ORIGINAL ARTICLE

Population attributable fraction of pelvic inflammatory disease associated with chlamydia and gonorrhoea: a cross-sectional analysis of Australian sexual health clinic data

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ABSTRACT

Objectives Pelvic inflammatory disease (PID) is an important cause of female infertility and can occur when micro-organisms such as chlamydia or gonorrhoea ascend to the upper genital tract. PID has been used as an outcome measure in chlamydia screening trials; however, few data have quantified the PID burden that could be avoided by preventing chlamydia. We estimated the population attributable fraction (PAF) of PID associated with a current chlamydia or gonorrhoea infection among females 16–49 years attending an Australian sexual health clinic (SHC) (2006–2013).

Methods Using multivariable logistic regression, PAF estimates were adjusted for age and behavioural factors. Two separate analyses were undertaken: one among 'chlamydia-tested' women and one among a subset of chlamydia-tested women who were also tested for gonorrhoea ('chlamydia+gonorrhoea-tested'). A sensitivity analysis using multiple imputation was conducted to assess the impact of missing data on results.

Results Among 15 690 chlamydia-tested women, 1279 (8.2%, 95% CI 7.7% to 8.6%) were chlamydia positive, 436 (2.8%, 95% CI 2.5% to 3.0%) had PID diagnosed and the adjusted PAF for chlamydia was 14.1% (95% CI 9.9% to 18.0%). Among the chlamydia +gonorrhoea-tested subset (n=8839), 681 (7.7%, 95% CI 7.2% to 8.3%) tested positive for chlamydia only, 30 (0.3%, 95% CI 0.2% to 0.5%) for gonorrhoea only, 22 (0.2%, 95% CI 0.2% to 0.4%) for chlamydia and gonorrhoea and 419 (4.7%, 95% CI 4.3% to 5.2%) had PID diagnosed. The adjusted PAF was highest for chlamydia only (12.4%, 95% CI 8.4% to 16.2%) compared with gonorrhoea only (0.9%, 95% CI −0.1% to 1.8%) or concurrent infections (1.0%, 95% CI 0.0% to 1.9%).

Conclusions In this high chlamydia prevalence SHC population, eliminating a current chlamydia infection might at most reduce PID by about 14%.

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BACKGROUND

Pelvic inflammatory disease (PID) is an important cause of tubal factor infertility and ectopic pregnancy.[1] Occurring when pathogens ascend to the upper genital tract, PID often follows the sexually transmitted infections (STIs) *Chlamydia trachomatis* (chlamydia) and *Neisseria gonorrhoeae* (gonorrhoea) with a causal role for *Mycoplasma genitalium* (MG) established[2] and bacterial vaginosis (BV) also considered a factor.[3]

Past studies have cultured chlamydia or gonorrhoea from the cervix of 29% and 26%, respectively (estimates vary), of acute PID cases.[1] More recently, nuclear acid amplification tests have detected these infections in 17% PID cases.[4] Largely affecting young heterosexuals, chlamydia is the most commonly diagnosed bacterial STI throughout the developed world with all age rates per 100 000 of 359 in Australia,[5] 447 in the USA[6] and 386 in the UK.[7] Gonorrhoea is more common via male-to-male transmission in many countries, with all age rates per 100 000 of 65 in Australia and 55 in the UK compared with 106 in the USA where rates are high among young heterosexuals.[5–7]

Estimates of the risk of PID from chlamydia or gonorrhoea vary, and there are questions about the natural history of these infections. PID may develop in 2%–5% of untreated chlamydia infections over 2 weeks,[8] and 10% over 1 year.[9] Although hampered by methodological or sample size issues, other evidence suggests up to 30% chlamydia infections could develop into PID.[10] PID has been diagnosed in 13% of chlamydia-infected or gonorrhoea-infected adolescents in the 7–15 days between testing and treatment[11] and modelling suggests 4%–7% gonorrhoea infections may develop into PID over 6–12 months.[12]

PID prevention is a key objective of STI screening or opportunistic testing.[13 14] It is important to determine the attribution of STIs and other PID risk factors in a population to understand the potential impact of control activities on this morbidity. Population attributable fraction (PAF) considers both magnitude of risk of an outcome (such as PID) associated with an exposure (such as chlamydia) and the exposure's population prevalence,[15] and could provide a measure of PID burden that might be avoided by preventing PID risk factors. Given that risk factor prevalence and their contribution to PID will vary between populations, the PAF for PID is likely to differ between risk groups, countries and settings. For example, the STI-associated PAF for PID might be higher in sexual-health-clinic (SHC) attendees than in the general population.

Our aim was to estimate the potentially avoidable PID burden if chlamydia or gonorrhoea were

eliminated from the population. We report population-level and individual-level risks associated with PID and a current chlamydia or gonorrhoea infection in female SHC attendees.

METHODS

Setting and study population

We conducted a cross-sectional analysis of routinely collected data from female patients 16–49 years during their first episode of care (first and follow-up visits in the next 30 days) at a large Australian SHC between January 2006 and June 2013. Current sex-workers were excluded.

Melbourne Sexual Health Centre (MSHC) is the major public SHC in the state of Victoria, Australia, and provides a free triage-based walk-in service. Attendees at higher sexual risk, with symptoms suggesting an STI, or females with pelvic pain are triaged in. Details of attendees triaged out of MSHC are not collected; however, over 85% of all attendees are triaged in. All new female patients are offered a chlamydia test. The decision to conduct gonorrhoea, MG or BV tests depends on the clinician's assessment and the patient's clinical presentation and sexual history. During the study, a total of 28 036 women were seen in MSHC and 18 586 (66%) met the inclusion criteria (figure 1): 55% were asymptomatic, 89.1% were tested for chlamydia, 50.5% for gonorrhoea, 39.1% for BV and 8.1% for MG. This analysis was limited to investigating chlamydia and gonorrhoea as the most common bacterial STIs tested and the focus of national testing recommendations.[16]

Primary outcome and exposure definition

The primary outcome was PID. The primary exposure was a current genital chlamydia or gonorrhoea infection. Clinical PID diagnosis was guided by Centers for Disease Control and Prevention criteria that include uterine tenderness, cervical motion tenderness or adnexal tenderness in sexually active women with pelvic pain and also signs of cervicitis or abundant vaginal leukocytes.[13] Chlamydia and gonorrhoea diagnoses were based on laboratory results: (i) chlamydia on strand displacement amplification from urine, high vaginal swabs (HVS) and cervical swabs; (ii) gonorrhoea on HVS and cervical swab culture. Test results for MG (urine, HVS and cervical swab PCR) and BV (Nugent's score of 7–10 or 4–6 with clue-cells)[17] were collected for PID cases.

Data collection and exclusions

Information on demographics, sexual behaviour (condom use, number of male sexual partners (MSPs)), current contraception (intrauterine device (IUD), hormonal), laboratory results and clinical diagnosis (including PID) were extracted from the computerised medical record. Self-reported symptoms (such as pain, vaginal discharge, intermenstrual bleeding, genital lesions) were recorded at triage. A binary 'symptoms at triage' variable was created. Behavioural data were self-entered by patient/s and diagnoses by clinician/s. Records without behavioural information were excluded. Because not all women were chlamydia and gonorrhoea tested, two datasets were prepared (figure 1): (1)

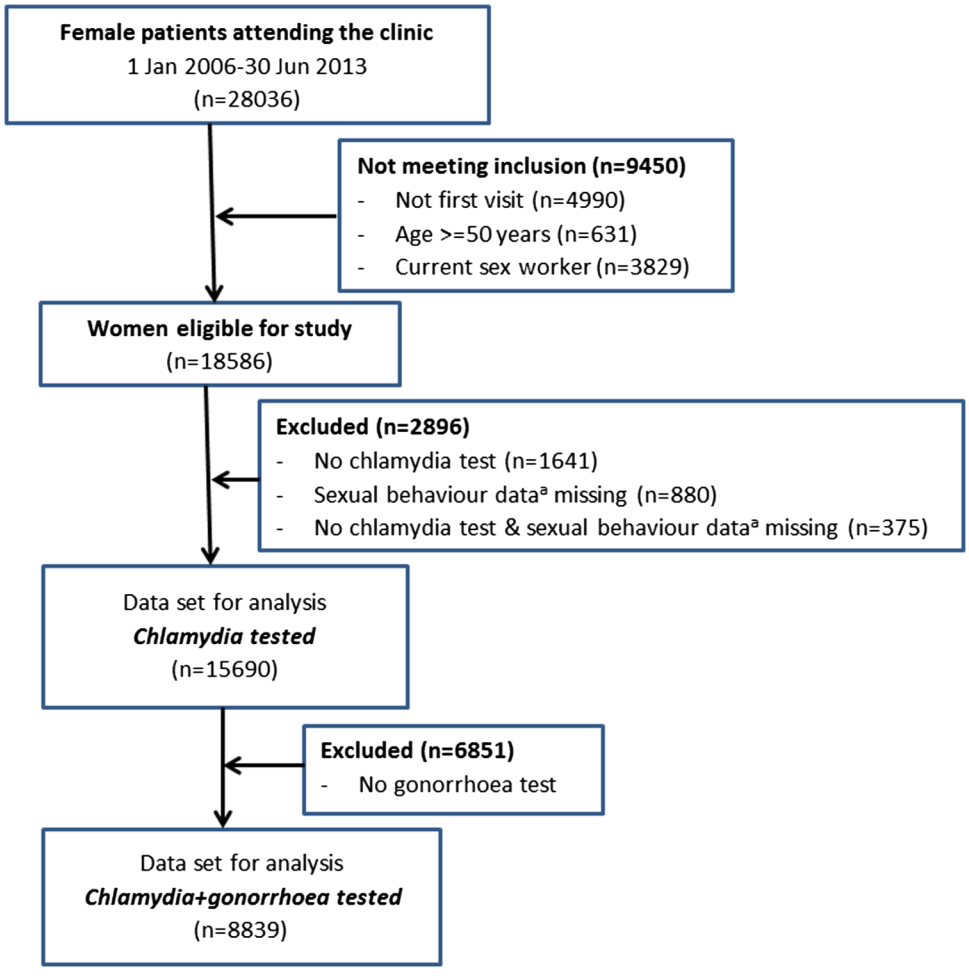

Figure 1 Flowchart of participants in the chlamydia-tested and chlamydia+gonorrhoea-tested datasets.

comprised all women tested for chlamydia ('chlamydia-tested') (n=15 690); (2) a subset of chlamydia-tested who were also tested for gonorrhoea ('chlamydia+gonorrhoea-tested') (n=8839).

Statistical analysis

Data were analysed using STATA statistical software V.13.0. The PID prevalence and 95% CIs were calculated. For each dataset, the population-level and individual-level risk associated between a current chlamydia or gonorrhoea infection and PID were investigated using univariable and multivariable logistic regression. Age, country of birth, number of MSPs (past 3, 12 months), condom use (consistent, inconsistent, no MSP/vaginal sex, past 3, 12 months) and contraception method were identified a priori as potential confounders. We investigated whether age modified the association between chlamydia or gonorrhoea and PID by comparing logistic regression models with and without an interaction term between age and chlamydia or gonorrhoea using the likelihood ratio test. No effect modification was found. To assess the impact of missing data we conducted a sensitivity analysis using multiple imputation[18] and compared the estimated OR from the complete-case analyses with those derived from multiple imputation. Online supplementary tables S1 and S2 provide details of the imputation model. We calculated the PAF of PID associated with chlamydia and/or gonorrhoea infection from the PID prevalence and OR estimates from the complete-case analyses for both datasets. Under the assumptions of causality and low PID prevalence, the PAF formula for cross-sectional analyses is:

$$\mathrm{PAF} = 1 - \frac{\sum_{i=1}^{n} \mathrm{pexp}_i}{\sum_{i=1}^{n} \mathrm{p}_i}$$

where n is the sample size, pexp_i is the predicted probability for the ith individual from the multivariable logistic model which included the exposure and p_i is the predicted probability for the ith individual from the multivariable logistic model without the exposure variable.[15] Because symptoms may prompt patients to seek medical care and be STI-tested, we undertook a subgroup analysis based on the 'symptoms at triage' variable to assess whether the PAF of PID associated with chlamydia or gonorrhoea varied between women reporting and not reporting symptoms at triage.

The Alfred Health Human Ethics Committee (EC00315) granted ethical approval (322/13).

RESULTS

Participants and PID cases

Between 2006 and 2013, 18 586 new female patients were seen in MSHC: 15 690 comprised the chlamydia-tested group among whom 1279 (8.2%, 95% CI 7.7% to 8.6%) were chlamydia positive and 436 (2.8%, 95% CI 2.5% to 3.0%) had PID diagnosed. Of these 436 PID cases, 94 (21.6%) were chlamydia-associated, of which 66 (70%) were co-diagnosed with PID and chlamydia at first visit and 28 (30%) were diagnosed with PID within the next 3–28 (median 7) days. The chlamydia+gonorrhoea-tested subset comprised 8839 women; 681 (7.7%, 95% CI 7.2% to 8.3%) tested positive for chlamydia alone, 30 (0.3%, 95% CI 0.2% to 0.5%) for gonorrhoea alone, 22 (0.2%, 95% CI 0.2% to 0.4%) for both gonorrhoea and chlamydia and 419 (4.7%, 95% CI 4.3% to 5.2%) had PID diagnosed. Of these 419 PID cases, 1.2% (95% CI 0.4% to 2.8%) were diagnosed with chlamydia+gonorrhoea co-infection, 19.6% (95% CI 15.9% to 23.7%) with chlamydia alone and 1.2% (95% CI 0.4% to 2.8%) with gonorrhoea alone. MG was detected in 2.9% (95% CI 1.5% to 4.9%) of PID cases, BV in 15.5% (95% CI 12.1% to 19.3%) and no pathogen in 61% (95% CI 55.8% to 65.3%). Table 1 provides the characteristics and PID prevalence for both datasets. Almost one-half (47%) of chlamydia-tested and two-thirds (66%) of chlamydia+gonorrhoea-tested women reported symptoms.

Table 1 Prevalence of PID by patient characteristics for chlamydia-tested and chlamydia+gonorrhoea-tested women

	Chlamydia-tested (N=15 690) PID/patients		Chlamydia +gonorrhoea-tested* (N=8839) PID/patients	
	n/N	Per cent	n/N	Per cent
	436/15 690	2.8	419/8839	4.7
Age group (years)				
16–29	359/12 080	3.0	345/6596	5.2
30–49	77/3610	2.1	74/2243	3.3
Country of birth				
Australia	188/6529	2.9	182/3591	5.1
Other	248/9161	2.7	237/5248	4.5
Current contraception				
Any hormonal	119/4362	2.7	114/2185	5.2
IUD	18/263	6.8	17/157	10.8
Other/not reported	299/11 065	2.7	288/6497	4.4
Symptoms self-reported at triage				
No	49/8348	0.6	46/3005	1.5
Yes	387/7342	5.3	373/5834	6.4
STI contact				
No	397/14 652	2.7	383/8322	4.6
Yes	39/1038	3.8	36/517	7.0
Chlamydia test results				
Negative	342/14 411	2.4	NA	
Positive	94/1279	7.4	NA	
Chlamydia and gonorrhoea test results				
Negative	NA		327/8106	4.0
Chlamydia positive only	NA		82/681	12.0
Gonorrhoea positive only	NA		5/30	16.7
Chlamydia and gonorrhoea positive	NA		5/22	22.7
Male sexual partners, last 3 months				
None	10/1239	0.8	10/660	1.5
1	231/8059	2.9	225/4628	4.8
≥2	195/6392	3.1	187/3551	5.3
Condom use with male partners, last 3 months				
No male partners/vaginal sex	11/1351	0.8	11/715	1.5
Always	44/2572	1.7	44/1267	3.5
Not always	381/11 767	3.2	364/6857	5.3
Male sexual partners, last 12 months				
None	3/514	0.6	3/273	1.1
1	117/4059	2.9	113/2457	4.6
2	90/3418	2.6	86/1873	4.6
≥3	226/7699	2.9	217/4236	5.1
Condom use with male partners, last 12 months				
No male partners/vaginal sex	5/612	0.8	5/323	1.6
Always	38/2299	1.7	38/1149	3.3
Not always	393/12 779	3.1	376/7367	5.1

*Chlamydia+gonorrhoea tested group is a subset of the chlamydia-tested group.
IUD, intrauterine device; NA, not applicable; PID, pelvic inflammatory disease; STI, sexually transmitted infection.

Individual factors associated with increased risk of a PID diagnosis

Among chlamydia-tested women, multivariable analysis found PID diagnosis was more likely (table 2) with chlamydia infection (adjusted odds ratio (AOR) 3.0, 95% CI 2.4 to 3.9), an IUD (AOR 2.6, 95% CI 1.6 to 4.2) and younger age (AOR 1.3, 95% CI 1.0 to 1.6) and less likely with consistent condom use (AOR 0.6, 95% CI 0.4 to 0.8).

Among the chlamydia+gonorrhoea-tested subset, PID diagnosis was more likely (table 2) with chlamydia infection only (AOR 3.0, 95% CI 2.3 to 3.9), gonorrhoea only (AOR 4.4, 95% CI 1.7 to 11.6), chlamydia+gonorrhoea co-infection (AOR 6.2, 95% CI 2.2 to 17.0), an IUD (AOR 2.6, 95% CI 1.5 to 4.4) and younger age (AOR 1.4, 95% CI 1.1 to 1.9).

Population attributable fraction

The adjusted PAF for PID (table 3) for chlamydia was 14.1% (95% CI% 9.9 to 18.0%) for chlamydia-tested women. For chlamydia+gonorrhoea-tested women, the PAF was higher for chlamydia only (12.4%, 95% CI 8.4% to 16.2%) than gonorrhoea only (0.9%, 95% CI −0.1% to 1.8%) or chlamydia+gonorrhoea co-infection (1.0%, 95% CI 0.0% to 1.9%) (table 3). Stratified by age group, the adjusted chlamydia PAF among chlamydia-tested women was 14.5% (95% CI 9.8% to 19.1%) for women aged 16–29 years and 11.7% (95% CI 3.2% to 19.4%) for those aged 30–49 years. Stratified by symptoms at triage, the chlamydia PAF for women not reporting symptoms was 27.8% (95% CI 11.6% to 41.0%) and for women reporting symptoms it was 13.2% (95% CI 9.1% to 17.1%).

Sensitivity analysis

Online supplementary table S1 presents the demographic characteristics and PID prevalence among the 18 586 eligible women and two analytical subgroups. The proportion 16–29 years and Australian born was similar between all groups. Online supplementary table S2 presents the estimated AORs

Table 2 Factors associated with PID among chlamydia-tested and chlamydia+gonorrhoea-tested women

	Chlamydia-tested (N=15 690)					Chlamydia+gonorrhoea-tested* (N=8839)				
	Univariable		Multivariable			Univariable		Multivariable		
	OR	95% CI	AOR	95% CI	p Value	OR	95% CI	AOR	95% CI	p Value
Age group (years)										
16–29	1.4	1.1 to 1.8	1.3	1.0 to 1.6	0.058	1.6	1.3 to 2.1	1.4	1.1 to 1.9	0.006
30–49	1.0		1.0			1.0		1.0		
Country of birth										
Australia	1.1	0.9 to 1.3				1.1	0.9 to 1.4			
Other	1.0					1.0				
Current contraception										
Any hormonal	1.0	0.8 to 1.3	0.9	0.7 to 1.1	0.210	1.2	0.9 to 1.5	1.0	0.8 to 1.3	0.789
IUD	2.6	1.6 to 4.3	2.6	1.6 to 4.2	<0.001	2.6	1.6 to 4.4	2.6	1.5 to 4.4	<0.001
Other/not reported	1.0		1.0			1.0		1.0		
Chlamydia test results										
Negative	1.0		1.0			NA				
Positive	3.3	2.6 to 4.1	3.0	2.4 to 3.9	<0.001	NA				
Chlamydia and gonorrhoea test results										
Negative	NA					1.0		1.0		
Chlamydia positive only	NA					3.3	2.5 to 4.2	3.0	2.3 to 3.9	<0.001
Gonorrhoea positive only	NA					4.8	1.8 to 12.5	4.4	1.7 to 11.6	0.003
Chlamydia and gonorrhoea positive	NA					7.0	2.6 to 19.1	6.2	2.2 to 17.0	<0.001
Male sexual partners, last 3 months†										
None	1.0					1.0				
1	3.6	1.9 to 6.8				3.3	1.7 to 6.2			
≥2	3.9	2.0 to 7.3				3.6	1.9 to 6.9			
Condom use with male partners, last 3 months										
No male partners/vaginal sex	0.2	0.1 to 0.4	0.3	0.1 to 0.5	<0.001	0.3	0.2 to 0.5	0.3	0.2 to 0.6	<0.001
Always	0.5	0.4 to 0.7	0.6	0.4 to 0.8	<0.001	0.6	0.5 to 0.9	0.7	0.5 to 1.0	0.026
Not always	1.0		1.0			1.0		1.0		
Male sexual partners, last 12 months†										
None	1.0					1.0				
1	5.1	1.6 to 16.0				4.3	1.4 to 13.7			
2	4.6	1.5 to 14.6				4.3	1.4 to 13.8			
≥3	5.2	1.6 to 16.1				4.9	1.5 to 15.3			
Condom use with male partners, last 12 months†										
No male partners/vaginal sex	0.3	0.1 to 0.6				0.3	0.1 to 0.7			
Always	0.5	0.4 to 0.7				0.6	0.5 to 0.9			
Not always	1.0					1.0				

*Chlamydia+gonorrhoea-tested group is a subset of the chlamydia-tested group.
†Male sexual partners, last 3 and 12 months, and condom use, last 12 months, omitted from final multivariable models due to collinearity.
NA, not applicable; PID, pelvic inflammatory disease.

Table 3 PAF of PID associated with chlamydia and gonorrhoea infection

	Overall		No symptoms at triage*		Symptoms at triage†	
	PAF % (95% CI)	Adjusted PAF‡ % (95% CI)	PAF % (95% CI)	Adjusted PAF‡ % (95% CI)	PAF % (95% CI)	Adjusted PAF‡ % (95% CI)
Chlamydia-tested						
Chlamydia positive	14.6 (10.4 to 18.6)	14.1 (9.9 to 18.0)	28.3 (12.2 to 41.4)	27.8 (11.6 to 41.0)	13.6 (9.5 to 17.5)	13.2 (9.1 to 17.1)
Chlamydia+ gonorrhoea-tested subset						
Chlamydia and/or gonorrhoea positive	14.9 (10.7 to 18.9)	14.2 (10.0 to 18.3)	25.5 (0.9 to 38.8)	24.4 (8.0 to 37.9)	14.1 (9.9 to 18.1)	13.6 (9.4 to 17.6)
Chlamydia positive only	13.0 (9.0 to 16.8)	12.4 (8.4 to 16.2)	19.6 (4.8 to 32.0)	18.5 (3.5 to 31.2)	12.6 (8.6 to 16.5)	12.2 (8.2 to 16.1)
Gonorrhoea positive only	0.9 (−0.1 to 1.9)	0.9 (−0.1 to 1.8)	1.9 (−2.3 to 5.8)	1.8 (−2.3 to 5.8)	0.8 (−0.1 to 1.7)	0.8 (0.1 to 1.7)
Chlamydia and gonorrhoea positive	1.0 (0.1 to 1.9)	1.0 (0.0 to 1.9)	4.1 (−1.4 to 9.3)	4.1 (−1.3 to 9.2)	0.6 (−0.2 to 1.4)	0.6 (−0.2 to 1.4)

*Chlamydia infection was detected in 746 (8.9%, 95% CI 8.3% to 9.6%) and PID was diagnosed in 49 (0.6%, 95% CI 0.4% to 0.8%) of 8348 chlamydia-tested women not reporting symptoms at triage.
†Chlamydia infection was detected in 533 (7.3%, 95% CI 6.7% to 7.9%) and PID was diagnosed in 387 (5.3% 95% CI 4.8% to 5.8%) of 7342 chlamydia-tested women reporting symptoms at triage.
‡Adjusted for age group, contraception, condom use, last 3 months.
PAF, population attributable fraction; PID, pelvic inflammatory disease.

from multiple imputation. The estimated AORs for PID from chlamydia-tested, chlamydia+gonorrhoea-tested and multiple imputation complete-case analyses were very similar. For example, the chlamydia AOR was 3.2 (95% CI 2.5 to 4.0) in the first imputation model with missing chlamydia test result values imputed compared with 3.0 (95% CI 2.3 to 4.9) in chlamydia-tested women.

DISCUSSION

This study found that in high-risk female SHC patients, up to 14% of clinically diagnosed PID was associated with a current chlamydia infection and about 1% with gonorrhoea. Among women not reporting symptoms at triage, the chlamydia PAF was 28% compared with 13% for women reporting symptoms. It is likely the lower PAF in symptomatic women is because factors other than chlamydia (such as symptoms, another STI) influenced PID diagnosis whereas for asymptomatic women, chlamydia detection facilitated PID diagnosis. At the individual level, our multivariable analysis showed PID diagnosis was more likely with chlamydia or gonorrhoea infection, an IUD, inconsistent condom use and in younger women.

This is the first Australian study, and we believe internationally, to estimate the PAF of PID associated with chlamydia or gonorrhoea using clinical data. PAF represents the proportion of disease in a population that might be avoided if particular risk factors were eliminated.[15] At the individual level, we found a 4.4-fold and 3-fold increased risk of PID for women with gonorrhoea or chlamydia, respectively. This is consistent with a recent Australian study showing higher PID hospitalisation rates following gonorrhoea or chlamydia compared with no infection.[19] Despite a strong individual association between gonorrhoea and PID, our gonorrhoea PAF was small reflecting its low prevalence (<0.5%) in this population and consistent with the pattern of largely male-to-male gonorrhoea transmission in Australia.[5] Chlamydia was more prevalent in our population, and this is reflected in our PAF estimates with a larger burden of PID in this population potentially avoidable by eliminating a chlamydia rather than a gonorrhoea infection.

The burden of PID related to STIs at population level will vary between populations depending on the underlying prevalence of STIs and other risk factors. Our PAF estimates are based in a high-risk SHC population and may not reflect the general population. Around half our study population reported symptoms at triage and three or more MSPs in the past year. This is higher than observed among women attending Australian general practices where 6% are symptomatic and 13% report three or more MSPs in a year.[20] The chlamydia prevalence in our sample (7.3% in symptomatic, 8.9% in asymptomatic women) was also higher compared with 4.4% in Australian general practice.[20] Although our PAF estimates suggest that removing chlamydia might reduce the PID burden by 14% (95% CI 10% to 18%), most PID in this high-risk population was not associated with chlamydia. Elsewhere, modelling has estimated that around 20% (5% –40%) of PID among UK women is caused by chlamydia.[21] Of concern is our finding that around two-thirds of chlamydia-associated PID was co-diagnosed at first visit, suggesting symptoms rather than awareness of STI risk prompted the visit. Reduction in chlamydia-associated PID morbidity is possible only if women present early in their infection's course, highlighting the ongoing need for improving community awareness around STI risk, indications for testing and ensuring testing is accessible.

PID prevention is widely viewed as a potential measure of the impact of chlamydia screening or opportunistic testing. Such programs could prevent PID indirectly if they lead to decreased chlamydia prevalence, or directly if chlamydia is detected and treated before PID develops.[22] Success of direct prevention depends on the duration between chlamydia acquisition and PID development, which can be weeks.[11 23] Some countries have conducted chlamydia screening or opportunistic testing trials focussing on young asymptomatic adults in community settings and included PID as an outcome measure[9 14 24 25] Results from a UK trial (PID incidence in chlamydia-screened (1.3%) vs unscreened (1.9%)) suggested chlamydia screening might reduce PID incidence over 1 year[9] while a Dutch trial reported a low 1 year PID incidence (1.9%) that did not alter over time.[24] Furthermore, a Swedish population-based cohort found a low cumulative PID incidence (to age 35) (5.6% in women ever chlamydia positive vs 4% in chlamydia negative)[26] and concluded the benefits of chlamydia screening may have been overestimated.

So, what do our results mean for opportunistic chlamydia screening in general-practice settings? Our subanalysis showed that chlamydia elimination for high-risk symptomatic female

SHC attendees with a PID prevalence of 5.3% (53 cases per 1000 patients) might avoid 13% of PID, or 6.9 cases per 1000 patients. Given women attending Australian general practice are more likely to be asymptomatic[20] and if we assume the general-practice PID prevalence is comparable with that observed among women not reporting symptoms in this study (0.6%), then with a PAF of 28%, chlamydia elimination might only avoid 1.7 cases per 1000 patients. However, this is most likely overestimated because chlamydia prevalence in general practice (4.4% in women)[20] is considerably lower than we observed for women not reporting symptoms (8.9%). Furthermore, it is only PID cases diagnosed after chlamydia detection and treatment that could be directly prevented by screening.

Our analysis is strengthened by the large sample size and sensitivity analysis showing missing data did not impact on the association with PID. Another strength is our adjusted PAF estimates accounted for the effects of potentially confounding variables on the relationship between chlamydia or gonorrhoea and PID.

This study has a number of limitations. The cross-sectional design means the temporal relationship between STIs and most PID is unknown and not all women were chlamydia and gonorrhoea tested, potentially biasing PAF estimates to higher-risk women. Our decision to undertake a cross-sectional analysis was influenced by the clinical setting; female non-sex-workers are only triaged into MSHC if at STI risk and repeat visits limited to the next 2–4 weeks. Restricting our study to first episode of care maximised data completeness. Second, PID diagnosis was clinical, which can vary in accuracy between clinicians.[27] If clinicians were oversensitive to PID when STIs were diagnosed, the PAF could be overestimated. Third, although past or repeated chlamydia infection are both PID risk factors,[28] we were unable to measure their contribution; possibly the PAF would be higher if previous infection was considered.

We found that an IUD in situ was associated with increased PID risk. The role of IUDs in PID has been debated with higher PID rates reported in IUD users than in non-users. This risk appears greatest in the 3 months post insertion,[1] relevant to copper/levonorgestrel-releasing IUDs and for women with an STI during insertion.[29] However, a recent review found no evidence that IUD use increases PID risk in excess of risk from an STI.[29] Observational studies may be hampered by detection bias. It is possible that clinicians in this study had a lower threshold for PID diagnosis when they knew a woman had an IUD.

Interestingly, we found no pathogen in 61% PID cases. Almost a quarter had chlamydia and/or gonorrhoea which is similar to UK sex-workers with clinically diagnosed PID,[28] but lower than past US and European studies (1970s–1990s) where chlamydia was cultured from 5% to 51% and gonorrhoea from 5% to 80% PID cases.[1] MG and BV were detected in some PID cases in this study suggesting an aetiological role, although evidence has established one for MG[2] but not BV.[3] The fact that no infection was diagnosed for over half our PID cases raises questions about sensitivity and specificity of PID clinical diagnosis and highlights the need for a gold standard diagnostic test. Several groups are investigating PID diagnostic biomarkers, but are some way off.[30] It is also possible for some PID cases with no pathogen detected that a pathogen had cleared from the lower genital tract but had ascended to the upper genital tract.

Justification of chlamydia (and gonorrhoea) screening often includes prevention of female reproductive morbidity. PAF provides a measure of PID burden that might be avoided by preventing these STIs. In this high chlamydia prevalence population, most PID diagnoses were not associated with chlamydia and chlamydia elimination might at most reduce PID by 14%. Our results suggest that in a general-practice setting with low chlamydia prevalence, widespread chlamydia screening would only prevent a small number of PID cases raising questions about the cost-effectiveness of chlamydia screening. Nevertheless, improved community awareness around STI risk and indications for testing is essential to reach high-risk women, to diagnose and treat infections promptly and avoid progression to PID.

Key messages

- Population attributable fraction (PAF) can provide a measure of pelvic inflammatory disease (PID) burden in a population that might be eliminated by preventing chlamydia or gonorrhoea infection.
- Most PID in women attending an Australian sexual-health-clinic was not associated with chlamydia. Chlamydia elimination in this high chlamydia prevalence population might only reduce PID by 14%.
- In general-practice settings with low chlamydia prevalence, chlamydia elimination could only prevent a small number of PID cases.
- Reduction in sexually transmitted infection (STI)-associated PID morbidity is possible only if women present early in their infection. Improved community awareness around STI risk and indications for testing is essential.

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