0.001
Unknown	703	557	146	
Number of chlamydia tests (lifetime)				<0.001
1-2	582 (29%)	359 (23%)	223 (49%)	
3-5	1,137 (56%)	927 (60%)	210 (46%)	
6 or more	294 (15%)	268 (17%)	26 (5.7%)	
Chlamydia infection with symptoms[#]				<0.001
Asymptomatic	767 (38%)	757 (49%)	10 (2.2%)	
Symptomatic	797 (40%)	797 (51%)	0 (0%)	
Serology+ only	449 (22%)	0 (0%)	449 (98%)	
Number of chlamydia infections[#]				
1	1,138 (57%)	1,128 (73%)	10 (2.2%)	
2 or more	426 (21%)	426 (27%)	0 (0%)	
Serology+ only	449 (22%)	0 (0%)	449 (98%)	
Age at first chlamydia infection[#]				
13-22	706 (45%)	706 (45%)	0 (0%)	

	Overall, N = 2,013[1]	Not imputed, N = 1,554[1]	Imputed, N = 459[1]	p-value[2]
23-31	775 (50%)	775 (50%)	0 (0%)	
32-41	73 (4.7%)	73 (4.7%)	0 (0%)	
No infection / Serology+ only	459	0	459	
Chlamydia IgG antibodies (serology)[#]				
Negative	478 (24%)	473 (30%)	5 (1.1%)	
Positive	912 (45%)	461 (30%)	451 (98%)	
Unknown[^]	623 (31%)	620 (40%)	3 (0.7%)	

Chlamydia-positive was defined as a positive screening-PCR outcome in the CSI study (screening-PCR), and/or the presence of chlamydia IgG antibodies (serology) and/or a self-reported chlamydia infection (self-reported). Variables were assessed using data from baseline unless marked as assessed by the most recent data collection indicated with [#]. Lifetime variables were based on data from sexual debut until baseline questionnaireIf ≥5% was missing in one of the subgroups an extra category `unknown` was included. [$]Educational level: theoretical (higher professional education, university level education) vs practical (all other educations). + migration background classified as 'Western' if both parents had a Western country of birth i.e. a country from Europe [excluding Turkey], North America, Oceania, Indonesia and Japan, 'non-Western' if at least one parent had a non-Western country of birth, and 'unknown' if one parent was Western while the country of birth of the other parent was unknown or when the country of birth of both parents was unknown. [^]No serum sample submitted or not sufficient amount of serum to be tested. [1]Mean (SD) n (%); [2]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test; * = statistically significant, p<0.05. SD = standard deviation. CSI = chlamydia screening implementation. CT = *Chlamydia trachomatis.* IUD = Intrauterine Device. IgG= Immunoglobulin G. BMI = Body mass index.

Table S5 - Characteristics of the study population by diagnosis status

Among those with an asymptomatic versus serology+ only chlamydia infection.

	Overall, N = 1,216[1]	**Asymptomatic,** N = 767[1]	**Serology+ only ,** N = 449[1]	**p-value**[2]
Age (years) mean (SD)[#]	35.37 (4.36)	34.95 (4.32)	36.09 (4.34)	<0.001
Chlamydia status[#]				
Self-reported + screening-PCR	125 (10%)	125 (16%)	0 (0%)	
Self-reported + screening-PCR + CT-IgG	53 (4.4%)	53 (6.9%)	0 (0%)	
Self-reported + CT-IgG	167 (14%)	167 (22%)	0 (0%)	
Self-reported only	418 (34%)	418 (54%)	0 (0%)	
Screening-PCR + CT-IgG	1 (<0.1%)	1 (0.1%)	0 (0%)	
Screening-PCR only	3 (0.2%)	3 (0.4%)	0 (0%)	
CT-IgG only	449 (37%)	0 (0%)	449 (100%)	
Migration background				0.13
Non-western	231 (19%)	159 (21%)	72 (16%)	
Western	921 (76%)	568 (74%)	353 (79%)	
Unknown	64 (5.3%)	40 (5.2%)	24 (5.3%)	
Educational level[$]				0.013
Practical	284 (23%)	198 (26%)	86 (19%)	
Theoretical	930 (76%)	568 (74%)	362 (81%)	
Unknown	2 (0.2%)	1 (0.1%)	1 (0.2%)	
Smoking (lifetime)				<0.001
Every day	147 (12%)	108 (14%)	39 (8.7%)	
Yes, but not continuously	679 (56%)	437 (57%)	242 (54%)	
Never	390 (32%)	222 (29%)	168 (37%)	
BMI				0.7
<25	910 (75%)	579 (75%)	331 (74%)	
25-30	199 (16%)	120 (16%)	79 (18%)	
>30	102 (8.4%)	65 (8.5%)	37 (8.2%)	
Unknown	5 (0.4%)	3 (0.4%)	2 (0.4%)	
Age at sexual debut mean (SD)	16.72 (2.26)	16.51 (2.06)	17.07 (2.55)	<0.001
Lifetime sex partners				<0.001
<6	116 (9.5%)	55 (7.2%)	61 (14%)	
6-12	337 (28%)	188 (25%)	149 (33%)	
>=12	763 (63%)	524 (68%)	239 (53%)	
Condom use with casual partners (last 12 months)				<0.001

	Overall, N = 1,216[1]	**Asymptomatic,** N = 767[1]	**Serology+ only ,** N = 449[1]	**p-value**[2]
Always, mostly	536 (44%)	329 (43%)	207 (46%)	
Sometimes	443 (36%)	320 (42%)	123 (27%)	
Never/not often	86 (7.1%)	51 (6.6%)	35 (7.8%)	
No casual partners	150 (12%)	67 (8.7%)	83 (18%)	
Unknown	1 (<0.1%)	0 (0%)	1 (0.2%)	
Gonorrhea positivity (n%)[#]	35 (2.9%)	27 (3.5%)	8 (1.8%)	0.080
Use of IUD[#]				0.9
Never	648 (53%)	408 (53%)	240 (53%)	
At least once	568 (47%)	359 (47%)	209 (47%)	
Pregnancy[#]				0.026
Ever pregnant	804 (66%)	494 (64%)	310 (69%)	
Never pregnant nor tried	355 (29%)	228 (30%)	127 (28%)	
Tried or trying and failed to become pregnant	57 (4.7%)	45 (5.9%)	12 (2.7%)	
Planned (at least once)[#]				0.001
Not planned (at least once)	610 (50%)	412 (54%)	198 (44%)	
Planned (at least once)	606 (50%)	355 (46%)	251 (56%)	
Age at first pregnancy (years) mean (SD)[#]	29.02 (5.73)	28.72 (5.86)	29.49 (5.48)	0.2
Number of chlamydia tests (lifetime)				<0.001
1-2	412 (34%)	190 (25%)	222 (49%)	
3-5	666 (55%)	462 (60%)	204 (45%)	
6 or more	138 (11%)	115 (15%)	23 (5.1%)	
Chlamydia specific variables				
Repeat chlamydia infections[#]				
Single	637 (52%)	637 (83%)	0 (0%)	
Multiple	130 (11%)	130 (17%)	0 (0%)	
Serology+ only	449 (37%)	0 (0%)	449 (100%)	
Age at first chlamydia infection[#]				
13-22	297 (39%)	297 (39%)	0 (0%)	
23-31	421 (56%)	421 (56%)	0 (0%)	
32-41	39 (5.2%)	39 (5.2%)	0 (0%)	
Not reported/Serology+ only	459	10	449	
Chlamydia antibodies (serology)[#]				
Negative	252 (21%)	252 (33%)	0 (0%)	
Positive	670 (55%)	221 (29%)	449 (100%)	

	Overall, N = 1,216[1]	**Asymptomatic,** N = 767[1]	**Serology+ only ,** N = 449[1]	**p-value[2]**
Unknown[^]	294 (24%)	294 (38%)	0 (0%)	

Asymptomatic was defined as screening-PCR+ and/or self-reported + without symptoms while serology+ only was defined as presence of chlamydia IgG antibodies without any other chlamydia indicators. Variables were assessed using data from baseline unless marked as assessed by the most recent data collection indicated with [#]. Lifetime variables were based on data from sexual debut until baseline questionnaire If ≥5% was missing in one of the subgroups an extra category `unknown` was included. [$]Educational level: theoretical (higher professional education, university level education) vs practical (all other educations). + migration background classified as 'Western' if both parents had a Western country of birth i.e. a country from Europe [excluding Turkey], North America, Oceania, Indonesia and Japan, 'non-Western' if at least one parent had a non-Western country of birth, and 'unknown' if one parent was Western while the country of birth of the other parent was unknown or when the country of birth of both parents was unknown. [^]No serum sample submitted or not sufficient amount of serum to be tested. [1]Mean (SD) n (%); [2]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test; * = statistically significant, p<0.05. SD = standard deviation. CSI = chlamydia screening implementation. CT = *Chlamydia trachomatis*. IUD = Intrauterine Device. IgG= Immunoglobulin G. BMI = Body mass index.

Table S6 - Characteristics of the study population by symptoms status

Among those with only asymptomatic infections(s) versus those who experienced symptomatic chlamydia infection(s).

	Overall, N = 1,5641	**Asymptomatic**, N = 767[1]	**Symptomatic,** N = 797[1]	**p-value[2]**
Age (years) mean (SD)[#]	34.63 (4.49)	34.95 (4.32)	34.31 (4.64)	0.009
Chlamydia status[#]				
Self-reported + screening-PCR	230 (15%)	125 (16%)	105 (13%)	0.2
Self-reported + screening-PCR + CT-IgG	112 (7.2%)	53 (6.9%)	59 (7.4%)	
Self-reported + CT-IgG	350 (22%)	167 (22%)	183 (23%)	
Self-reported only	868 (55%)	418 (54%)	450 (56%)	
Screening-PCR + CT-IgG	1 (<0.1%)	1 (0.1%)	0 (0%)	
Screening-PCR only	3 (0.2%)	3 (0.4%)	0 (0%)	
CT-IgG only	0 (0%)	0 (0%)	0 (0%)	
Migration background				<0.001
Non-western	387 (25%)	159 (21%)	228 (29%)	
Western	1,091 (70%)	568 (74%)	523 (66%)	
Unknown	86 (5.5%)	40 (5.2%)	46 (5.8%)	
Educational level[$]				<0.001
Practical	474 (30%)	198 (26%)	276 (35%)	
Theoretical	1,089 (70%)	568 (74%)	521 (65%)	
Unknown	1 (<0.1%)	1 (0.1%)	0 (0%)	
Smoking (lifetime)				0.2
Every day	219 (14%)	108 (14%)	111 (14%)	
Yes, but not continuously	858 (55%)	437 (57%)	421 (53%)	
Never	487 (31%)	222 (29%)	265 (33%)	
BMI				0.094
<25	1,142 (73%)	579 (75%)	563 (71%)	
25-30	273 (17%)	120 (16%)	153 (19%)	
>30	145 (9.3%)	65 (8.5%)	80 (10%)	
Unknown	4 (0.3%)	3 (0.4%)	1 (0.1%)	
Age at sexual debut mean (SD)	16.40 (2.12)	16.51 (2.06)	16.29 (2.18)	0.020
Lifetime sex partners				0.2
<6	131 (8.4%)	55 (7.2%)	76 (9.5%)	

	Overall, N = 1,5641	Asymptomatic, N = 767[1]	Symptomatic, N = 797[1]	p-value[2]
6-12	383 (24%)	188 (25%)	195 (24%)	
>=12	1,050 (67%)	524 (68%)	526 (66%)	
Condom use with casual partners (last 12 months)				0.8
Always, mostly	658 (42%)	329 (43%)	329 (41%)	
Sometimes	672 (43%)	320 (42%)	352 (44%)	
Never/not often	101 (6.5%)	51 (6.6%)	50 (6.3%)	
No casual partners	132 (8.4%)	67 (8.7%)	65 (8.2%)	
Unknown	1 (<0.1%)	0 (0%)	1 (0.1%)	
Gonorrhea positivity (n%)[#]	82 (5.2%)	27 (3.5%)	55 (6.9%)	0.003
Use of IUD[#]				0.2
Never	856 (55%)	408 (53%)	448 (56%)	
At least once	708 (45%)	359 (47%)	349 (44%)	
Pregnancy[#]				0.3
Ever pregnant	1,000 (64%)	494 (64%)	506 (63%)	
Never pregnant nor tried	484 (31%)	228 (30%)	256 (32%)	
Tried or trying and failed to become pregnant	80 (5.1%)	45 (5.9%)	35 (4.4%)	
Planned (at least once)[#]				0.011
Not planned (at least once)	891 (57%)	412 (54%)	479 (60%)	
Planned (at least once)	673 (43%)	355 (46%)	318 (40%)	
Age at first pregnancy (years) mean (SD)[#]	27.80 (6.15)	28.72 (5.86)	26.90 (6.29)	<0.001
Number of chlamydia tests (lifetime)				0.033
1-2	360 (23%)	190 (25%)	170 (21%)	
3-5	933 (60%)	462 (60%)	471 (59%)	
6 or more	271 (17%)	115 (15%)	156 (20%)	
Chlamydia specific variables				
Repeat chlamydia infections[#]				<0.001
Single	1,138 (73%)	637 (83%)	501 (63%)	
Multiple	426 (27%)	130 (17%)	296 (37%)	
Chlamydia antibodies (serology)[#]				0.2
Negative	478 (31%)	252 (33%)	226 (28%)	
Positive	463 (30%)	221 (29%)	242 (30%)	
Unknown[^]	623 (40%)	294 (38%)	329 (41%)	
Age at first chlamydia infection[&]	**Overall, N = 1,5641**	**Asymptomatic, N = 783[1]**	**Symptomatic, N = 781[1]**	**p-value[2]**
<18	107 (6.8%)	37 (4.7%)	70 (9.0%)	<0.001

	Overall, N = 1,5641	Asymptomatic, N = 767[1]	Symptomatic, N = 797[1]	p-value[2]
18 – 22	721 (46.1%)	402 (51.3%)	319 (40.8%)	
23 - 41	736 (47.1%)	344 (43.9%)	392 (50.2%)	

Asymptomatic was defined as screening-PCR+ and/or self-reported+ without symptoms while symptomatic was defined as screening-PCR+ and/or self-reported+ with symptoms. Variables were assessed using data from baseline unless marked as assessed by the most recent data collection indicated with [#]. Lifetime variables were based on data from sexual debut until baseline questionnaire If ≥5% was missing in one of the subgroups an extra category `unknown` was included. [$]Educational level: theoretical (higher professional education, university level education) vs practical (all other educations). + migration background classified as 'Western' if both parents had a Western country of birth i.e. a country from Europe [excluding Turkey], North America, Oceania, Indonesia and Japan, 'non-Western' if at least one parent had a non-Western country of birth, and 'unknown' if one parent was Western while the country of birth of the other parent was unknown or when the country of birth of both parents was unknown. [^]No serum sample submitted or not sufficient amount of serum to be tested. [&] Numbers are different from numbers by symptoms group in the rest of Table S6 because women who experienced an asymptomatic infection before their first symptomatic infection are now categorized as asymptomatic.

[1]Mean (SD) n (%); [2]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test; * = statistically significant, $p<0.05$. SD = standard deviation. CSI = chlamydia screening implementation. CT = *Chlamydia trachomatis*. IUD = Intrauterine Device. IgG= Immunoglobulin G. BMI = Body mass index.

Table S7 - Sensitivity analysis pelvic inflammatory disease (PID)

Association between chlamydia positivity and hospitalized pelvic inflammatory disease (PID) in women participating in NECCST. Women who had already experienced non-hospitalized PID episodes were excluded from the analyses.

	N*	Person-years	HR‖	95%CI	P value	aHR‖#	95%CI	P value
PID Hospitalized								
Chlamydia negative	53	77,747	Ref			Ref		
Chlamydia positive	38	23,229	2.47	1.56 – 3.94	0.0002	2.08	1.28 – 3.41	0.0038

Chlamydia positive was defined as a positive PCR-test outcome in the CSI study (screening-PCR), and/or the presence of chlamydia IgG and/or a self-reported chlamydia infection. For these analyses, multiple imputations were used to estimate time of first chlamydia infection in women without a known first year of chlamydia infection. *Median cases of 15 multiple imputation datasets. ‖ Estimated from 15 multiple imputation datasets. # models adjusted for educational level, age (linear) and number of lifetime chlamydia tests. HR = Hazard Ratio. NECCST = Netherlands chlamydia cohort study. CI = Confidence Interval. aHR= Adjusted Hazard Ratio.

Table S8 - Association between stratified chlamydia positivity and outcomes in women participating in NECCST

Outcomes were pelvic inflammatory disease, ectopic pregnancy and tubal factor infertility. Chlamydia positivity was stratified by chlamydia status subgroups for diagnosis or repeat infection.

	Events	Time	Crude hazard ratio			Adjusted Hazard Ratio[a,b,c]		
	N*	Person-years[#]	HR‖	95%CI	P value	aHR‖	95%CI	P value
Pelvic Inflammatory Disease								
Chlamydia negative	146	78,201	Ref			Ref		
Diagnosis								
Chlamydia positive								
Asymptomatic	23	8,958	1.25	0.79 - 1.98	0.34	1.06	0.66 - 1.69	0.82
Symptomatic	53	9,109	2.99	2.16 - 4.14	< 0.00001	2.29	1.62 - 3.25	< 0.00001
Serology+ only	14	5,605	1.36	0.78 - 2.39	0.28	1.35	0.78 – 2.35	0.28
Repeat infection								
Chlamydia positive								
Single	58	14,748	2.01	1.46 - 2.76	< 0.0001	1.65	1.18 – 2.30	0.003
Multiple	18	3,286	2.68	1.62 - 4.43	0.00016	1.90	1.11 – 3.25	0.019
Serology+ only	14	5,605	1.36	0.78 - 2.39	0.28	1.35	0.78 – 2.35	0.28
Ectopic pregnancy								
Chlamydia negative	52	78,897	Ref			Ref		
Diagnosis								
Chlamydia positive								
Asymptomatic	13	9,151	1.74	0.93 - 3.26	0.084	1.77	0.92 - 3.41	0.088
Symptomatic	18	9,485	2.43	1.39 - 4.23	0.002	2.14	1.17 - 3.92	0.014
Serology+ only	8	5,694	1.89	0.87 - 4.10	0.106	1.85	0.86 - 3.98	0.12
Repeat infection								
Chlamydia positive								
Single	24	15,175	2.03	1.23 - 3.36	0.006	1.92	1.13 – 3.29	0.018
Multiple	7	3,427	2.31	1.02 - 5.22	0.044	2.32	0.96 – 5.61	0.06
Serology+ only	8	5,694	1.89	0.87 - 4.10	0.106	1.85	0.86 - 3.98	0.12
Tubal factor infertiliy								
Chlamydia negative	25	79,002	Ref			Ref		
Diagnosis								
Chlamydia positive								

Asymptomatic	9	9,144	2.3	1.04 - 5.07	0.04	2.26	1.01 - 5.10	0.05
Symptomatic	17	9,490	4.38	2.31 - 8.32	< 0.0001	4.45	2.27 - 8.73	< 0.0001
Serology+ only	8	5,694	1.28	0.37 - 4.45	0.69	1.27	0.37 - 4.40	0.70
Repeat infection								
Chlamydia positive								
Single	24	15,165	3.89	2.17 - 6.97	< 0.0001	3.75	2.04 – 6.87	< 0.0001
Multiple	2	3,434	1.23	0.28 - 5.45	0.78	1.21	0.26 – 5.55	0.80
Serology+ only	8	5,694	1.28	0.37 - 4.45	0.69	1.26	0.36 – 4.39	0.71

Chlamydia positive was defined as a positive PCR-test outcome in the CSI study (screening-PCR), and/or the presence of chlamydia IgG and/or a self-reported chlamydia infection. Symptomatic was defined as screening-PCR+ and/or self-reported+ with symptoms. Asymptomatic was defined as screening-PCR+ and/or self-reported + without symptoms. Serology+ only was defined as presence of chlamydia IgG antibodies without any other chlamydia indicators. For these analyses, multiple imputations were used to estimate time of first chlamydia infection in women without a known first year of chlamydia infection. *Median cases of 15 multiple imputation datasets. [#] person-years for pelvic inflammatory disease, ectopic pregnancy, tubal factor infertility and pregnancies. ‖ Estimated from 15 multiple imputation datasets. [a]PID Model adjusted for educational level, age (linear) and number of lifetime chlamydia tests. [b]Ectopic pregnancy model adjusted for age (linear), migration background, educational level, number of lifetime sex partners, number of lifetime chlamydia tests and IUD insertion. [C]TFI model adjusted for age (linear) and number of lifetime chlamydia tests.

NECCST = Netherlands chlamydia cohort study. CI = Confidence Interval. aHR= Adjusted Hazard Ratio.

Table S9 - Sensitivity analysis - Association between chlamydia positivity and complications (pelvic inflammatory disease, ectopic pregnancy, tubal factor infertility) in women participating in NECCST based on: 1. data of chlamydia positives based on screening-PCR results and chlamydia negatives only; and 2. data of chlamydia positives based on self-reported diagnosis and chlamydia negatives only. Women with Serology+ only serology+ only infections were excluded in these analyses.

	Crude HR (95%CI)	p value	Adjusted[a] HR (95%CI)	p value	Crude HR (95%CI)	p-value	Adjusted[b] HR (95%CI)	p value
	Model 1: Pelvic inflammatory disease[a] (n=142)				Model 2: Pelvic inflammatory disease[a] (n=192)			
Chlamydia								
Negative	Ref.		Ref.		Ref.		Ref.	
Positive	2·03 (1·20-3·44)	0·009	1·37 (0·79-2·38)	0·25	2·19 (1·59-3·02)	< 0.0001	1·78 (1·26-2·51)	0·001
	Model 1: Ectopic pregancy[b] (n=51)				Model 2: Ectopic pregancy[b] (n=73)			
Chlamydia								
Negative	Ref.				Ref.			
Positive	1·27 (0·44-3·63)	0·65	0·90 (0·30-2·75)	0·85	2·46 (1·50-4·05)	0·0006	2·33 (1·34-4·04)	0·004
	Model 1: Tubal factor infertility[c] (n=26)				Model 2: Tubal factor infertility[c] (n=48)			
Chlamydia								
Negative	Ref.				Ref.			
Positive	1·78 (0·49-6·38)	0·36	1·45 (0·40-5·31)	0·61	3·71 (2·04-6·73)	< 0.0001	4·03 (2·21-7·64)	< 0.0001

Chlamydia positive was defined as a positive PCR-test result in the screening study (screening-PCR) (model 1), or a self-reported chlamydia infection (self—reported) (model 2). [a] PID Model adjusted for educational level, age and number of lifetime chlamydia tests. [b] Ectopic pregnancy model adjusted for age, migration background, educational level, number of lifetime sex partners, number of lifetime chlamydia tests and IUD insertion. [C] TFI model adjusted for age and number of lifetime chlamydia tests.

NECCST = Netherlands chlamydia cohort study. CI = Confidence Interval. aHR= Adjusted Hazard Ratio.

Table S10 - Sensitivity analysis - Association between chlamydia positivity and complications (pelvic inflammatory disease, ectopic pregnancy, tubal factor infertility) in women participating in NECCST based on data of with and without women with serology+ only infections.

	With serology+ only infections aHR (95% CI)	Without serology+ only infections aHR (95% CI)
PID	1·62 (95% CI 1·20 - 2·17)	1·71 (95% CI 1·24 - 2·34)
EP	1·81 (95% CI 1·08 - 3·05)	1·81 (95% CI 1·09 - 3·05)
TFI	2·75 (95% CI 1·53 - 4·94)	3·37 (95% CI 1·82 - 6·22)

[a] aHR for Pelvic inflammatory disease model adjusted for age (linear), educational level, and number of lifetime chlamydia tests.

[b] aHR for Ectopic pregnancy model adjusted for age (linear), migration background, educational level , number of lifetime sex partners, number of lifetime chlamydia tests and IUD insertion.

[c] aHR for Tubal factor infertility adjusted for age (linear) number of lifetime chlamydia tests.

Table S11 - Risk estimates for potential confounders in models with chlamydia.

For each outcome potential confounders are assessed one-by-one together with chlamydia. Gray/white boxed indicate different models.

Covariates		**Pelvic inflammatory disease**		**Ectopic pregnancy**		**Tubal factor infertility**	
		aHR (95%CI)	**p-value**	**aHR (95%CI)**	**p-value**	**aHR (95%CI)**	**p-value**
Chlamydia (unadjusted)	Negative	Ref.		Ref.		Ref.	
	Positive	**1.95 (1.47 - 2.59)**	**< 0.001**	**2.11 (1.34 - 3.31)**	**0.002**	**2.90 (1.63 - 5.01)**	**< 0.001**
Chlamydia	Negative	Ref.		Ref.		Ref.	
	Positive	**1.91 (1.44 - 2.54)**	**< 0.001**	**1.83 (1.17 - 2.87)**	**0.010**	**2.66 (1.51 - 4.71)**	**< 0.001**
Migration background	Western	Ref.		Ref.		Ref.	
	Non-Western	1.17 (0.82 - 1.66)	0.380	**2.46 (1.53 - 3.94)**	**< 0.001**	1.69 (0.88 - 3.27)	0.110
	Unknown	**1.81 (1.11 - 2.95)**	**0.020**	1.81 (0.77 - 4.25)	0.171	1.8 (0.62 - 5.18)	0.270
Chlamydia	Negative	Ref.		Ref.		Ref.	
	Positive	**1.76 (1.32 - 2.33)**	**< 0.001**	**1.84 (1.18 - 2.88)**	**0.008**	**2.69 (1.52 - 4.74)**	**0.001**
Education level	Practical	Ref.		Ref.		Ref.	
	Theoretical	**0.44 (0.33 - 0.57)**	**< 0.001**	**0.39 (0.25 - 0.59)**	**< 0.001**	0.6 (0.33 - 1.08)	0.090
Chlamydia	Negative	Ref.		Ref.		Ref.	
	Positive	**1.84 (1.38 - 2.46)**	**< 0.001**	**2.31 (1.46 - 3.64)**	**< 0.001**	**2.76 (1.54 - 4.94)**	**< 0.001**
Number of lifetime chlamydia tests	1 - 2	Ref.		Ref.		Ref.	
	3 - 5	1.22 (0.87 - 1.69)	0.240	0.86 (0.52 - 1.43)	0.560	1.67 (0.85 - 3.29)	0.130
	6 or more	1.32 (0.96 - 1.8)	0.090	0.63 (0.37 - 1.08)	0.090	1.17 (0.58 - 2.36)	0.650
Chlamydia	Negative	Ref.	Ref.	Ref.	Ref.	Ref.	
	Positive	**1.91 (1.44 - 2.52)**	**< 0.001**	**2.14 (1.38 - 3.33)**	**< 0.001**	**2.86 (1.63 - 5.03)**	**< 0.001**
Age of sexual debut (linear)		0.9 (0.85 - 0.96)	0.002	1.08 (0.99 - 1.18)	0.100	1.00 (0.88 - 1.14)	0.945
Chlamydia	Negative	Ref.		Ref.		Ref.	
	Positive	**1.92 (1.45 - 2.54)**	**< 0.001**	**2.35 (1.51 - 3.67)**	**< 0.001**	**2.61 (1.48 - 4.61)**	**0.001**
Number of lifetime sex partners	<6	Ref.		Ref.		Ref.	
	6 - 12	1.06 (0.64 - 1.75)	0.820	0.63 (0.35 - 1.11)	0.110	0.55 (0.18 - 1.7)	0.300
	>12	1.26 (0.79 - 2.03)	0.330	**0.3 (0.17 - 0.55)**	**< 0.001**	1.24 (0.48 - 3.25)	0.650
Chlamydia	Negative	Ref.	Ref.	Ref.		Ref.	
	Positive	**1.92 (1.45 - 2.54)**	**< 0.001**	**1.97 (1.26 - 3.09)**	**< 0.001**	**2.71 (1.53 - 4.79)**	**0.001**
Gonnorhea	Negative	Ref.	Ref.	Ref.		Ref.	
	Positive	1.56 (0.82 - 2.98)	0.173	2.4 (1.02 - 5.63)	0.045	2.39 (0.83 - 6.9)	0.104

Chlamydia	Negative	Ref.		Ref.			
	Positive	**1.96 (1.48 - 2.59)**	**< 0.001**	**2.08 (1.34 - 3.24)**	**0.001**	**2.86 (1.63 - 5.01)**	**< 0.001**
Use of IUD	Never	Ref.		Ref.			
	At least once	0.97 (0.75 - 1.26)	0.813	0.72 (0.47 - 1.1)	0.129	1.31 (0.75 - 2.26)	0.334
Chlamydia	Negative	Ref.	Ref.		Ref.	Ref.	
	Positive	**1.93 (1.46 - 2.56)**	**< 0.001**	**2.07 (1.33 - 3.22)**	**0.002**	**2.79 (1.59 - 4.9)**	**0.001**
BMI	<25	Ref.	Ref.	Ref.	Ref.	Ref.	
	25-30	0.95 (0.66 - 1.36)	0.763	1.17 (0.68 - 2.01)	0.572	0.94 (0.43 - 2.05)	0.864
	>30	1.55 (1.03 - 2.33)	0.036	1.34 (0.66 - 2.73)	0.410	2.28 (1.08 - 4.82)	0.032
Chlamydia	Negative	Ref.		Ref.		Ref.	
	Positive	**1.85 (1.39 - 2.45)**	**< 0.001**	**2.04 (1.31 - 3.18)**	**0.002**	**2.79 (1.58 - 4.91)**	**0.001**
Smoking	Daily	Ref.		Ref.		Ref.	
	Yes, but not continuously	0.48 (0.34 - 0.69)	**< 0.001**	0.7 (0.37 - 1.33)	0.272	0.99 (0.4 - 2.42)	0.977
	Never	0.4 (0.27 - 0.59)	**< 0.001**	0.68 (0.34 - 1.34)	0.265	0.75 (0.29 - 1.99)	0.561
Chlamydia	Negative	Ref.	Ref.	Ref.	Ref.	Ref.	
	Positive	**1.93 (1.46 - 2.56)**	**< 0.001**	**2.17 (1.39 - 3.39)**	**0.001**	**2.82 (1.59 - 4.98)**	**0.001**
Condom use with casual partners (last 12 months)	Always	Ref.	Ref.	Ref.	Ref.	Ref.	
	Sometimes	0.99 (0.74 - 1.34)	0.960	1.12 (0.69 - 1.83)	0.645	1.42 (0.75 - 2.66)	0.273
	Never/not often	1.51 (0.94 - 2.45)	0.090	0.64 (0.19 - 2.12)	0.464	1.97 (0.72 - 5.4)	0.181
	No casual partners	0.81 (0.53 - 1.24)	0.326	1.81 (1.04 - 3.16)	0.036	1.22 (0.5 - 2.96)	0.65

Table S12 - Risk estimates for confounders included in final multivariable models

		Multivariable cox models		
	Categories	aHR	95% CI	p-value
Pelvic inflammatory disease[a]				
Chlamydia	Negative	Ref.		
	Positive	1·62	1·20 – 2·17	0·001
Age	Linear	0·93	0·87 – 0·99	0·03
Education	Practical	Ref.		
	Theoretical	0·45	0·34 – 0·59	< 0·001
Number of lifetime chlamydia tests	1 - 2	Ref.		
	3 - 5	1·20	0·86 – 1·68	0·27
	6 or more	1·32	0·96 – 1·82	0·09
Ectopic pregnancy[b]				
Chlamydia	Negative	Ref.		
	Positive	1·84	1·14 – 2·95	0·012
Age	Linear	1·05	0·96 – 1·15	0·29
Migration background	Non-western	Ref.		
	Western	0·54	0·33 – 0·89	0·02
Education	Practical	Ref.		
	Theoretical	0·48	0·31 – 0·77	< 0·001
Number of lifetime chlamydia tests	1 - 2	Ref.		
	3 - 5	0·98	0·58 – 1·65	0·94
	6 or more	0·83	0·47 – 1·46	0·52
Number of lifetime sex partners	<6	Ref.		
	6 -12	0·82	0·45 – 1·48	0·50
	>12	0·50	0·26 – 0·95	0·03
IUD use	Never	Ref.		
	At least once	1·15	0·74 – 1·78	0·52
Tubal factor infertility[c]				
Chlamydia	Negative	Ref.		
	Positive	2·75	1·53 – 4·94	0·001
Age	Linear	1·01	0·89 – 1·15	0·88

Number of lifetime chlamydia tests	1 - 2	Ref.		
	3 - 5	1·68	0·85 – 3·30	0·13
	6 or more	1·18	0·58 – 2·40	0·64