

# **Genital chlamydia infection in young people: a review of the evidence**

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## **Executive summary and recommendations**

### **Introduction**

Chlamydia is the most commonly notifiable sexually transmissible infection (STI) in Australia. The NSW Government convened a working group in 2010 tasked with developing an action plan focused on strategies for the control of chlamydial infection in people aged less than 30 years (hereafter referred to as young people). To inform the plan, we conducted a review that covered the epidemiology of chlamydia in young people in NSW; the relationship between chlamydia and adverse reproductive health outcomes, and the evidence on the effectiveness of a range of interventions that have been used to prevent chlamydia or its adverse outcomes.

### **Epidemiology of genital chlamydia in young heterosexuals in NSW: a literature review**

- Chlamydia is the most common notifiable infection in NSW.
- The numbers of both chlamydia notifications and Medicare-rebated chlamydia tests in young people have increased by more than 300% over the past ten years in NSW.
- There were no NSW chlamydia notification data available in Aboriginal and Torres Strait Islander people.
- Analyses of sentinel surveillance data from NSW sexual health services show that the proportion of those tested positive for chlamydia increased by 28% in females and 11.9% in males between 2004 and 2010.
- Repeat surveys on sexual behaviour in young people in Australia (2002 and 2008) found a reduction in age at first sex and an increase in the number of sex partners. Condom use remained stable with around 50% reporting always using them for sex in the past year.
- Chlamydia prevalence in two community and six clinic-based studies involving young people ranged from 3-12%. However, since most estimates are in sub-populations or at-risk populations, they are unlikely to represent the true general population prevalence.
- In Australia, annual rates of hospital separations for PID declined between 1998-99 and 2007-08 (from 0.80 to 0.61 per 1,000 women in 15 to 24 year olds and from 0.99 to 0.65 in 25 to 34 year olds).
- In one prospective cohort study of young Australian women, chlamydia incidence was estimated to be 4.5 per 100 person years, and the re-infection rate at 12 months was 22%.
- Medicare data show most young people attended a GP in NSW in 2008 (86% of women and 67% of men), but only 7.3% were tested for chlamydia.
- Data from a sentinel surveillance network of 25 general practice clinics in 2008 showed that the recording of Aboriginal and Torres Strait Islander status was less than 15%.
- Based on chlamydia prevalence studies, it is likely the number of infections in NSW in 2009 was closer to 60,000 rather than the 14,948 reported, meaning that 45,000 infections in one year were not diagnosed and treated.

### **Sequelae of chlamydia infection in women: a literature review**

- Based on 27 studies reviewed, there is limited high quality evidence regarding the association between chlamydia infection and reproductive sequelae to provide robust and generalisable risk estimates.
- From one study we estimated that untreated chlamydial infections increased the risk of pelvic inflammatory disease (PID) by 6.5-25 folds, compared to no infection.
- Based on this study as well as other data we calculated that the proportion of PID in young Australian women attributable to chlamydial infection ranges between 17% and 47%.

- From four available studies, treated chlamydial infections increased the risk of PID by between 25% and 150%, compared to no infection.
- From one study, repeated chlamydial infections increased the risk of PID by about 4-6 fold, compared to a single infection.
- Severe PID increases the likelihood of ectopic pregnancy and infertility, but there is uncertainty about the role of chlamydia in the causation of severe PID.
- There is conflicting evidence regarding the relationship between chlamydial infection and ectopic pregnancy.
- One study suggests a 30% increase in the risk of infertility after chlamydial infection

### **Strategies to improve adherence to diagnosis and management guidelines for pelvic inflammatory disease: a systematic review**

- Timely diagnosis and treatment of PID is important to prevent long term reproductive sequelae. However due to the broad range of clinical presentations, PID, particularly mild to moderate disease, is often difficult to diagnose.
- Evidence-based guidelines for the diagnosis and management of PID in Australia exist but research suggests that adherence to PID management guidelines by practitioners and patients is poor, although NSW and Australian data are limited.
- We systematically searched the literature and identified three studies which evaluated strategies to improve practitioner and patient adherence to such guidelines.
- An abbreviated summary of PID treatment provided to practitioners improved the management but not the diagnosis of PID in hypothetical case scenarios.
- One study found that a video on PID self-care administered to patients did not improve compliance with antibiotics and follow-up.
- One study found that a multi-faceted intervention involving a practice protocol, provision of 14 days of observed antibiotic treatment, written instructions for patients and active follow-up resulted in a greater proportion of patients receiving the recommended antibiotics and improved follow-up attendance.
- None of these trials were conducted in Australia.

### **Effectiveness of chlamydia screening in reducing adverse outcomes: a systematic review**

- Systematic screening programs have been established to detect asymptomatic cases, with the twin goals of reducing transmission and reproductive tract morbidity.
- There is a consistent body of evidence, including randomised controlled trials (RCT) and observational studies, showing that screening for chlamydia can reduce chlamydia prevalence and PID incidence in young females.
- Three of the five studies that used PID as the primary outcome after screening found significant reductions of 35%-56%.
- All four studies that tracked chlamydia prevalence following screening found significant reductions.
- No study examined the impact of more than one round of screening.

### **Interventions to increase chlamydia screening in primary care: a systematic review**

- We identified 15 reports describing 16 interventions; ten were RCTs and five were observational studies. Seven interventions were associated with significant increases in screening rates.

- Interventions that involved system changes to enable all patients to be offered a chlamydia test had the greatest impact; they included a multifaceted quality improvement program that included provision of a urine jar to patients at registration (65% in intervention clinics vs. 21% in the control clinics among female adolescents and 49% vs. 5% among male adolescents); and doctors offering a test to all presenting young male clients, prior to consultation (29% in the intervention clinics vs. 4% in the control clinics).
- Other strategies showed more modest increases including linking screening to routine Pap smears (6.9% vs. 4.5%), computer alerts for doctors (12.2% vs. 10.6% in young females), education workshops for clinic staff ( $p < 0.001$ , in young females) and internet-based continuing medical education (15.5% vs. 12.4%, in young females).
- Linking chlamydia screening with Pap smears resulted in increased testing, but often outside the recommended target age groups for chlamydia screening.
- Other strategies that could be considered but were not the subject of published evaluations include: cash incentives, reminder systems in general practice clinics, practice-nurse led interventions and quality improvement programs in Aboriginal populations.
- Two large-scale studies are underway in NSW primary care clinics - ACCEPt and SHIMMER - that are multi-faceted testing interventions aimed at increasing chlamydia testing.

### **Interventions to increase re-screening for chlamydial infections: a systematic review and meta-analysis**

- Chlamydia re-screening is important to detect and treat re-infections. Repeated chlamydial infections increase the risk of PID by about 4-6 fold.
- Despite clinical guidelines recommending re-screening around 3 months after treatment, re-screening rates remains low in sexual health services in Australia (<20%).
- We identified eight RCTs and four controlled observational studies, all conducted in the US, which evaluated strategies to increase re-screening within 3 months of treatment.
- Overall mailed screening kits were most effective at increasing re-screening followed by the use of reminder strategies. Specifically:
  - Results of four RCTs assessing mailed screening kits with or without reminders had a summary effect estimate of 1.3 (95%CI:1.1-1.5), i.e. a 30% improvement in rescreening.
  - One RCT evaluated the effect of a reminder and found a relative risk (RR) of 9.7 (95%CI:1.3-71.3) from a very low base.
  - Three controlled observational studies also assessed the impact of reminder strategies and found RRs of 1.97 (95%CI:1.76-2.21), 1.01 (95%CI:0.66-1.55), and 1.88 (95%CI:1.58-2.24); i.e. nearly a 2-fold improvement in two studies, and no significant effect in the third. A summary effect was not calculated for these studies due to significant heterogeneity.
  - Four other studies showed no evidence of a significant increase in re-testing; one RCT assessed the effect of a \$20 patient incentive, two RCTs assessed motivational interviewing with or without reminders, and one controlled observational study assessed the promotion of clinical guidelines in improving rescreening uptake.
- Another strategy that could be considered but was not assessed in quantitative studies is the use of text messaging as a reminder.

### **Effectiveness of home-based screening using self-collected mail-in specimens at increasing testing uptake: review of the literature**

- RCTs (all conducted in the US) have found that higher chlamydia testing rates can be achieved with home-based sampling compared to clinic-based testing.

- One study found 56.3% of women in the home-based sampling group had a chlamydia test compared to 32.9% in the clinic group (RR=1.7, 95%CI:1.4-2.0).
- Another study found more men completed testing when they were sent an invitation letter with a request card (3.6%, RR=5.6, 95%CI:3.6-7.8) or invitation letter with a home testing kit (7.8%, RR=11.1, 95%CI: 7.3-16.9) compared to usual clinic care (0.8%).
- A study among women showed repeated home-based sampling at 6, 12 and 18 months increased testing rates compared to a clinic group (RR=1.38, 95%CI:1.23-1.55).
- Home-based sampling was well-accepted among young people and often preferred compared to clinic testing.
- A number of screening programs involving home-based sampling have reported lower chlamydia testing rates than the trials above. In the Netherlands, in a population based mail out, 34% of young people who received the home-testing kit returned a sample for testing after the first mail out and in France the response to a similar program was 29%
- Home-based sampling using self-collected mail-in specimens may be a good option to increase testing in young high-risk individuals, particularly those with less access to clinical services.
- Home-screening program on a population basis require costly large scale registries like cervical cancer screening, and mechanisms to provide treatment and offer partner notification for those testing positive.

### **Health promotion interventions to improve STI knowledge, reduce risk behaviours and chlamydia or other STIs in young people: a literature review**

- There are a number of different strategies that have been used to modify sexual risk behaviour by young people. The following findings emerged from published literature reviews:
  - Comprehensive health promotion programs which were community based and had multiple components were most effective in changing sexual behaviour, and produced multiple desired effects like increased knowledge and skills, delay in first sex, increased use of condoms and contraceptives, and reduced numbers of sexual partners.
  - Two-thirds of the 48 school curriculum-based programs that support use of condoms and contraceptives in addition to encouraging abstinence were associated with statistically significant changes in delaying the initiation of sex, increasing condom and contraceptive use, reducing the frequency of sex, and reducing number of sexual partners. An in-depth analysis of programs revealed a number of program characteristics (related to development, content and implementation) that were consistently associated with effective programs.
  - Abstinence-only school curriculum based programs have not led to any change in sexual risk behaviour.
  - Availability of condoms and contraceptives in schools increases their accessibility and uptake but whether this leads to an actual increase in use has not been confirmed.
  - Programs based at STI, family planning or reproductive health clinics were associated with an increase in the use of condoms and contraceptives and also a decrease in incidence of STIs. The interventions included STI counselling and testing (98%), education (85%), skill training (condom use - 75% and communication skills - 58%), and motivational components (risk awareness - 60%, risk feedback - 33%, and attitudes towards condom use and/or reducing number of sexual partners - 31%).

### **Modelling chlamydia prevention interventions to reduce chlamydia prevalence/incidence: a literature review**

- One Australian mathematical modelling study explored the coverage levels and target groups required for screening to reduce chlamydia prevalence in the population.

- The modelling predicted that the introduction of extensive screening of young people in Australia can reduce chlamydia transmission and prevalence. The coverage required to lead to a substantial reduction in prevalence varied according to age group and whether both sexes were included.
  - If 40% of men and women <25 years were screened annually, the prevalence of chlamydial infection would decrease rapidly over 10 years in all age groups, with >50% of the reduction being achieved during the first 4 years.
  - A 50% reduction in the overall prevalence of chlamydial infection in the population within 10 years could also be achieved by a variety of combinations of coverage levels and target groups including annually screening ~80% of females <20 years old, 30% of females <25 years old, 20%–30% of females <30 years old, 60% of males and females <20 years old, 20% of males and females <25 years old, or <20% of males and females <30 years old.
- No Australian modelling study has explored the potential impact of partner notification, or condom use.
- Modelling studies in other countries have highlighted that screening should be coupled with enhanced partner management to minimise re-infection and to reduce the cost of the screening program.

## **Recommendations**

1. Because the incidence is high (~4% per year in young women) and re-infection rates are high (22%), regular chlamydia screening and re-screening after a chlamydial infection is vital.
2. Screening programs should employ strategies that result in system changes to increase chlamydia testing rates in primary care, as a very high proportion of young people do attend their general practitioner or primary care clinic at least once a year.
3. Home-based screening should be considered for young people who don't access health services regularly.
4. Any screening program in the future should be coupled with enhanced contact tracing to minimise re-infection and ongoing transmission.
5. Before embarking on large scale national chlamydia screening programs it would be prudent to wait for the results of the ACCEPt and SHIMMER studies.
6. Interventions that reduce sexual risk-taking behaviour of young people need to be considered
7. Enhancing curriculum based education programs should be considered, with a similar content and duration to overseas programs demonstrated to consistently decrease sexual risk factors.
8. Comprehensive health promotion programs that are community-based and have multiple components should be considered.
9. Clinic-based motivational interviewing should also be considered.
10. More uniform ways to diagnose PID and catalogue PID in medical records is required for monitoring and surveillance purposes.
11. Data collections systems need to be enhanced; to be able to evaluate future strategies, particularly improved recording of Aboriginal and Torres Strait Islander status in NSW notification data. Systems are also needed to monitor chlamydia incidence and potential sequelae.
12. Modelling that compares a range of prevention strategies (condom use, partner notification, and screening), combinations of these strategies, and a variety of methods and targets groups within these strategies using Australian data, should be considered to more accurately inform public health decision making in Australia.

## Chapter 1: Epidemiology of genital chlamydia in young heterosexuals in NSW

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### Abstract

**Introduction:** The NSW government convened a working group in 2010 tasked with developing an action plan focused on strategies to control chlamydial infection in young people aged <30 years. To inform the plan, we conducted a review on the epidemiology of chlamydia among this target group in NSW.

**Methods:** Electronic search engines were used to identify studies conducted since 2000 which reported on any of ten pre-specified prevention indicators related to: sexual health knowledge and behaviour, chlamydia testing rates and notifications, positivity, prevalence or incidence in <30 years olds in NSW. Grey literature was also searched. The indicators were selected based on international guidelines.

**Results:** In the last decade, the number of chlamydia notifications in 15-29 year olds in NSW increased by 336.3%, from 3,222 notifications in 2001 to 14,057 in 2010. Medicare data showed a parallel trend in chlamydia testing in young people aged 15-34 years, increasing from 35,384 tests rebated in 2000 to 154,218 in 2010, a 336% increase. One community-based study in NSW estimated chlamydia prevalence in young males and females to be 3.1% (95%CI:1.0-8.0%) and six studies based on clinic populations found the prevalence ranged from 3 to 12%. Analyses of data from a national sentinel surveillance system in sexual health services showed an increase of 28% in chlamydia positivity in young women aged 15-29 between 2004 and 2010 in NSW. The only cohort study among young Australian women (including a subset of NSW women) showed the incidence of chlamydia was high (~4% per year) and the re-infection rate was 22% by 12 months. The number of hospital admissions for PID has remained steady in the last five years, nationally. Despite the number of tests increasing, 2008/09 data from sentinel surveillance shows only 7.3% of 16-29 year olds attending general practices in NSW were tested for chlamydia in a 12 month period. No time trends were available specifically for behaviour data for young people in NSW. However, the national survey of secondary students and sexual health, reporting on Year 10 and Year 12 students from all of Australia in 2002 and 2008, showed that the age of sexual initiation is decreasing, the number of young people with multiple partners is increasing and condom use is fairly stable in young people. We did not identify ongoing estimates of chlamydia incidence, chlamydia-related sequelae or testing rates in Aboriginal and Torres Strait Islander people attending Aboriginal health services in NSW.

**Conclusion:** This review showed that in NSW the greatest burden of chlamydia is among young people aged 15-29 years. While part of the increase in chlamydia notifications mostly reflects increased testing (the more you test, the more you diagnose) analyses of sentinel surveillance data shows that the prevalence of infection in the population is also likely to be increasing. National behavioural surveys suggest a trend towards greater risk-taking behaviour. Despite this, an unacceptably low proportion of young people are being tested for chlamydia in general practice in NSW. There are many gaps in the available data that need to be addressed to plan and evaluate prevention programs.

## **Introduction**

Most chlamydia infections are asymptomatic and sustain transmission within a community if left undiagnosed and untreated.(1-3) In addition, untreated persons are at risk of serious long-term sequelae; especially pelvic inflammatory disease (PID) in women(4-7) which leads to infertility, ectopic pregnancy, recurrent PID, and chronic pelvic pain.(8-10) Chlamydia is the most commonly notified infection in Australia.(11) Over the past decade 110,862 chlamydia notifications have been reported in New South Wales (NSW),(12) and the highest rates of notification are observed in young people aged 20-24 years, followed by young people aged 15-19 years and 25-29 years.(13)

Primary prevention strategies are efforts to prevent chlamydial infection and can be achieved by health promotion and testing. *Health promotion* encompasses strategies that aim to change behaviours that reduce the risk of acquiring or transmitting infection, such as *decreasing the number of sex partners* and the *use of condoms*, particularly with new partners. The aim of *testing and treating* people with genital chlamydia is to prevent the infection being passed onto sexual partners and for pregnant women onto their babies. Chlamydia testing strategies are essential to chlamydia prevention, as infections among women and men are usually asymptomatic. Secondary prevention strategies are efforts to prevent complications among persons infected with chlamydia, such as pelvic inflammatory disease, infertility, and ectopic pregnancy, and can be achieved through detection and treatment of asymptomatic chlamydial infection; and treating the female partners of men with infection.

Sexually transmissible infections' (STI) surveillance systems provide routine information on key indicators that can guide the planning and evaluation of primary and secondary prevention initiatives intended to reduce STI transmission. To understand the transmission dynamics of STIs, it is very important to understand the sexual behaviours of the population. Information regarding knowledge and behaviour of a populations, help in understanding how epidemics are generated and inform prevention and disease control strategies.

The NSW government convened a chlamydia working group in 2010, with the responsibility of developing an action plan focused on strategies to control chlamydia infection in young heterosexual people aged <30 years in the state. To inform the action plan and inform future prevention and service programs, we conducted a systematic review on the ten core indicators related to the epidemiology of chlamydia among <30 year olds in NSW.

## **Methods**

### ***Indicators***

We focused on the following ten prevention indicators, consistent with international guidelines(14), among young people in NSW:

### **Impact**

1. Annually reported chlamydia cases (chlamydia notifications)
2. Percentage of 15-29 year olds infected with chlamydia at a given time (chlamydia prevalence)
3. Percentage of new chlamydia infections in 15-29 year olds at a given time (chlamydia incidence)
4. Annual cases of pelvic inflammatory disease among chlamydia-infected 15-29 year old women

## Knowledge and behaviour

5. Percentage of 15-29 year olds tested for chlamydia in the last 12 months
6. Percentage of 15-29 year olds who both correctly identify ways of preventing sexual transmissions of chlamydia and who reject major misconceptions about chlamydia transmission
7. Percentage of 15-29 year olds who correctly identify the potential sequelae associated with chlamydia
8. Percentage of 15-29 year olds who have had sexual intercourse before the age of 16
9. Percentage of 15-29 year olds who had more than one recent sexual partner
10. Percentage of 15-29 year olds reporting always using condom recently

We also describe these indicators in Aboriginal and Torres Strait Islander people as they are a priority population identified in the National STI strategy(15), NSW STI strategy(16), and are accorded a priority by having a dedicated strategy (Third National Aboriginal and Torres Strait Islander Blood Borne Viruses and STIs Strategy)(17). In addition, where available, we include information and data for travellers/backpackers, sex workers, prisoners and homeless people, as they are important sub-groups in the young population of NSW.

### ***Data sources***

The following data sources were used to describe the epidemiology of chlamydia (on any of the above ten prevention indicators) in young people in NSW:

#### *Grey Literature*

Australian Bureau of Statistics: Data on 2009 population size and demographics were sourced from the Australian Bureau of Statistics.(18)

Passive Surveillance: The National Notifiable Disease Surveillance System(12) is an ongoing population-based surveillance system, which collates the number of new chlamydia diagnoses reported by doctors and laboratories and the age, sex and area of residence of each case.

Sentinel Surveillance: The Australian Collaboration for Chlamydia Enhanced Sentinel Surveillance (ACCESS) project(19) is a sentinel surveillance system established to monitor the extent and outcome of chlamydial infection in six networks of clinical sites (general practices, sexual health services, family planning centres, antenatal clinics, Aboriginal community controlled health services, and laboratories). Each network provides unique information on testing uptake and chlamydia positivity in a range of populations.

Australian Study of Health and Relationships: This national survey was conducted in 2001/2002, among a representative sample of 19,307 Australians aged 16-59 years through computer assisted telephone interviews, across all states and territories. The intention is for the survey to be repeated periodically, with the next round in 2011/2012. For the purpose of this Chapter, data from young people aged 16-29 years were extracted from the NSW report of the study.(20) The NSW data are compared with the National data (Table 1.5).

National survey of secondary students and sexual health: This repeated national survey of Australian secondary students on HIV/AIDS and sexual health was conducted in 2002 and 2008 among 2,926 students from year 10 and 12 (median age 15 and 17 respectively); recruited from more than 100 secondary schools from every jurisdiction in Australia.(21) In this Chapter, findings of the 2008 survey are compared with those from 2002.

**Survey among Young Aboriginal and Torres Strait Islander people:** This community-based survey of knowledge, risk behaviour and access to services was conducted among young Aboriginal and Torres Strait Islander people (aged 16-30 years) in NSW in 2007/08. A total of 293 surveys were collected via recruitment through two community events.(22)

**Sexual health clinic data:** A retrospective analysis of sexual health clinic data by McNulty et al in 2010, reported on the sexual behaviour of young backpackers/travellers (aged 18-30 years) visiting the Sydney Sexual Health Centre in Sydney, NSW from 1998 to 2006; and compared the findings to young non-backpackers visiting the centre, during the same time period.(23)

**NSW Young People In Custody Health Survey:** A survey was conducted among 242 young people (mean age: 17 years) in any of the nine juvenile detention centres or subject to community control orders in NSW, in 2003.(24) Interviews and assessments were conducted by registered psychologists and nurses from the Department of Juvenile Justice and Justice Health.

**Sexual health and behaviours of Australian prisoners study:** Computer-assisted telephone interviews were conducted with 1,118 men and 199 women in NSW prisons in 2006-07.(25-26) These data are not age specific and come from general prison population of NSW (median age: 33 years) and are only used in this Chapter when data were not available from the NSW young people in custody health survey.

**PID hospitalisations:** Hospitalisation for PID was defined as having an International Classification of Disease 10 (ICD10-AM) code in the main diagnosis field for 'salpingitis and oophoritis' or 'acute inflammatory diseases of the uterus' or 'parametritis and pelvic cellulitis' or 'inflammatory disease of the ovary, fallopian tube, pelvic cellular tissue and peritoneum' or chlamydial infection of pelviperitoneum and other genitourinary organs in women.<sup>1</sup> For this report, PID hospitalisations data were not available for all ICD-10 codes in NSW. Therefore we used national Australian Institute for Health and Welfare hospitalisation data, using the ICD-10 codes (including A56.1) and ABS census population estimates.(27)

### *Peer-reviewed literature*

**Medline and EMBASE:** The electronic bibliographic databases Medline and EMBASE were also searched from 2000 to the end of January, 2011. The following search terms were used:

- (chlamydia.mp. or exp Chlamydia/ or exp Chlamydia trachomatis/) AND (exp New South Wales/ep [Epidemiology])

Further searches were conducted to identify prevalence and incidence studies. Terms *Prevalence* and *Incidence* were combined (separately) with the original search terms to identify these studies. Studies were included if they reported on sexual health knowledge, sexual behaviour, chlamydia testing rates and chlamydia notifications, positivity, prevalence or incidence in <30 years olds in NSW.

**Review process:** Using the search terms chlamydia and New South Wales, 60 articles were identified excluding duplicates. In addition, reference lists of these articles were reviewed to identify other relevant articles and six articles were identified through this hand-search (Figure 1.1). Of these 66 articles the following studies were excluded; those which did not contain epidemiological data (n=19), did not report on genital chlamydia (n=2), did not have any data from NSW (n=15), and 26 articles were prevalence studies.

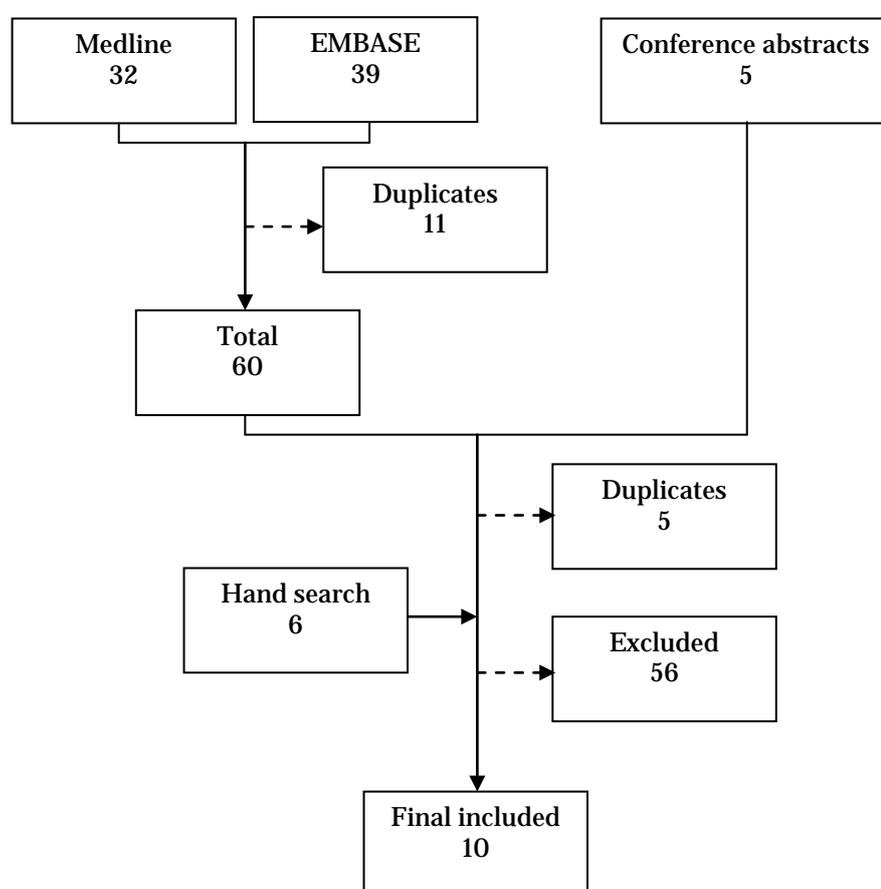
<sup>1</sup> ICD-10 codes: N70.0, N70.1, N70.9, N71.0, N71.1, N71.9, N73.0, N73.1, N73.2, N73.8, N73.9, N74.4, A56.1

**Conference abstracts:** Programs of the Australian Sexual Health Conference, from 2005 to 2010, were hand-searched for relevant prevalence and incidence studies. Five studies were shortlisted for inclusion. However, all five of them were found to be duplicates and were already identified through the other search strategy.

From the 26 prevalence studies, the following were excluded: studies which did not include young people in NSW; studies which only reported on routine testing data; studies which reported prevalence earlier than 2000 and studies where the participants included those older than 29 years and data related to those aged <30 years were not reported separately. However, studies reporting on routine data were included if the testing rate was above 70%. (28)

Only ten peer-reviewed papers were included in the review. Combined with the grey literature, a total of 33 papers/reports and data sources were included in this Chapter.

**Figure 1.1: Search results – peer-reviewed databases**



### **Data analysis**

Descriptive analyses were undertaken for most data sources.

ACCESS data for NSW were not publicly available, so were purposely extracted in 15-29 year old heterosexual young people in NSW who were new patients at 12 NSW sexual health services. The proportion of young heterosexuals who were tested for chlamydia on their first visit was calculated (chlamydia testing). The proportion of new patients diagnosed with chlamydia (chlamydia positivity) was also calculated by dividing the total number of new chlamydia diagnoses by the total number of tests. Indeterminate chlamydia results were excluded from the analysis. Analysis was conducted using STATA 10 (StataCorp, College Station, TX, USA).

## Results

### Characteristics of NSW population

#### Demographics

In 2009, NSW had the highest number of young people aged 15-29 years (1,519,544)(29), overseas migration (83,787)(29), Aboriginal and Torres Strait Islander people (161,910)(30) and prisoners (11,127)(31) compared to other states and territories in Australia (Table 1.1).

**Table 1.1: Population demographics in NSW compared to other states and territories, 2009 (29)**

Population demographics	NSW	VIC	QLD	SA	WA	TAS	NT	ACT
Total population	7,190,482	5,501,387	4,475,132	1,634,835	2,272,556	505,360	227,646	355,311
Population growth rate <sup>2</sup>	1.64	2.14	2.44	1.33	2.66	0.89	2.26	1.86
Overseas migration (n)	83,787	77,502	53,265	17,349	38,078	2,046	1,909	3,775
Young people age 15-29 years (n)	1,519,544	1,187,839	956,781	329,987	492,454	94,910	55,795	85,890
Females aged 15-29 years (n)	743400	577936	467819	161199	235230	46727	26993	41921
Median age of population (18)	37.1	37.0	36.2	39.1	36.3	39.6	31.2	34.7
Aboriginal and Torres Strait Islanders (n) (30)	161,972	35,909	156,517	29,785	74,885	19,653	67,475	4,600

In 2006, 70.1% of the NSW population was born in Australia, 8.8% were born in other English speaking countries and 21% were born in non-English speaking countries; Year 12 was the highest school qualification for 46.7% of the adult population.(32) In 2006, 72.6% of the population of NSW lived in major cities, 26.8% lived in regional areas and 0.6% lived in remote areas.(33)

NSW has the highest number of Aboriginal and Torres Strait Islander people in Australia. In 2006, 57% of Aboriginal and Torres Strait Islander people in NSW were less than 25 years of age and only 35% and 21% of those aged 15 years and over stated Year 10 and Year 12 or equivalent respectively as their highest level of schooling.(34)

The 2003 NSW Young People In Custody Health Survey,(24) showed that the mean age of young detainees was 17 years for males and 16 years for females, the majority were Australian born, and the population was disproportionately Aboriginal and/or Torres Strait Islander people (42%). In 2006, 545,000 international visitors visited Australia out of which 407,000 visited Sydney.(35)

#### **Indicator 1: Chlamydia notifications**

In NSW, the number of chlamydia notifications has increased by 336.3% over the past decade, from 3,222 notifications in 2001 to 14,057 in 2010; with a 23.4% increase between 2009 and 2010 (12) (Table 1.2). In 2010, notification rates were highest in 20-24 years olds (1265.7 per 100,000 population) followed by 15-19 year olds (912.8 per 100,000) and 25-29 years (660.7 per 100,000). Aboriginal and Torres Strait Islander status was unavailable for 95% of NSW chlamydia notifications in 2009.

Based on chlamydia notifications between 1998 and 2003, Schleihauf et al conducted a spatiotemporal cluster analysis to investigate the differences in geographical distribution of the infection in NSW.(36) They reported a significant clustering of chlamydia cases in a grouping of 270

<sup>2</sup> Increase in population in 2009 compared to start of 2009; includes natural increase (births minus number of deaths) and net overseas migration

postal areas along the eastern coast of NSW, from the Sydney area to the NSW northern border. People living in this cluster were 5 times more at risk of having a chlamydia notification, compared to people living outside the cluster.

**Table 1.2: Trends in chlamydia notifications, testing and positivity in 15-29 year olds in NSW**

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	ptrend	
Number of chlamydia notifications (12)	3,222	4,005	5,651	7,381	8,439	8,977	9,473	10,666	11,387	14,057	<0.0001	
Chlamydia notification rate per 100,000 population* (12)	236.8	294.5	414.5	539.88	612.51	642.8	662.25	722.83	762.99	945.5	<0.0001	
Chlamydia tests rebated by Medicare in 15-34 year olds (37)	35,384	41,697	57,317	71,258	78,302	#	#	115,809	154,218	166,318	<0.0001 <sup>β</sup> <0.0001 <sup>§</sup>	
Chlamydia tests rebated by Medicare per 100,000 15-34 year olds	1908.9	2234.9	3055.0	3791.6	4149.9	#	#	5899.2	7661.3	8130.9	<0.0001 <sup>β</sup> <0.0001 <sup>§</sup>	
Chlamydia testing rates in young heterosexuals at sexual health services‡	Males	-	-	-	79.7%	82.2%	81.2%	81.7%	79.0%	77.4%	88.3%	0.23
	Females	-	-	-	73.7%	78.8%	79.2%	79.8%	77.5%	74.6%	84.2%	0.05
Chlamydia positivity rates in young heterosexuals at sexual health services‡	Males	-	-	-	10.9%	11.3%	11.5%	11.1%	10.6%	11.3%	12.2%	0.44
	Females	-	-	-	8.5%	9.5%	10.3%	9.9%	10.2%	10.0%	10.9%	0.02

\* Age standardised rate per 100 000 population

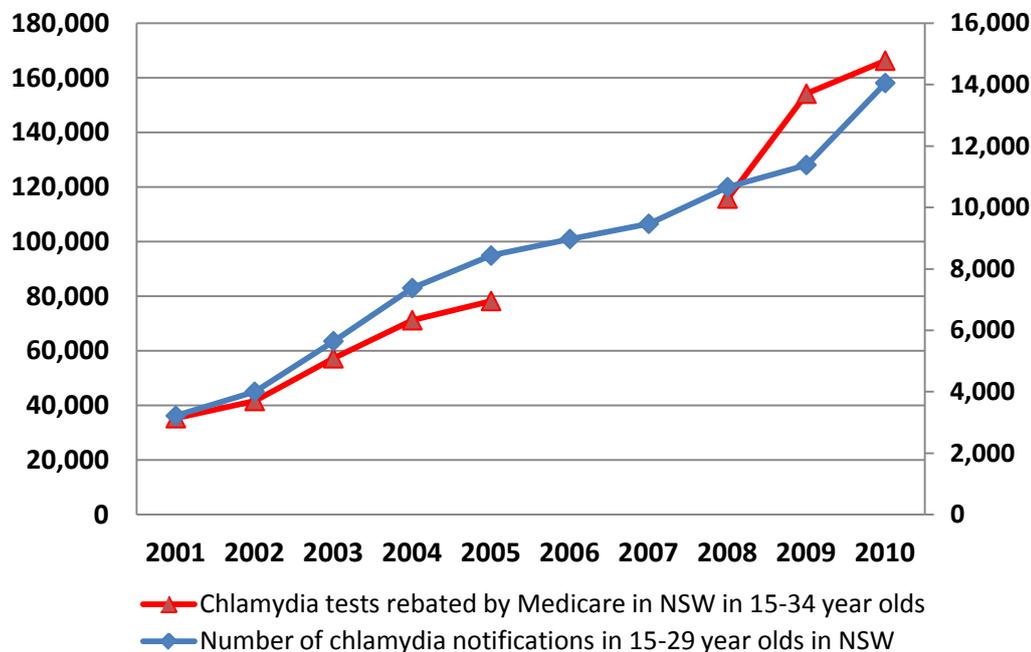
‡ Data from 12 SHS in NSW – ACCESS data – first visits only

# Gap from Nov 2005 to April 2007 due to testing being rolled into a multiple test item number; reported rebates 626 in 2006 and 65,585 in 2007

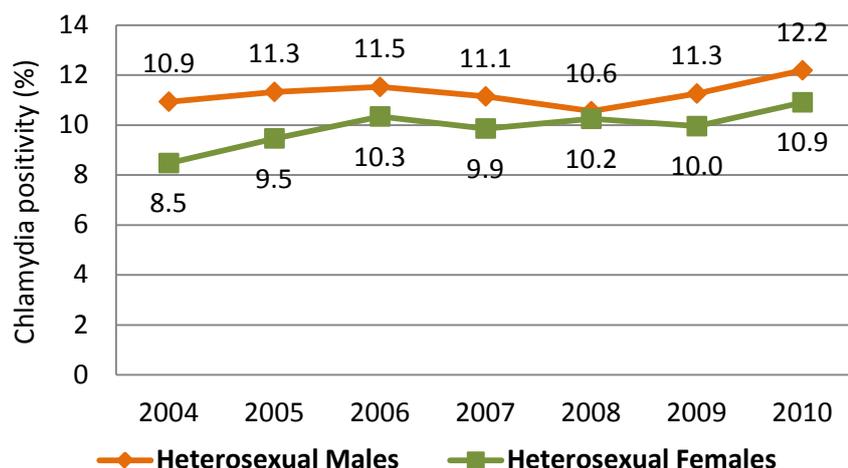
β ptrend for 2001-2005

§ ptrend for 2008-2010

**Figure 1.2a: Trends in chlamydia notifications and testing\* in NSW, 2001-2010**



\* Data from 15-34 year olds; Gap from Nov 2005 to April 2007 due to testing being rolled into a multiple test item number; reported rebates were 626 in 2006 and 65,585 in 2007

**Figure 1.2b: Trends in chlamydia positivity in 15-29 year old heterosexual new patients attending 12 sexual health clinics in NSW, 2004-2010****Indicator 2: Chlamydia prevalence**

In our review, we identified and included six studies/reports which estimated the prevalence of chlamydia in young people recruited from clinical settings and two studies which recruited young people from community, over specific defined time periods in NSW (See table 1.3).

*Clinic-based studies*

Donovan et al reported prevalence of chlamydia in heterosexual patients attending the Sydney Sexual Health Clinic from 1994 to 2000.(38) The prevalence was reported to be 3.5% in females (median age: 25 years) and 6.6% in males (median age: 28 years) in 2000. A study was conducted by Kang et al in 333 homeless or at risk of homelessness young people (14-25 years) in NSW attending three youth health centres (two outer suburban, one rural), between 2000 and 2003.(39) The study found the prevalence of chlamydia to be 5.7% (95%CI: 3.0-8.4%). In this study all young people diagnosed with chlamydia were asymptomatic. A cross-sectional study conducted by Bateson et al in 2004, estimated the prevalence of chlamydia in 621 young women attending five family planning services in NSW,(40) and found the prevalence of chlamydia to be 5.6% (95%CI: 3.8-7.4). In addition, the study identified recent change in partners in past 3 months and reported 3 or more partners in the last year as an independent predictor of chlamydial infection.

Lenton et al, conducted a cross-sectional study among pregnant women attending antenatal services in the remote far west of NSW, between 2004 - 2006.(41) The median age of eligible women was 21 years and the prevalence of chlamydia was 2.7% (95%CI: 1.0-5.9) overall among 218 women and 9.1% (95%CI: 2.5-21.7) among the 44 Aboriginal and Torres Strait Islander women tested.

Findings from the ACCESS system(19), show that among 15-29 year old female heterosexuals attending 12 NSW sexual health clinics for the first time, chlamydia prevalence in those tested (or chlamydia positivity) increased significantly by 28%, from 8.5% in 2004 to 10.9% in 2010. In 15-29 year old male heterosexuals, chlamydia positivity increased, non-significantly, by 11.9%, from 10.9% in 2004 to 12.2% in 2010 (Table 1.2, Figure 1.2b). The antenatal clinic network of the ACCESS system involved consecutive sampling of young women attending one hospital antenatal clinic in NSW.(42) At this hospital, a total of 56 women aged 16-24 years, were tested at the clinic between October 2008 and March 2009; and the overall prevalence of 8.9% (95%CI:3.5-18.5); higher in

women aged 16-19 years (16.7%, 95%CI:1.9-55.8) compared with 20-24 year olds (8.0%, 95%CI:2.8-17.9).

### Community-based studies

Martin et al, conducted a study among young people aged 16-24 years to ascertain the acceptability of self-collected urine samples as a means of testing and to determine the rate of positivity in the sample.(43) Young people could request a self-testing kit to be posted to them via phone, website or could collect one directly at an outreach event. A total of 277 kits were requested and 131 samples were returned, in the target age-group (16-24 years) four participants tested chlamydia positive (3.1%; 95%CI:1.0-8.0). In another study, Davies et al recruited and tested 432 young international travellers from hostels across Sydney in 2009.(44) They reported an overall prevalence of 3.5% (95%CI: 2.0-5.7) among the young travellers. Prevalence was higher in females (3.9%) than in males (3.1%).

**Table 1.3: Chlamydia prevalence studies in young people in NSW, 2000-2009**

Author, year, reference	Years of study	Setting	Study design	Target population	Sex	Sample size	Median age	Chlamydia prevalence	95% CI
<i>Clinical setting</i>									
Donovan et al 2002 (38)	2000	Sexual health clinic	Routine chlamydia testing data: ~80-85% new patients tested	Patients attending sexual health clinic	F	800	25	3.5%	2.3%-5.0%
					M	1,114	28	6.6%	5.3%-8.3%
Kang et al. 2006 (39)	2000-2003	Youth health centres	Consecutive sampling: 82% tested	Homeless or at-risk of homelessness young people (14-25 years)	M & F	333	-	5.7%	3.0%-8.4%
Bateson et al. 2006 (40)	2004	Family planning clinics	Consecutive sampling: 67% tested	Women aged 16-24 years	F	621	20*	5.6%	3.8%-7.4%
Lenton et al. 2007 (41)	2004-2006	Antenatal clinics	Cross-sectional study: 52% tested	Pregnant women	F	218	21	2.7%	1.0%-5.9%
				Indigenous pregnant women	F	44	-	9.1%	2.5%-21.7%
ACCESS, 2009 (42)	2008-2009	Hospital antenatal clinic	Consecutive sampling: 38.6% women tested	Pregnant women (16-24 years)	F	56	-	8.9%	3.5%-18.5%
ACCESS	2010	Sexual health clinics	Routine chlamydia testing data: 84.2% of female and 88.3% of male new patients tested	Patients attending sexual health clinic (15-29 years)	F	2,640	22	10.9%	9.7%-12.2%
					M	2,674	24	12.2%	11.0%-13.5%
<i>Community setting</i>									
Martin et al. 2009 (43)	2006-2007	Community	Community sampling	Young people (16-24 years)	M & F	277	20	3.1%	1.0%-8.0%
Davies et al. 2011 (44)	2009	Hostels	Community sampling	International backpackers in Sydney	M	225	24	3.1%	1.3%-6.3%
					F	207	23	3.9%	1.7%-7.5%

\* Mean Age

### Indicator 3: Chlamydia incidence

No ongoing studies of genital chlamydia incidence were identified in NSW.

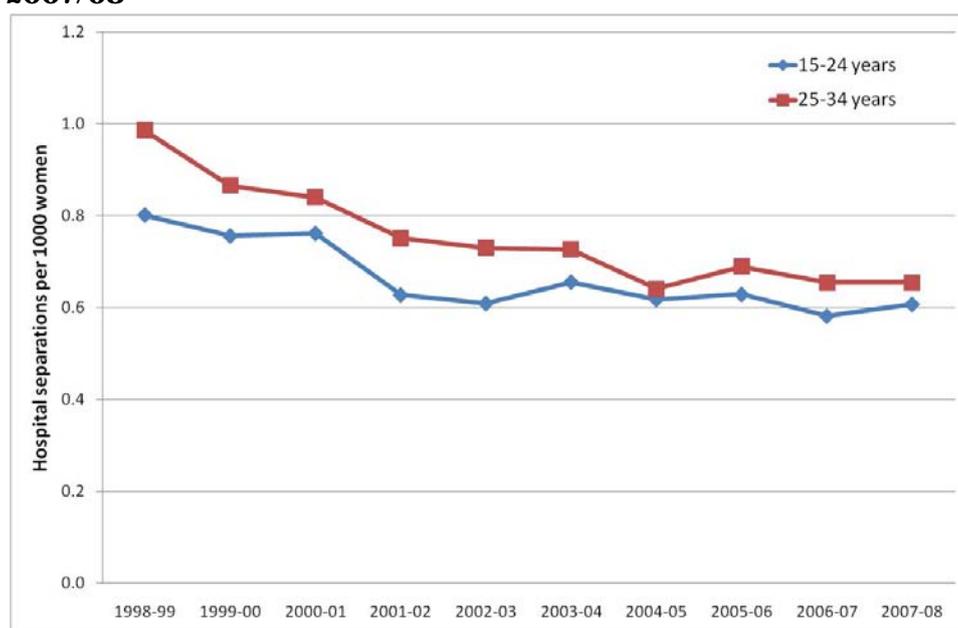
There has been only one prospective cohort study of chlamydia incidence in heterosexuals, ever conducted in Australia. The study was conducted among 16-25 year old women recruited from general practices, sexual health and family planning clinics in three states (NSW, Victoria and ACT).(45) Although the study does not provide NSW specific estimates; there were 38 incident cases

of chlamydial infection in 1,116 women, giving an overall chlamydia incidence of 4.5 per 100 person years (95%CI: 3.1-6.7) in 2008/2009.

#### **Indicator 4: Chlamydia sequelae**

Overall there has been a significant decreasing trend in annual rates of hospital separations for PID from 1998/99 to 2007/08. In 15 to 24 year old women rates decreased from 0.80 to 0.61 per 1,000 women over the entire time period ( $p < 0.001$ ), and in 25 to 34 year olds from 0.99 to 0.65 ( $p < 0.001$ ). From 2004 onwards annual rates of hospital separations for PID have remained steady (Figure 1.3).(27)

**Figure 1.3: Annual rates of hospital separations for PID in Australia by age-group, 1998/99 - 2007/08**



#### **STI knowledge and sexual behaviour**

##### **Indicator 5: Percentage of 15-29 years tested for chlamydia in the last 12 months**

The 2007/2008 survey among young Aboriginal and Torres Strait Islander people described self-reported testing and showed that 35.1% young people reported being tested for an STI in the past 12 months, prior to the survey; and another 24.3% reported being tested for an STI but not in the past 12 months.[22]

Testing rates from a range of clinical setting were available and showed in NSW in 2008, 1,037,032 16-29 individual patients visited a general practitioner, representing 87% of women and 67% of males aged 16-29 years in NSW.(46) Of these 7.3% were tested for chlamydia, which is the second lowest testing rate in Australia (Table 1.4). A higher proportion of young females (10.2%) were tested in general practice in NSW than young males (3.7%).

The extent of testing in Aboriginal and Torres Strait Islander people attending general practice clinics in NSW is not well understood, due to the poor recording of Aboriginal and Torres Strait Islander status. Among 27 general practice clinic participating in the ACCESS study, Aboriginal and Torres Strait Islander status was only recorded in 15% of patients.(47)

In 2010, 5,082 young people aged 15-29 years attended 12 sexual health services participating in ACCESS in NSW, and 88.3% of males and 84.2% of females were tested for chlamydia (Table 1.2).

Data from other networks of ACCESS (Aboriginal community controlled health services, and family planning clinics) only included 1-2 services in NSW so are not reported here.

Data from the Medicare Benefits Schedule shows that there was a 336% increase in the number of tests rebated by Medicare, from 2001 to 2010, among young people aged 15-34 years in NSW (Table 1.2). A total of 35,384 chlamydia tests were rebated among young people in NSW in 2000, this number increased to 154,218 in 2010 (Figure 1.2a).(37)

**Table 1.4: Chlamydia testing rate in 15-29 years old in general practices, Oct 07 - Sept 08\***

	Consultations	Tests	Rate
TAS	69,689	1,761	2.5
NSW	1,037,032	75,532	7.3
SA	232,156	17,489	7.5
VIC	783,066	66,048	8.4
ACT	56,272	5,144	9.1
QLD	629,050	67,693	10.8
WA	304,750	36,927	12.1
NT	27,340	9,123	33.4
TOTAL	3,139,354	279,717	8.9

\* Unique consultations and tests

***Indicator 6: Percentage of 15-29 year olds who both correctly identify ways of preventing sexual transmissions of chlamydia and who reject major misconceptions about chlamydia transmission,***

***and***

***Indicator 7: Percentage of 15-29 year olds who correctly identify the potential sequelae associated with chlamydia***

Young people in NSW: The Australian Study of Health and Relationships (2001/2002), found that the level of STI knowledge was low in young people in NSW. The mean score (on a 0-10 scale range) was: 4.4 for men and 5.7 for women aged 16-19 years and 5.9 for men and 6.6 for women aged 20-29 years.(20)

Australian young people: The secondary students and sexual health survey (conducted in 2002 and 2008), showed that an average of 7.2 of 11 STI knowledge questions were answered correctly by young Australians, compared to the average score of 6.2 in 2002.(21) In 2008, the average score was higher for females (7.5) compared to males (6.7). A majority of students (91%) knew that both men and women can pass on STIs without having any obvious symptoms but only 47% of students knew that both men and women can suffer from chlamydia and only 55% knew that chlamydia can lead to infertility in women.

Aboriginal and Torres Strait Islanders: The 2007/08 community-based survey among young Aboriginal and Torres Strait Islander people,(22) showed that more than 70% of participants, correctly answered knowledge questions related to STIs. The survey also showed that 71.3% of young Aboriginal and Torres Strait Islander people knew that a person can have an STI without any obvious symptoms and a lower proportion (63.1%) knew that STIs can make it hard for women to get pregnant.

***Prisoners:*** The 2006-07 study of Australian prisoners found that among NSW prisoners of all ages, half of men (50%) and more than half women (58.3%) inmates thought that chlamydia affects only women; and only 51.8% men and 62.3% women knew that chlamydia can lead to infertility in women.(25)

***Indicator 8: Percentage of 15-29 year olds who have had sexual intercourse before the age of 16***

***Young people in NSW:*** According to the Study of Health and Relationships, in NSW, 26.7% men and 17.9% women aged 16-19 years had their first vaginal sex before the age of 16 and 24.3% men and 14.7% women aged 20-29 years had their first vaginal sex before the age of 16.(20)

***Australian young people:*** According to the secondary students survey,(21) 34.0% of male and 43.1% female students have ever had sexual intercourse in 2008; compared to 36.4% male and 33.3% female students in 2002.

***Prisoners:*** The 2003 NSW young people in custody health survey showed that the median age of first intercourse was 13 years for males and 14 years for females.(24)

***Indicator 9: Percentage of 15-29 year olds who had more than one recent sexual partner***

***Young people in NSW:*** The Study of Health and Relationships showed that in 2000/2001 in NSW, 13% of men and 4.6% of women aged 16-19 years and 8.9% of men and 4.9% of women aged 20-29 years, who were in a regular relationship, had more than one sexual partner in last 12 months.(20)

***Australian young people:*** According to the secondary students survey, the proportion of young people reporting more than three sexual partners in the past 12 months, increased from 19.9% in 2002 to 29.7% in 2008.(21) The survey also showed that in 12.1% of young people, the last sexual partner was someone they had not met before. This proportion has increased from the 2002 survey in which it was 10.8%.

***Aboriginal and Torres Strait Islanders:*** The 2007/08 community-based survey among young Aboriginal and Torres Strait Islander people showed that 27.3% of 16-30 year olds reported having more than three casual partners and 63.5% reported having at least one casual sex partner in past six months.(22)

***Prisoners:*** The 2003 NSW custody survey found prisoners had a high number of lifetime sexual partners according to the 2003 NSW young people in custody health survey: 24% of female and 18% of male inmates had more than six lifetime partners and 12% females and 50% males had more than 11 partners.(24)

***Travellers:*** The sexual health clinic retrospective analysis by McNulty et al, 2010 reported that young backpacker travellers in Sydney had higher number of sexual partners, with 39% (49% of men and 30% of women) reporting two or more sexual partners in the last three months compared with 30% (36% of men and 22% of women) of comparison non-backpacker patients ( $p < 0.001$ ). (23)

***Indicator 10: Percentage of 15-29 year olds reporting always using condoms***

***Young people in NSW:*** The Study of Health and Relationships (2001/2002), found that 76% of men and 80% of women aged 16-19 years and 45.6% of men and 39.2% of women aged 20-29 years, always used condoms with a casual partner in past six months. However, 83.7% men and 36.0%

women aged 16-19 years and only 20.7% men and 7.4% women aged 20-29 years, always used condoms with a regular partner.(20)

***Australian young people:*** According to the 2008 secondary students survey, only 50.5% of sexually active secondary school students always used condoms in the last one year, 42.6% reported using them only sometimes and a small proportion (6.9%) never used condoms.(21) This was similar to the 2002 survey which reported that 52.1% students always used condoms, 38.9% used it sometimes and 9% never used condoms

***Aboriginal and Torres Strait Islanders:*** The community-based Aboriginal and Torres Strait Islander survey in young people in NSW showed that 40% of 16-30 year olds reported using condoms with casual partners in past six months on every occasion whereas 20% had never used condoms with casual partners.(22)

***Prisoners:*** The 2003 NSW custody survey showed that 49% men and 57% women either never used condoms or used them less than half of the time when they engaged in penetrative sex with regular partners; whereas, 33% of young men and 44% of young women either never used condoms or used them less than half of the time when they had penetrative sex with casual partners.(24)

***Travellers:*** The sexual health clinic retrospective analysis found that two third of both backpackers and non-backpacker young people reported unprotected anal or vaginal sex in the last three months; 22% men and 23% women backpackers always used a condom in the last three months compared to 21% men and 18% women non-backpackers.(23)

**Table 1.5: Sexual behaviour indicators among young people, NSW comparison with national data (20, 48-51)**

Indicator			NSW	National
STI knowledge score	16-19 years	Male	4.4	4.5
		Female	5.7	5.8
	20-29 years	Male	5.9	6.0
		Female	6.6	6.6
Percentage who have had sexual intercourse before the age of 16	16-19 years	Male	26.7%	26.9%
		Female	17.9%	24.8%
	20-29 years	Male	24.35	22.6%
		Female	14.7%	17.2%
Percentage who were in a regular relationship and had more than one sexual partner in the last 12 months	16-19 years	Male	13.0%	21.4%
		Female	4.6%	8.0%
	20-29 years	Male	8.9%	9.6%
		Female	4.9%	5.6%
Percentage reporting 100% condom use with casual partners in past 6 months	16-19 years	Male	76.0%	65.2%
		Female	80.0%	43.9%
	20-29 years	Male	45.6%	43.6%
		Female	39.2%	37.3%

\* Very small sample size

## Discussion

This review showed that in NSW, the greatest burden of chlamydia infection is among young people aged 15-29 years. While part of the increase in chlamydia notifications is likely to reflect increased testing (the more you test, the more you diagnose) analyses of sentinel surveillance data, shows that the prevalence of infection in young people attending sexual health clinics has increased slightly over

the past decade. National secondary schools surveys also suggest a trend towards higher risk behaviour. Despite this, an unacceptably low proportion of young people are being tested for chlamydia in general practice. There are many gaps in available data, which need to be filled for planning and evaluation of prevention programs.

### *Implications for prevention programs*

According to the Royal Australian College of General Practitioners' Guidelines for Preventive Activities in General Practice, all sexually active women under 25 years of age should be opportunistically screened for chlamydia.(52) However, only 7.3% of young people who attend GP clinics get tested each year in NSW. This shows that there is a need for interventions to increase chlamydia testing in young people in the general practice setting in the state. *Chapter 5* looks at the interventions which can be utilized to increase chlamydia testing in general practice.

Our review shows that the level of knowledge regarding STIs is moderate among young people in NSW. Studies have suggested that the level of chlamydia knowledge influences people's decisions about chlamydia testing. Acceptability of testing increases if people know that chlamydia is a common, asymptomatic and a serious condition; if they know the testing process and understand its importance; and if they know that chlamydia can lead to long-term sequelae especially infertility.(53) However, preliminary results from a study conducted by National Centre in HIV Social Research, shows that knowledge is not the only factor which influences testing decisions; rather it shows that young people are influenced by their perceptions of personal risk and what others think about people who have a test. Thus, in addition to increasing knowledge and perceptions of personal risk, interventions should address testing related stigma and reinforce the positive norms of their peers towards STI testing.

Though NSW trend data are not available; there appears to be a trend towards greater sexual risk-taking behaviour in young people in Australia. More young people are becoming sexually active at a younger age; more young people have multiple sex partners; and though condom use has remained somewhat stable it's far less than ideal. Interventions that reduce sexual risk-taking behaviour of young people should be considered. *Chapter 8* summarizes the interventions that are effective in decreasing the sexual risk-taking in young people. The chapter shows that the effect of such interventions could be important especially when combined with other prevention strategies.

### *Implications for surveillance systems*

Surveillance systems are never perfect and vary considerably according to the area of public health being monitored and the available resources. From a scientific and public health perspective, it is clear that chlamydia epidemics can differ considerably over place and time, and the monitoring systems that are used to guide prevention initiatives need to reflect the current state of the epidemic in a given setting. The relationship between prevalence and incidence, and the behavioural and demographic profiles of at-risk individuals, are required to make valid comparisons over time. Passive surveillance data can be used as an indicator of population prevalence if the testing rates are high enough, and sentinel surveillance can be used as an indicator of prevalence in the populations accessing the clinics if the testing rates are high enough. This review identified that a number of important indicators could not be measured with existing surveillance data, namely chlamydia incidence, and clinic-based testing rates and notifications in Aboriginal and Torres Strait Islander people (Box 1.1).

In NSW, both doctors and laboratories notify cases of chlamydia. Each notification includes age, sex and area of residence of the patient. The system provides the number of new diagnosis over a

defined time period but depends very strongly on access to health services and the patterns of testing in a population, and thus has substantial limitations as an indicator of prevention programs, particularly because it does not provide a denominator to interpret surveillance trends. Only 5% of notification data from NSW have Aboriginal and Torres Strait Islander status recorded. Nationally, the chlamydia diagnosis rate in the Aboriginal and Torres Strait Islander population in 2009 was 999 per 100,000 population which was more than three times that of the non-Indigenous rate of 287 per 100,000.(54) There is therefore a strong need to improve reporting of Aboriginal and Torres Strait Islander status in NSW notification data.

Recognising the limitations of routine case-reporting, surveys which aim to estimate chlamydia prevalence are often conducted to support the planning and evaluation of STI prevention programs. The populations involved in surveys are generally defined by demographic or behavioural characteristics or by a link to a defined setting such as a clinical service or institution that can be used as a site of recruitment to the survey. The ideal surveys are population-based. However, such surveys are very costly and resource intensive and therefore are likely to take place every five years only, precluding the ability to track intermediate term trends. No population-based estimates of chlamydia prevalence in young people were available from NSW. The most relevant data comes from studies conducted in specific sub populations. However, since these estimates are in sub-populations or at-risk populations, they are unlikely to represent the true population estimates. The only population-based prevalence study in Australia was conducted by Hocking et al in 2003/2004 among women aged 18 to 35 years in Victoria, who were recruited by telephone interviews from a random sample of households.(55) Just under half (43%) of women, who agreed to participate, self-collected and posted urine samples through mail for chlamydia testing. The prevalence among sexually active women aged 18–24 years was found to be 3.7% (95%CI: 1.2%-8.4%) and was 0.2% (95%CI: 0.0%-1.1%) among 25–35 year olds.

In clinical sites, the chlamydia positivity rate may be used as a proxy for prevalence among the people attending the service, when testing rates are high.(28) The routine nature of the data also allows for rapid epidemiological assessment of populations affected and changes in the burden of disease. In NSW, data have been successfully collated from NSW sexual health services and are used for this purpose, demonstrating a steady or even small increase in the prevalence of infection in those tested. The main methodological disadvantage of using indicators collected from clinical sites is that they represent high risk populations and thus will never provide populations estimates of prevalence. That being said, prevention programs aim to target those at highest risk.

The central objective of chlamydia prevention programs is to reduce the extent of transmission. Accordingly, incident chlamydia infection rates are a key programmatic indicator as they reflect the rate of transmission and help determine both the need for intervention programs and their effectiveness. But incidence is very difficult to measure in practice. Direct measurement of incidence requires the use of repeat STI testing in the setting of cohort studies, which are not generally incorporated into routine surveillance systems as they are too expensive to be undertaken as ongoing population monitoring initiatives. Prospective cohort studies are complex, and require long and costly follow-up. As such, there has only been one prospective cohort study of chlamydia incidence in heterosexuals ever conducted in Australia.(45)

A number of alternative approaches can be used to provide chlamydia incidence estimates including repeat testing, and mathematical techniques. Both these methods have strengths and weaknesses. The use of repeat-testing data is appealing for estimating chlamydia incidence for several reasons; it includes large sample sizes and high risk populations, who may otherwise not participate in cohorts or other research. In addition, risk behaviour data are routinely recorded. For example, the ACCESS

system will be able to produce chlamydia incidence estimates for MSM and sex workers who undergo frequent screening. However, the method has some weaknesses such as: many young people have low repeat testing rates, selection bias may occur due to changes in the client profile or testing patterns over time and people may seek testing and treatment for infections outside the clinic that is being monitored. Mathematical modelling can also be used to estimate incidence. Mathematical algorithms which compile all biological and epidemiological available data sources and estimate incidence are appealing as they are cheaper, but are dependent on the accuracy of information required to parameterise the equations.

Australia has no formal surveillance system to monitor the syndromes associated with STIs. As described in *Chapter 3*, methods to measure the extent of PID vary considerably and have involved collation of data from primary health care clinics, extraction of data from hospital databases, case-control studies, special surveys, cohorts and data linkages studies. However, most of these assessments are not repeated and therefore do not strictly fit the definition of surveillance. All these methods have strengths and weaknesses. The difficulties associated with measuring PID are described in more detail in *Chapter 3*. From the national hospital data presented in this Chapter it is difficult to interpret what the decreasing trend since 1998/9 mean, as only a subset of the PID cases will be chlamydia related. Also since 2004, hospital admissions due to PID have stabilised.

#### ***Box 1.1: Gaps and Recommendations***

##### ***What was missing?***

1. Population chlamydia prevalence estimates
2. Chlamydia incidence estimates
3. Notification data related to Aboriginal and Torres Strait Islander people

##### ***Recommendations***

1. Explore feasibility of integrating chlamydia testing with existing ongoing behavioural surveys
2. Explore mathematical techniques to estimate incidence
3. Enhance current notification data to capture Aboriginal and Torres Strait Islander status

## **Conclusion**

Young people aged 15-29 years clearly constitute the greatest proportion of the population affected with and at-risk of chlamydial infection. In spite of the increasing numbers of notifications and probable increase in prevalence, a very low proportion of young people get tested for chlamydia in the general practice setting. Less than ideal STI knowledge and increasing sexual risk behaviour in this population increases their susceptibility to acquire chlamydial infections. Lack of prevalence and incidence data hinders our understanding of the impact of prevention programs on chlamydia transmission.

## Chapter 2: Chlamydia infection and sequelae

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### Abstract

**Introduction:** Chlamydial infections may result in long term clinical sequelae, in both men and women. Complications following genital chlamydia infection in women include pelvic inflammatory disease, which may lead to scarring; resulting in infertility, ectopic pregnancy, and chronic pelvic pain. In Australia, chlamydial infections affect predominantly young women of reproductive age; we therefore reviewed the evidence regarding the likelihood of sequelae following infection in women.

**Methods:** A comprehensive review was published by Haggerty et al in 2010. The authors searched the Medline database for studies from 1950 to 2008. We updated this review and classified studies into sequelae following untreated chlamydial infection, treated infection, repeat infections, and sequelae following PID. Given substantial heterogeneity between studies we did not attempt to conduct a meta-analysis but described individual study results. To allow comparisons between studies, where raw data were available, we calculated rates and relative risks.

**Results:** Twenty four studies were included in the review by Haggerty et al. and we added three further relevant studies. All were observational studies although some were conducted within the setting of a trial. The study populations, methods and quality of included studies varied considerably. Few studies included a control group so that risk ratios could be estimated, and few adjusted estimates for appropriate confounders. Seven small studies estimated the rate of PID after an untreated chlamydial infection and their results ranged from 0% after one year to 30% after 7 weeks. Four studies estimated the rate of PID after a treated chlamydial infection; rates ranged from 1.1% to 18.8% over follow-up periods ranging from 1-14 years. Two studies showed that there was an increased risk of ectopic pregnancy after a chlamydial infection (HR=1.26 and HR=1.82) and one showed there was a decreased risk (HR=0.55). In one study, chlamydial infection was significantly associated with hospitalisations for infertility (HR=1.31). Two studies showed the risk of PID increased with more chlamydial infections. After the second and the third chlamydial infection, compared to the first infection, the risk of PID (OR=4.0 and OR=6.4 respectively) and ectopic pregnancy (OR=2.1 and OR=4.5 respectively) increased; and compared to no infections, the risk of ectopic pregnancy increased after one and two or more infections (HR=1.8 and HR=3.4 respectively). Six studies looked at rates of sequelae after PID of any cause. Estimates ranged from: 1.9%-16% of women were subsequently diagnosed with infertility (follow-up period from 1-15 years), 0.6%-9.1% of women were subsequently diagnosed with ectopic pregnancy (follow-up period from 3-10 years approximately) and 16.7%-56% of women were subsequently diagnosed with chronic pelvic pain (follow-up period from 1-15 years).

**Conclusion:** This review shows that there is limited quality evidence to provide robust estimates of the likelihood of PID and other reproductive health sequelae following chlamydial infections. On the balance of published studies it appears that untreated chlamydial infections increase the risk of PID compared to treated chlamydial infection, and treated chlamydial infections increase the risk of PID compared to no infection. Compared to a single infection, repeated chlamydial infections also appear to increase the risk of PID and the risk of ectopic pregnancy. Severe PID of any cause increases the likelihood of subsequent ectopic pregnancy and infertility; however, it is unclear how

**much severe PID is caused by chlamydia. Further studies are warranted to provide better estimates of the magnitude of the risk of long term reproductive and gynaecological sequelae.**

## Introduction

*Chlamydia trachomatis* is the most commonly notified infection in Australia,(56) with 73,543 notifications in 2010(12). Chlamydia causes cervicitis and urethritis in women and urethritis in men; and can cause rectal and pharyngeal infections; it also has the potential to be transmitted in labour, causing pneumonia and eye infections in neonates. Important clinical consequences of genital chlamydial infection may arise from largely asymptomatic infections not being diagnosed and treated quickly; such complications include pelvic inflammatory disease (PID)(4-7), and other gynaecological and reproductive health morbidity, which result from scarring from PID, like infertility, ectopic pregnancy, and chronic pelvic pain.(8-10)

Understanding the relationship between untreated and treated chlamydial infection and these sequelae are essential to inform policy and programmatic responses and also to evaluate the impact of any interventions which aim to prevent chlamydial infection and associated morbidity. However there are many challenges to understanding the relationships between chlamydia infection and sequelae. Firstly, there are problems with measuring the presence of genital chlamydia infections. The majority of women with genital chlamydial infection are asymptomatic. Therefore, the presence of chlamydia is often only detectable through testing. Further, among women who test positive the time of infection cannot be determined, and in a proportion of these women the infection will spontaneously clear. Women who test negative can also become infected subsequent to their test. Secondly, the diagnostic criteria used to identify cases of PID are often inconsistent between studies. Lastly, although chlamydia can cause PID which can then lead to long term sequelae, a proportion of chlamydia infected women develop long term sequelae without having ever had PID.

A recent published review (Haggerty et al) assessed the evidence base relating to the rate of sequelae after *Chlamydia trachomatis* genital infection in women(57). They found large variations in the incidence of PID following chlamydia. They also found many consistencies in evidence surrounding other chlamydia-related sequelae. With this being a fast moving field of research enquiry, we conducted a review of the literature firstly by reviewing all studies included in the review by Haggerty et al(57). We then updated this by conducting a search of literature up to January 2011, as well as including studies that we were aware of as relevant to the question but which had not been covered by the Haggerty review.

## Methods

Haggerty et al (2010) searched the Medline database for studies from 1950 to 2008 using the following two search strategies:

- (*Chlamydia trachomatis*) and (*pelvic inflammatory disease or salpingitis or endometritis or infertility or ectopic pregnancy*)
- (*Pelvic inflammatory disease or salpingitis or endometritis*) and (*infertility or ectopic pregnancy*)

Studies were limited to those involving non-pregnant women only. We summarised the findings of the Haggerty et al (2010) review and included additional studies published in English, up until January 2011.

We focused this Chapter on pelvic inflammatory disease, infertility and ectopic pregnancy, and grouped studies according to whether they examined the following associations:

- Untreated chlamydial infection and PID;

- Treated chlamydial infection and PID;
- Chlamydial infection and ectopic pregnancy and infertility;
- Repeat chlamydial infection and PID, ectopic pregnancy, infertility and pelvic pain;
- PID and ectopic pregnancy, infertility and pelvic pain.

Where relevant, we described studies in categories defined by length of follow-up period, or PID diagnosis method. Also to allow for comparisons between studies, if authors had not estimated effect measures but data was available to do so, we calculated this and note this in the text.

## **Results**

We included 24 studies from the Haggerty review. We added three further relevant studies published between 2002 and 2010.

### ***A. Untreated chlamydial infection and PID***

There were seven studies which examined the relationship between untreated chlamydial infection and PID (Table 2.1; Figure 2.1). (1, 58-63) Studies were conducted between 1980 and 2007, with four conducted before 2000; four were in the US and three in Europe. Studies had varying study populations with four based in STI clinics or hospitals and three in more generalisable populations (university students, attendees of a counselling bureau and attendees of a health service for a job placement). Only one study included women who were symptomatic for chlamydial infection (61) and only two studies included a control or comparison group (1, 62).

The older studies diagnosed chlamydia by culture techniques (58-61); in two, diagnoses were made by Nucleic Acid Amplification Tests (NAAT) (1, 62); and in one diagnosis was by a mixture of NAAT or culture (63). PID was ascertained using clinical criteria in six studies (1, 58-61, 63), one study also included laparoscopic diagnosis (1); and one used self-report (62). The sample sizes ranged from 20 to 115. Three studies were conducted before the need to treat chlamydia was universally accepted (58-59, 62), three conducted their studies by using the window of time between testing and treatment (60-61, 63), and one used stored samples that were tested later (1).

The highest estimate of PID after an untreated chlamydial infection was 30% after 7 weeks and the lowest was 0% after one year. Since the follow-up period after chlamydial infection varied considerably (from an average of 13 days to 12 months), results are shown according to short and long follow up periods. The three studies with short follow-up periods (median time ~14 days) found that the percentage of women subsequently diagnosed with PID ranged from 2%-4.5%. (60-61, 63) The four studies with mid- to long-term follow-up periods (7 weeks to 1 year) found that the percentage of women diagnosed with PID ranged from 0% - 30%. (58-59, 62)

The most recent and likely most generalisable study, published in 2010, reported on findings from the POPI (Prevention Of Pelvic Infection) trial and reported that 9.5% (4.7%-18.3%) of women with untreated chlamydial infection at up to 1 year of follow-up were diagnosed with PID. (1) Compared to a control group of women who had no chlamydia infection diagnosed, women with untreated chlamydial infection were approximately six times more likely to develop PID compared to women without a chlamydial infection (calculated RR=6.5).

**Table 2.1: PID after an untreated chlamydial infection in women**

Author surname, year	Country	Study design	Age (years)	Symptomatic	Setting	Duration of Follow-up	Sample size n	% diagnosed with PID at follow up (95%CI)
<b>Short-term follow-up</b>								
Hook et al, 1994 (60)	US	Prospective cohort, time between testing and treatment	-	No	STI clinics	Median 14 days	93	3.2% (0.8%-8.5%)
Bachman et al, 1999 (61)	US	Retrospective cohort, time between testing and treatment	22 (Median)	Yes	Hospital emergency department and gynaecology service	Between testing & treatment	67	4.5% (1.1%-11.7%)
Geisler et al, 2008 (63)	US	Prospective cohort, time between testing and treatment	21 (Median)	No	STI clinics	Median 13 days	115	2% (0.3%-5.6%)
<b>Mid- and Long-term follow-up</b>								
Stamm et al, 1984 (58)	US	Prospective cohort nested in a gonorrhoea treatment clinical trial	14-47	Yes (Gonococcal infection)	STI clinics	7 weeks	20	30% (13%-53%)
Rahm et al, 1986 (59)	Sweden	Prospective natural history study	Adolescents	No	Community - attendees of counselling bureau	12 weeks	109	3.7% (1.2%-8.6%)
Morre et al, 2002 (62)	Netherlands	Prospective natural history study	18-40	No	Community - attendees of health services prior to a job engagement	1 year	30	0% (0%-9.5%)
Oakeshott et al, 2010 (1)	UK	Prospective cohort nested in chlamydia screening RCT	16-27	No	Community - educational institutes	1 year	74	9.5% (4.7%-18.3%)

RCT=Randomized Controlled Trial, STI=Sexually Transmissible Infection, PID=Pelvic Inflammatory Disease, CI=Confidence Interval

## ***B. Treated chlamydial infection and PID***

In total, we identified four studies which assessed the risk of PID after at least one detected and treated chlamydial infection.(1, 64-66) Two studies were conducted in the US and two in Europe. Three of the four were community based studies, with women recruited from the general population.(1, 64-65) Coded hospital diagnoses were used to identify PID in two studies whereas in the other two the diagnosis(64-65) was based on clinical investigations along with coded hospital diagnosis (biopsy in one(66) and laparoscopy findings(1) in the other). The four studies were much larger than those on untreated chlamydia infections, with sample sizes of 63 to 2,965. They were also more current with all conducted after 1995 (Table 2.2; Figure 2.1).

From the four studies the percentage of women diagnosed with PID ranged from 1.1% to 18.8% over follow-up periods ranging from 1-14 years. In the retrospective analysis of registry data by Low et al. PID hospitalisations occurred in 5.6% of women who had ever tested positive, compared to 4.0% in women who tested negative and 2.9% in women who were never tested.(65) In the study of army recruits, seven women out of 643 (1.1%) who tested positive for chlamydia were hospitalized for PID - a rate of 7.1 per 1000 person years.(64) The other two studies focused on the percentage of women diagnosed with PID on the basis of clinical diagnosis. Findings from the POPI trial showed that one out of 63 women diagnosed with chlamydia at baseline developed PID (1.6%) over the 12 month follow-up period.(1) In the other prospective cohort study, high-risk women were retested for chlamydia every 6-12 months and 23 of 122 women (18.8%) with chlamydial infection were diagnosed with PID; this compared to 7% of women who did not have chlamydial or gonorrhoeal infections.(66)

Only one of the four studies provided a confounder adjusted risk estimate of PID following a treated chlamydial infection (HR=1.27, 95%CI: 1.04-1.55) (65). For the remaining three studies, based on the data available, we were able to calculate the crude relative risk of developing PID after a treated chlamydial infection and it ranged from 1.27-2.69.

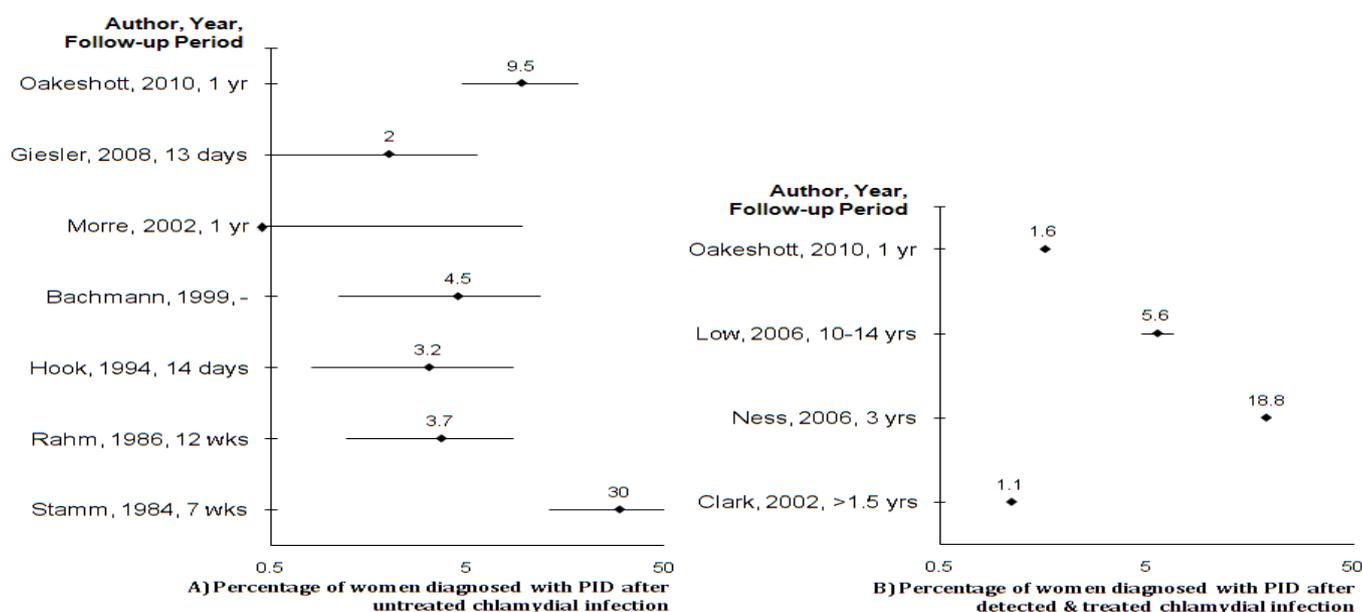
**Table 2.2: PID after detected and treated chlamydial infection in women**

Author surname, year	Country	Study design	Age (years)	Symptomatic	Diagnosis of PID	Setting	Duration of Follow-up	Sample size n	% diagnosed with PID at follow up (95%CI)
Clark et al, 2002 (64)	US	Prospective cohort study	80% <25 years	No	Hospital codes	Community - army recruitment	>1.5 years	643	1.1%*
Ness et al, 2006 (66)	US	Prospective cohort study	13-36	No	Hospital codes and Clinical investigations	Clinics (Family planning, University, Gynaecology, STI)	Median 3 years	122	18.8%
Low et al, 2006 (65)	Sweden	Retrospective population based cohort study	15-24	No	Hospital codes	Community - whole county	10-14 years	2,965	5.6% (4.7% - 6.7%)
Oakeshott et al, 2010 (1)	UK	Prospective cohort nested in chlamydia screening RCT	16-27	No	Hospital codes and Clinical investigations	Community - educational institutes	1 year	63	1.6%

\* Calculated from data available in the paper

RCT=Randomized Controlled Trial, STI=Sexually Transmissible Infection, PID=Pelvic Inflammatory Disease, CI=Confidence Interval

**Figure 2.1: Percentage of women diagnosed with PID after A) an untreated B) detected and treated chlamydial infection**



### C. Chlamydial infection and ectopic pregnancy and infertility

Three studies were included which assessed the risk of ectopic pregnancy and infertility after a chlamydial infection. (65, 67-68) All three studies were large retrospective cohort studies conducted using whole population record linkage (Table 2.3; Figure 2.2). All studies were conducted in Europe, and all had a long follow-up period (>10 years) and a large sample size (>13,000). It was assumed that the women who tested positive for chlamydia in the studies were treated for it. None of the studies reported on chronic pelvic pain as an outcome of chlamydial infection, all three reported on ectopic pregnancy and only one reported on infertility (65).

The estimated hazard ratios (HR) of having an ectopic pregnancy associated with chlamydial infection were inconsistent across the three studies: in one study there was a reduction in risk

(HR=0.55, 95% CI:0.31-0.96)(67), and in the other two an increased risk [HR=1.26 (95%CI:0.94-1.67)(65) and HR=1.82 (95%CI:1.27-2.60)(68)] was reported. In one study, chlamydial infection was significantly associated with hospitalisations for infertility (HR=1.31, 95% CI:1.09-1.57)(65).

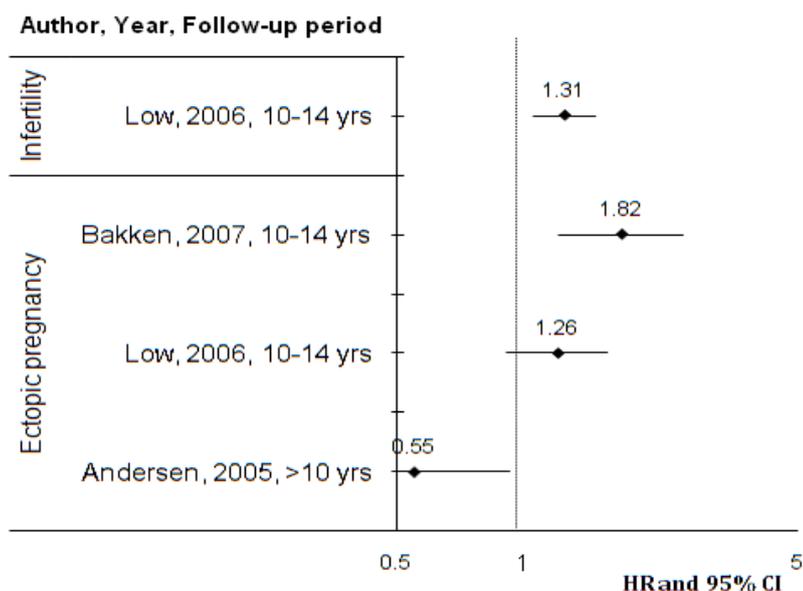
The included studies did not control for confounders completely: one only controlled for maternal age(67); one only for parity(68); and one for test status, education level, housing, income, births and census year(65).

**Table 2.3: Ectopic pregnancy and infertility after chlamydial infection among women**

Author surname, year	Country	Study design	Age (years)	Setting	Duration of Follow-up	Sample size n	Outcome - HR (95% CI)	
							Ectopic pregnancy	Infertility
Andersen et al, 2005 (67)	Denmark	Retrospective cohort study	15-24	Community - whole county	>10 years	13,693	0.55 (0.31-0.96)	-
Low et al, 2006 (65)	Sweden	Retrospective population based cohort study	<43	Community - whole county	10-14 years	43,715	1.26 (0.94-1.67)	1.31 (1.09 to 1.57)
Bakken et al, 2007 (68)	Norway	Retrospective cohort study	20-33	Community - whole county	10-14 years	20,762	1.82 (1.27-2.60)	-

HR=Hazard Ratio, CI=Confidence Interval

**Figure 2.2: Risk of ectopic pregnancy and infertility after chlamydial infection**



#### **D. Repeat chlamydial infection and PID, ectopic pregnancy, infertility and pelvic pain**

Three cohort studies examined the risk of PID and long term reproductive and gynaecological sequelae after repeated chlamydial infections(68-70); another cohort study assessed the risk of sequelae after repeat PID episodes(71) (Table 2.4; Figure 2.3). Two of these studies were community based whereas the other two were based on clinical populations. Studies were conducted in the US, Europe and Africa with a variable sample size (ranging from 302 - 20,762) and follow-up period (ranging from 17.6 months to 14 years).

Three studies measured rates of PID, ectopic pregnancy and infertility after repeated chlamydial infections(68-70). In the study by Kimani et al (1996) both single and repeated infection was found to be a risk factor for PID; however, the risk of PID among women with one chlamydial infection was

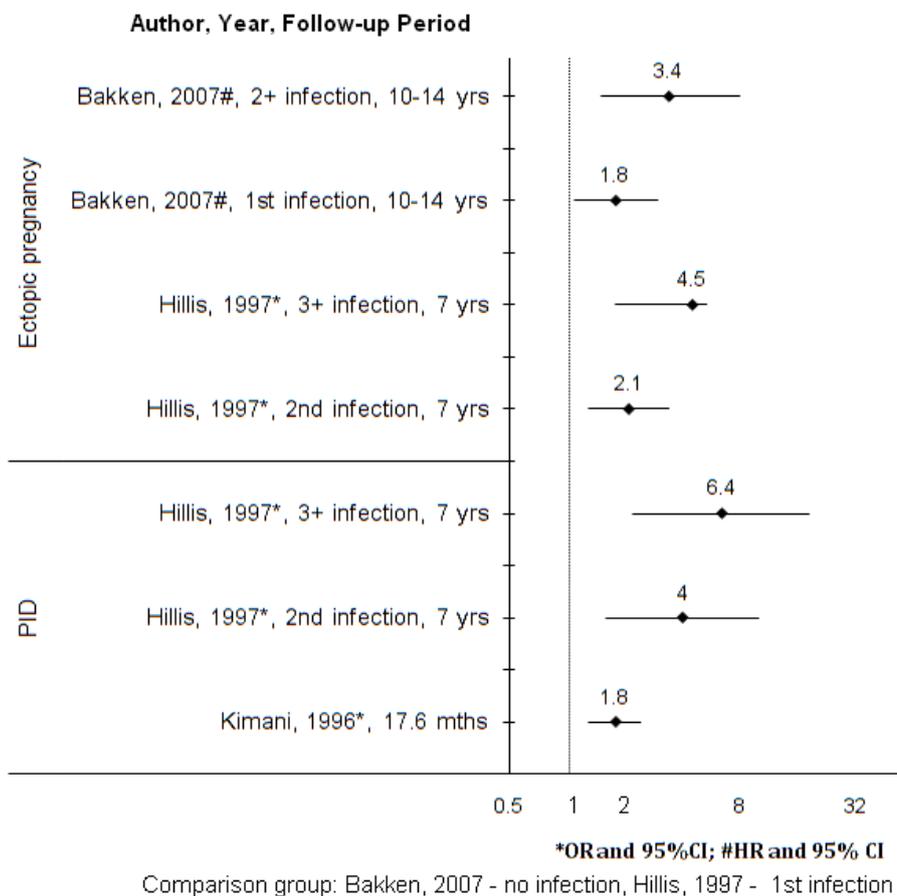
similar to women with repeated infections ( $p=0.15$ ). Hillis et al (1997) found that compared to the first infection, the risk of PID increased after the second and the third chlamydial infection (OR=4.0, 95%CI: 1.6-9.9 and OR=6.4, 95%CI:2.2-18.4 respectively).

The study by Bakken et al (2007) demonstrated that compared to women with no infections, women were at highest risk of having an ectopic pregnancy after two or more infections (adjusted HR=3.4, 95%CI:1.5-8.0), followed by one infection (adjusted HR=1.8, 95%CI:1.1-3.0). Hillis et al, showed that compared to a single infection, women with three or more infections were at highest risk of ectopic pregnancy (OR=4.5, 95%CI:1.8-5.3) followed by two chlamydial infections (OR=2.1, 95%CI:1.8-5.3).

Westrom et al (1992) showed that the risk of infertility increased after every PID episode (8% after the first, 19.5% after the second and 40% after the third episode).

Only two studies controlled for confounders. However, Hillis et al, only adjusted for gonococcal infection and country of birth without adjusting for age, race and repeat tests; whereas Bakken et al only adjusted for parity and age at first test.

**Figure 2.3: Outcome of repeat chlamydial infections**



**Table 2.4: PID and sequelae after repeat chlamydial infection**

Author surname, year	Country	Study design	Age (years)	Setting	Duration of Follow-up	Sample size n	Reference	Outcome (95% CI)		
								PID	Ectopic pregnancy	Infertility
Westrom et al, 1992 (71)	Sweden	Prospective cohort study	10-35	Hospital	13,400 women years	1,732	PID episodes	-	-	After 1 <sup>st</sup> =8% After 2 <sup>nd</sup> =19.5% After 3 <sup>rd</sup> =40%
Kimani et al, 1996 (69)	Kenya	Prospective cohort study	20-49	Treatment clinic	17.6 ± 11.1 months	302	Repeat chlamydial infection	OR=1.8 (1.3-2.4) p=0.0004	-	-
Hillis et al, 1997 (70)	US	Retrospective cohort study	10-44	Community - whole state	7 years	11,000	1 chlamydial infection	2 infections OR=4.0 (1.6-9.9) 3+ infections OR=6.4 (2.2-18.4)	2 infections OR=2.1 (1.3-3.4) 3+ infections OR=4.5 (1.8-5.3)	-
Bakken et al, 2007 (68)	Norway	Retrospective cohort study	20-33	Community - whole county	10-14 years	20,762	No chlamydial infection	-	1 infection aHR=1.8 (1.1-3.0) 2+ infection aHR=3.4 (1.5-8.0)	-

PID=Pelvic Inflammatory Disease, CI=Confidence Interval, OR=Odd's Ratio, aHR=Adjusted Hazard Ratio

### ***E. PID and ectopic pregnancy, infertility and pelvic pain***

A total of 12 studies were included which measured the risk of reproductive and gynaecological sequelae after PID. Six studies measured the risk of sequelae after PID of any cause(71-76) and six after chlamydia associated PID(9, 77-81).

***Sequelae following PID of any cause:*** Five of the six studies were conducted in Europe and the remaining one in the US. Five studies included data only from women hospitalized for PID and the remaining study included data from outpatient clinics. Women with PID were identified by laparoscopy in three studies(71-73), clinical diagnosis in two studies(75-76) and discharge diagnosis with surgical confirmation in one study(74). Only two studies out of six had a control group(71, 74). The studies varied in sample size, which ranged from 22 to 1,732, and follow-up time, which ranged from 1 year to 15 years (Table 2.5).

Five studies reported on the percentage of women diagnosed with infertility, three on ectopic pregnancy and three on chronic pelvic pain after an episode of PID. The percentage of women diagnosed with infertility ranged from 1.9%-16% in women diagnosed with PID (follow-up period from 1-15 years)(71, 73-76). Ectopic pregnancy in women with PID ranged from 0.6%-9.1% (follow-up period from 3-10 years approximately)(71, 75-76) and 16.7%-56% of women were diagnosed with chronic pelvic pain (follow-up period from 1-15 years)(73-74, 76).

One study assessed the association between the severity of PID and the probability of achieving a live birth, while accounting for subsequent episodes of PID.(72) The study found that after 12 years, 90% of women with mild, 82% of women with moderate and only 57% of women with severe PID could achieve a live birth. Women who had severe PID with subsequent diagnoses were 8 times more likely not to achieve live birth compared to women with a single mild episode of PID (RR=8.1; 95%CI:3.0-22.2).

Only two studies had a control group.(71, 74) Based on data available in these two studies, we calculated the relative risk of sequelae after PID. These studies suggest that PID of any cause increases risk in later life of infertility (RR=5, 95%CI: 2-18) and ectopic pregnancy (RR=9, 95%CI: 1-69 and RR=10, 95%CI: 1-70).

***Sequelae following chlamydia associated PID:*** Four of the six studies included were conducted in the US, one in Canada and one in Europe. The diagnosis of PID was clinical in three out of six studies(9, 78-79), laparoscopic in one study(77), and histological in two studies(80-81). Only two studies included a control group. The sample size of the studies varied from 50-780 and the follow-up period from 5 months to 14 years (Table 2.6; Figure 2.4).

Four studies reported on the risk of infertility after chlamydia related PID; two reported on chronic pelvic pain; one on recurrent PID and two on pregnancy as an outcome after PID. The four studies which reported on the risk of infertility, showed mixed results. Two studies showed that chlamydia associated PID was not significantly associated with elevated infertility compared to women without PID (OR=0.9, 95%CI:0.5-1.7(79) and OR=1.0, 95%CI:0.6-1.6(80)). In one of these studies, although there was no overall difference in infertility rates between chlamydia related and non-chlamydia related PID; chlamydial infection was found to be associated with delayed care seeking which in turn was found to be associated with impaired fertility(79). Another study reported that chlamydia related PID was significantly associated with developing infertility (RR=2.5, 95%CI:1.0-6.2)(78). In the fourth study, 7 out of 13 women with non-gonococcal PID had an adverse fertility outcome; and among them, women with evidence of past or current chlamydial infection had the highest infertility rate (3 out of 7 women)(77).

Two studies reported that chlamydia related PID was not significantly associated with an increase in chronic pelvic pain compared to women without PID (OR=0.6, 95%CI:0.4-0.9(80) and OR=0.69, 95%CI:0.49-1.1(81)). One study reported that chlamydia related PID was not associated with recurrent PID compared to women without PID (OR=0.6, 95%CI:0.4-0.9)(80).

Two studies reported on pregnancy as an outcome after chlamydia related PID. One reported that PID was not associated with reduced pregnancy compared to women without PID (OR=0.8, 95%CI:0.6-1.2)(80) and the other reported that compared to women with the lowest anti-chlamydia elementary bodies, women with the highest had lower pregnancy rates (HR=0.47, 95%CI:0.3-0.8).

**Table 2.5: Sequelae after PID (of any cause)**

Author surname, year	Country	Study design	Age (years)	Setting	Duration of Follow-up	Sample size n	% diagnosed		
							Infertility	Ectopic Pregnancy	Chronic pelvic pain
Westrom et al, 1992 (71)	Sweden	Prospective Cohort study	10-35	Hospital	13,400 women years	1,732	16%	9.1%	-
Stagey et al, 1992 (73)	UK	Prospective study	-	Hospital	1-3 years	22	33%	-	56%
Buchan et al, 1993 (74)	UK	Retrospective cohort study	-	Hospital	15 years	1,200	1.9%	-	16.7%
Lepine et al, 1998 (72)	Sweden	Prospective cohort study	15-35	Hospital	12 years	1,288	-	-	-
Ness et al, 2002 (76)	US	RCT	14-37	Emergency, gynaecology and STI clinics	35 months	831	18%	0.6%	29%
Heinonen & Leinonen, 2003 (75)	Finland	Prospective cohort study	16-50	Hospital	125 ± 44 months	39	11%*	1.8% <sup>#</sup>	-

\* Calculated from data available in the paper

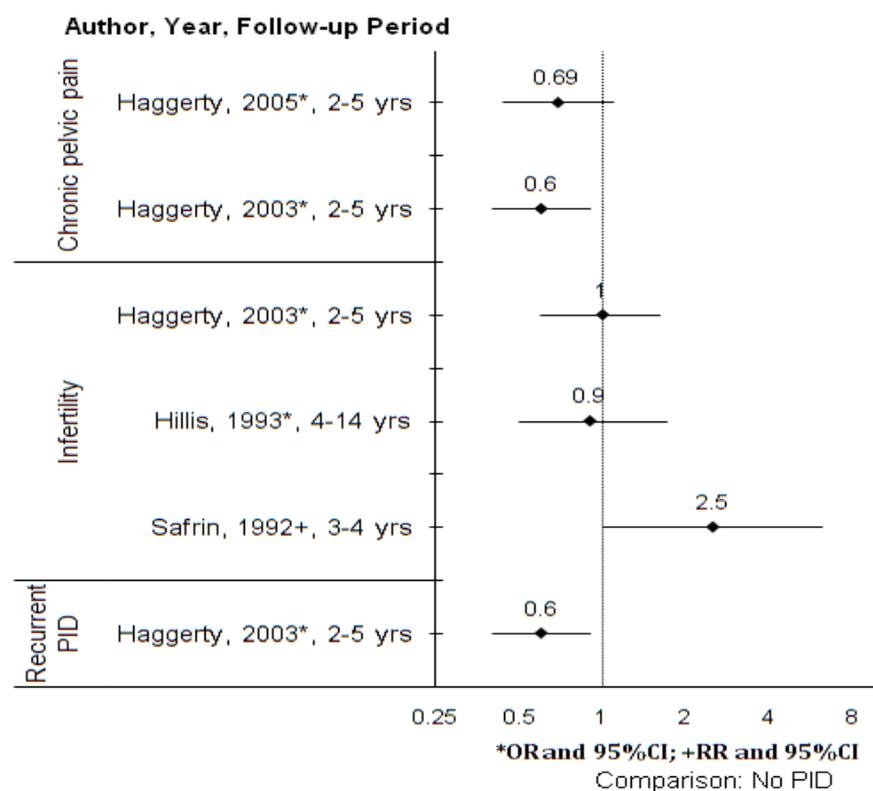
<sup>#</sup> Calculated from the number of ectopic pregnancies out of total pregnancies

RCT=Randomized Controlled Trial, STI=Sexually Transmissible Infection

**Table 2.6: Sequelae after chlamydia associated PID**

Author surname, year	Country	Study design	Age (years)	Setting	Duration of Follow-up	Sample size n	Outcome (95% CI)			
							Recurrent PID	Pregnancy	Infertility	Chronic pelvic pain
Brunham et al, 1988 (77)	Canada	RCT	16-34	Emergency, outpatient or women's clinic	5-7 months	50	-	-	3 of 7 infertile women had chlamydia	-
Safrin et al, 1992 (78)	US	Retrospective cohort study	-	Hospital	3-4 years	51	-	-	RR=2.5 (1.0-6.2)	-
Hillis et al, 1993 (79)	Sweden	Case-control study	-	Hospital	4-14 years	443	-	-	OR=0.9 (0.5-1.7)	-
Haggerty et al, 2003 (80)	US	Prospective cohort study	14-37	Emergency, gynaecology and STI clinics	2-5 years	614	OR=0.6 (0.4-0.9)	OR=0.8 (0.6-1.2)	OR=1.0 (0.6-1.6)	OR=0.6 (0.4-0.9)
Haggerty et al, 2005 (81)	US	Prospective cohort study	14-37	Emergency, gynaecology and STI clinics	2-5 years	780	-	-	-	OR=0.69 (0.44-1.10)
Ness et al, 2008 (9)	US	Prospective cohort study	14-37	Emergency, gynaecology and STI clinics	84 months	443	-	HR=0.47 (0.3-0.8)	-	-

RCT=Randomized Controlled Trial, STI=Sexually Transmissible Infection, PID=Pelvic Inflammatory Disease, CI=Confidence Interval, OR=Odd's Ratio, HR=Hazard Ratio

**Figure 2.4: Outcome of chlamydia-associated PID**

## Discussion

Our systematic review assessed the evidence regarding the relationship between chlamydial infection and related morbidity. From the included studies, it is clear that chlamydial infection leads to gynaecological and reproductive pathology but there is a great deal of uncertainty regarding the size of the risks. From the review we found that untreated chlamydial infections increase the risk of PID compared to treated chlamydial infection by about 6 fold, treated chlamydial infections increase

the risk of PID compared to no infection by about 2 fold, and repeated chlamydial infections increase the risk of PID compared to a single infection by about 4 fold. Severe PID of any cause increases the likelihood of ectopic pregnancy by about 10 fold and infertility by about 5 fold; however it is not certain how much severe PID is caused by chlamydia. The evidence for a direct relationship between chlamydial infection and ectopic pregnancy is equivocal and for chlamydia and infertility one study suggests a small increase in risk.

### Methodological aspects of included studies

Overall studies included in the review had a number of limitations that lend uncertainty to their results. Regarding their internal validity, firstly, most studies did not include control groups or the control groups were not necessarily appropriate. Secondly, some studies only used hospitalization data and therefore may have had inadequate ascertainment of the exposure or outcomes. Thirdly, outcomes were ascertained inconsistently with different diagnostic guidelines used across the studies particularly for PID. Fourthly, few studies accounted for potential confounders such as age or other sexually transmitted infections. Lastly, many studies involved small sample size leading to imprecise estimates of effect. There were also issues with the external validity of the studies, with many clinic-based studies being less generalisable; chlamydia was diagnosed by culture in the older studies and by NAAT in the later studies; and no study was conducted in Australia. Also studies had variable follow-up period making comparisons difficult.

### Does untreated chlamydia increase the risk of PID?

Results from these studies were inconsistent. First, the follow-up time was highly variable in the studies. If we extrapolated rates of PID from studies with shorter intervals to allow consistent comparisons to be made, we found unrealistic estimates. For example, in the study by Stamm et al (1984), (58) assuming a constant rate of 30% over a 7 week period, around 95% patients of untreated chlamydial infection will develop PID in one year which is implausibly high. The studies do suggest that rates of PID may not be constant over time and that a disproportionate amount of PID may occur early in the course of infection. This could be due to host factors, immune responses and difference in organism load(57). Second, some studies included symptomatic infections. This may result in higher rates of PID compared to asymptomatic infections. Third, some studies included only high risk women (women attending STI clinics versus women recruited from the community) who are probably more at risk of re-infections and co-infections, and thus at higher risk of developing PID.

Overall the studies suggest that the risk of PID increases after a chlamydial infection. Using data from the control arm of the most robust and generalisable study, the POPI trial, we estimated that the relative risk of PID associated with untreated chlamydial infection compared to no chlamydia infection was 6.5. However this calculation only takes account of the single chlamydia test that was performed as the trial intervention. Evidence on the proportion of women in the trial who had a positive chlamydia test at the time of diagnosis of PID suggest that the relative risks may be as high as 25.(1) Based on this study, and data on the prevalence of chlamydia infection in young women in the general population(55); we estimated the proportion of PID in young Australian women due to chlamydia could lie between 17%-47%.

### Does treated chlamydia increase the risk of PID?

The studies examining this question had reasonable sample sizes and their results were consistent, although limited adjustment was made for confounders. The studies included in this review showed PID rates of 1.1% to 18.8% over follow periods of 1-14 years after treated chlamydial infection. Again,

taking data from the POPI trial, 1.6% of women treated for chlamydia developed PID over 12 months, compared to 9.5% of women who were untreated. This data suggests that treating chlamydia infection reduces a woman's risk of PID. The other studies also suggest that compared to women without chlamydia infection, women with treated chlamydia infections still have higher risks of sequelae. This may occur because chlamydia can persist asymptotically for up to five years after infection,(82) so most infections in a previously unscreened population would already have been present for some time and might already have caused tubal damage before testing and treatment takes place.

#### Does chlamydia directly increase the risk of ectopic pregnancy and infertility?

Many women with infertility or ectopic pregnancy do not have a history of PID, thus it is also important to understand the direct association between chlamydia and long term sequelae. Studies which reported on ectopic pregnancies as an outcome of chlamydial infection had discordant results with two showing that women might have a lower or higher risk of ectopic pregnancy after a chlamydial infection, compared to women without a chlamydial infection and the third showing the opposite that is a decreased risk.

Infertility is a potentially serious and costly complication of a chlamydial infection and is difficult to measure.(83) Only one study was included in our review which showed a positive relationship between chlamydial infection and infertility. These findings are in contrast with a review by Wallace et al in 2008,(84) which also only included one study (case-control) but found no association between chlamydia and pregnancy rates. The study however had severe methodological limitations. These discrepancies highlight the need for further large and robust studies in this field.

#### Do repeated chlamydial infections increase the risk of PID and other sequelae?

All included studies suggested that the risk of sequelae increased after repeated chlamydial infections. Potentially, every chlamydial infection can cause damage to the upper genital tract leading to sequelae and with every additional infection the damage can increase. The most generalisable studies included were by Hillis et al (1997) and Bakken et al (2007) as they were both population based. They reported that the risk of PID and ectopic pregnancy increases with increasing numbers of chlamydial infections. However both studies also had limitations as they did not account for the number of tests done on women and had inadequate control of confounders. We can conclude that the evidence suggests increasing numbers of chlamydia infections increase the risk of PID.

#### Does PID increase the risk of infertility and other sequelae?

Interpreting studies examining the risk of reproductive sequelae following PID was difficult due to the fact that most studies reviewed focused on women with PID not specifically caused by chlamydia. As a number of factors and organisms cause PID; the relevance of these findings to the effect of chlamydia on the long term sequelae, ectopic pregnancy, infertility and pelvic pain, is limited. In addition, since these studies were based on women hospitalised with PID, they represent the incidence of sequelae following severe PID only. As most PID is not treated in hospitals(85) the overall population incidence of sequelae following PID could be very different from that derived from the published studies. In summary, these studies suggest that severe PID of any cause increases the risk of sequelae – infertility and ectopic pregnancy – later in life. In addition, Hillis et al (1993) report that PID treated early is less likely to lead to infertility compared to PID treated late.(79)

### Implications for chlamydia control and evaluation in Australia

Taking into account the 3.7% prevalence of chlamydia in young women in Australia(55), and a relative risk of PID of 6.5-25 comparing women with untreated chlamydia to women with no chlamydia, as estimated from the POPI trial(1), we estimated that 17%-47% PID in Australian women is attributable to a chlamydial infection. Thus, a proportion of PID cases should be avoidable by diagnosing and treating chlamydial infection early.

#### ***Box 3.1: Key messages***

- There is limited high quality evidence regarding the association between chlamydia infection and reproductive sequelae to provide robust risk estimates.
- From one study, we estimated that compared to women with no chlamydial infection, untreated chlamydial infections increased the risk of PID, by 6.5-25 fold and based on this study as well as other data we calculated the proportion of PID in young Australian women related to chlamydial infection may range between 17% and 47%.
- From four studies, treated chlamydial infections were found to increase the risk of PID, compared to no infection, by between 25 to 150%.
- From one study, compared to a single infection, repeated chlamydial infections were found to increase the risk of PID by about 4-6 fold.
- Severe PID of any cause increases the likelihood of ectopic pregnancy and infertility; however it is not certain how much severe PID is caused by chlamydial infection.
- There is conflicting evidence regarding the relationship between chlamydial infection and ectopic pregnancy. One study suggests the risk of infertility after chlamydial infection may be about 30% greater.

### **Conclusion**

In conclusion, there is evidence to show that chlamydial infection leads to PID and directly and indirectly to other sequelae like ectopic pregnancy and infertility. However, further studies are warranted to provide better estimates of the risk of long term reproductive and gynaecological sequelae.

## Chapter 3: Strategies to improve adherence to diagnosis and management guidelines for pelvic inflammatory disease

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### Abstract

**Introduction:** Timely diagnosis and treatment of pelvic inflammatory disease is important to prevent long term reproductive sequelae but evidence suggests poor adherence to established guidelines for diagnosis and management. Therefore we sought to systematically review the literature for studies describing strategies to improve the adherence to diagnosis and management guidelines for pelvic inflammatory disease (PID).

**Methods:** We searched the electronic databases MEDLINE, EMBASE, Cochrane Controlled Trials Register using the broad search terms, 'pelvic inflammatory disease', 'PID' 'salpingitis', 'adnexitis' AND 'diagnosis', 'management'. We also reviewed reference lists of review articles. All studies with a comparison or control group were considered for inclusion. Data from individual studies were reported but due to differences in study types no meta-analysis was conducted.

**Results:** Three studies met the inclusion criteria; two randomized controlled trials and an interrupted time-series. An abbreviated summary of PID treatment provided to practitioners was found to improve the management but not the diagnosis of PID in hypothetical case scenarios; a video on PID self-care administered to patients was not found to improve patient compliance with antibiotics and follow-up. The interrupted time-series found that following a multi-faceted intervention involving a practice protocol, provision of 14 days of antibiotics on-site, written instructions for patients and active follow-up, a greater proportion of patients received the recommended antibiotics (62% versus 91%) and attended for follow-up within 72 hours (10% versus 43%).

**Conclusion:** There is limited research on strategies to improve practitioner and patient adherence to PID diagnosis and management guidelines. Strategies making the management of PID more convenient such as summary guidelines and provision of treatment on-site appear to lead to better adherence.

## Introduction

Pelvic inflammatory disease (PID) is defined as inflammation of the female upper reproductive tract due to an infectious cause. It can occur as a consequence of a sexually transmitted infection, follow a gynaecological procedure, occur post-partum or rarely, result from haematological spread. In young women the most common causative organisms include the sexually transmitted infections *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.(86-89) Other organisms found to be associated with the development of PID include *Mycoplasma genitalium*, and anaerobic vaginal bacteria.(90)

Clinically PID has a wide spectrum of presenting complaints from a mild disease with non-specific lower abdominal discomfort to severe and florid sepsis with an acute abdomen. This reflects the fact that inflammation may involve one or many of the upper reproductive tract organs including the cervix, endometrium, fallopian tubes, ovaries, the peritoneum and the liver. PID may lead to scarring of the fallopian tubes resulting in infertility, ectopic pregnancy and chronic pelvic pain.(91) Timely treatment has been shown to reduce these complications.(87) Therefore the diagnosis and initiation of appropriate management are important for longer term reproductive health.

### Diagnosis of PID

Due to the broad range of clinical presentations, PID, particularly mild to moderate disease, is often difficult to diagnose. The symptoms and signs are often non-specific, and there is no gold standard which confirms the diagnosis. Symptoms include pelvic pain, fever, vaginal discharge and abnormal vaginal bleeding. Signs include lower abdominal tenderness, cervical motion tenderness, bilateral adnexal tenderness and occasionally a pelvic mass. Laparoscopy has been shown to be highly specific in diagnosing PID but it is invasive and costly in women with mild to moderate symptoms of disease. Furthermore, studies in women with a clinical diagnosis of PID comparing laparoscopy to histopathological findings showed laparoscopy had low sensitivity.(92) To assist in diagnosis, many studies have attempted to ascertain the predictive value of various components of the patient history, clinical signs, laboratory investigations and medical imaging modalities, but with differing 'gold standards', the results have been inconclusive.(92-94) Therefore current Australian, and other international clinical guidelines, recommend that practitioners have a high index of suspicion for diagnosis of PID and a low threshold for empirical treatment.

### Epidemiology of PID

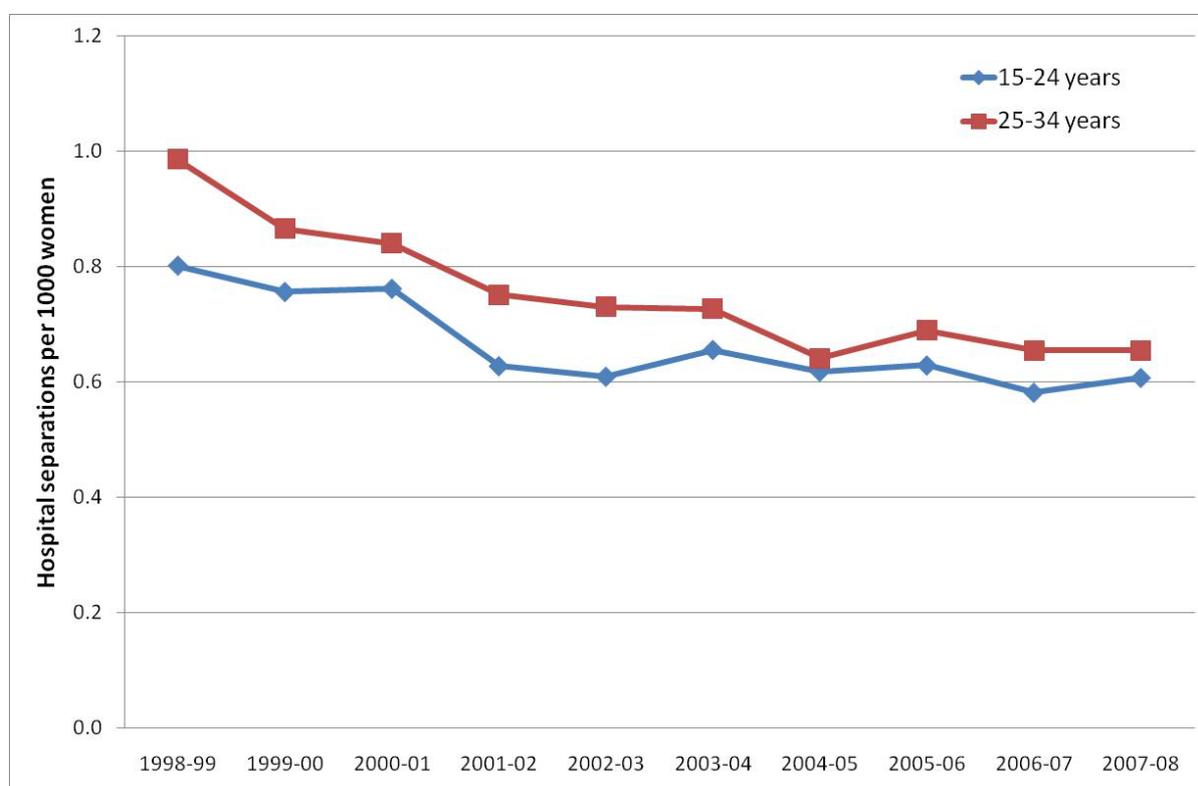
Due to the difficulty with diagnosis, reliable population-based data on the incidence of PID is limited and estimates depend on the study population and case definition. In NSW, routinely collected hospital admission data were examined for trends in PID between 1992 and 2001.(95) Hospitalisation for PID was defined as having an International Classification of Disease (ICD) code in the main diagnosis field for 'salpingitis and oophoritis' or 'acute inflammatory diseases of the uterus' or 'parametritis and pelvic cellulitis' or 'inflammatory disease of the ovary, fallopian tube, pelvic cellular tissue and peritoneum'<sup>3</sup>. Based on this definition, over the 10 year period, in women aged between 15 to 34 years, PID hospitalisations fell from 165 per 100,000 to 64 per 100,000 or a decrease of more than 60%.(95) Another Australian study extrapolated data from a random sample of Australian general practices included in the Bettering the Evaluation and Care of Health (BEACH Study) where diagnoses were coded according to the International Classification of Primary Care.(96) Between 1998 and 2002, general practitioner encounters for PID in women aged between 15 to 34 years decreased from an estimated 39.3 per 10,000 female-patient encounters in 1999–

<sup>3</sup> ICD-10 codes included: N70.0, N70.1, N70.9, N71.0, N71.1, N71.9, N73.0, N73.1, N73.2, N73.8, N73.9, N74.4

2000 to 19.4 per 10,000 in 2001–2002.(96) In addition, substantially more PID presentations were seen in general practice than in hospital.

More recent data on PID hospitalisations was publically available from the Australian Institute of Health and Welfare.(97) Using the same definitions for PID as the study conducted on NSW hospital separations between 1992 to 2001(85), but including the ICD-10 code A56.1 (chlamydial infection of pelviperitoneum and other genitourinary organs in women) and Australian census population estimates,(27) annual rates of hospital separations for PID from years 1998/99 to 2007/08 have continued to fall but at much more gradual rates (see Figure 3.1); in 15 to 24 year old women rates decreased from 0.80 to 0.61 per 1,000 women and in 25 to 34 year olds from 0.99 to 0.65. During this same time period chlamydia notifications(98) and testing rates, particularly in young women have increased substantially.(99) In developed countries, it is estimated that chlamydia may be responsible for about 30% of PID.(87) Therefore it has been suggested that some of the observed decrease in PID hospitalisations may reflect increased screening and treatment of chlamydia.(100)

**Figure 3.1: Hospital separations for PID<sup>i</sup> in Australia per 1,000 women from 1998/99 to 2007/08**



### Management of PID

Currently the diagnosis and management of PID in Australia is guided by the 2008 National Management Guidelines for Sexually Transmissible Infections.(86) These guidelines are similar to international guidelines including the US Centers for Disease Control (CDC) Sexually Transmitted Diseases Treatment Guidelines 2006,(101) and the British Association for Sexual Health and HIV Guidelines for the Management of PID(102) which are based on systematic reviews of the evidence.(103) All guidelines outline the symptoms and signs, appropriate diagnostic tests, and empirical broad-spectrum antibiotics that are available and appropriate, given local considerations regarding antibiotic resistance. The guidelines also offer advice on outpatient or inpatient treatment, contact tracing of sexual partners, and appropriate follow-up of patients (within 48 to 72 hours) to assess the response to treatment. Post-partum and post-procedural PID is treated differently from PID thought to be sexually acquired due to the different organisms presumed to be responsible.

Research suggests that adherence to PID management guidelines by practitioners and patients is poor, although NSW and Australian data are limited. In the US, studies that reviewed emergency department medical records found that less than half of patients seen with a diagnosis of PID had been prescribed antibiotics according to the CDC guidelines.(104) In the UK, audits of genitourinary departments (equivalent to Australian sexual health clinics) suggest reasonable adherence to British clinical practice guidelines.(105) However a study of over 200 GPs who were surveyed regarding their diagnosis and management of PID found that less than 50% were able to name two symptoms and two signs of PID, and less than 50% were able to correctly name an antibiotic regimen.(106)

In Australia, a study of specialist physicians in an urban walk-in sexual health clinic where patients could not choose their doctor, found that among the 23 doctors in the practice, the number of PID diagnoses made between doctors varied substantially compared to the number of diagnoses of genital warts. The authors of the report suggested the variability may have been attributable to under diagnosis of PID by some physicians.(107) In an audit based in another sexual health clinic, the authors concluded that PID may have been over-diagnosed, particularly in women who were sex workers.(108) Furthermore, an audit of medical records of women presenting with symptoms and signs of PID in remote Indigenous communities in Central Australia found that while symptoms and signs of PID were commonly recorded, the majority of women were not presumptively diagnosed with PID, nor managed in accordance with the local guidelines for PID.(109)

Given there are current evidence-based clinical guidelines for the diagnosis and management of PID, but substantial data suggesting poor adherence to these guidelines, this review aims to examine what strategies may improve adherence by practitioners and patients to PID diagnosis and management guidelines.

## **Aim**

To systematically review strategies that may improve the adherence of practitioners and patients to diagnosis and management guidelines for PID.

## **Methods**

Inclusion criteria: All studies that examined the effect of an intervention to improve adherence to diagnosis or management guidelines for PID. Only studies that had a control or comparison group were included.

Search Strategy: MEDLINE, EMBASE, Cochrane Register of Controlled Trials were searched from the year 2000 onwards. We also searched the reference lists of review articles. Search terms included 'pelvic inflammatory disease', 'salpingitis', 'adnexitis' and 'diagnosis' or 'management'. Studies were limited to the English language and humans. Titles and abstracts were reviewed and the full text examined if necessary.

Data extraction: As the nature of studies included in this review varied substantially, no attempt was made to combine the data in a meta-analysis. Rather, the studies are reviewed individually and their application to PID diagnosis and management in NSW is discussed.

## **Results**

After excluding duplicates, there were 1650 titles identified from the electronic databases and of these, 147 abstracts were reviewed. Fourteen full text articles were obtained and of these, three studies met the inclusion criteria and are outlined in Table 3.1.(110-112) The studies include a variety

of interventions aimed at the patient, the practitioner, or both. Two studies were randomised controlled trials (RCTs) and one was an interrupted time series study.

All of the studies included were conducted in the US between 2001 and 2008 and were aimed at paediatric and adolescent populations, or practitioners caring for these populations. Studies were based predominantly in hospital and outpatient facilities; one was based at a single hospital, the other two involved multiple centres. For the studies involving interventions with patients, the populations were young (mean age 16 or 17 years) and predominantly Black Americans, while for studies involving practitioners, they were practicing US paediatric emergency physicians.

**Table 3.1: Studies to improve adherence to diagnosis and management guidelines for PID**

Study ID	Study type	Year/ Setting	Population	n*	Intervention	Outcomes
Trent 2010(110)	RCT	US, large urban centre, ~2007	15-21 yr old women diagnosed with outpatient treatable PID in 5 hospital emergency departments or paediatric and adolescent medicine clinics	121	6 minute video using health belief model to acknowledge barriers and benefits to PID self-care in addition to standardized care	Medication completion, temporary sexual abstinence during the 14-day treatment period, partner notification, partner treatment, return for 72-hour follow-up.
Balamuth 2010(111)	RCT	US, 2008	Physicians working in paediatric emergency departments	237	Use of a PID treatment summary sheet versus the full CDC PID treatment guidelines	Correct completion of a multiple choice survey on PID diagnosis, treatment and follow-up
Trent 2006(112)	Interrupted time series	US, 2001-2003	Patient encounters for PID at a single paediatric outpatient department	127	Multilevel intervention: practitioner treatment algorithm and practice guideline, full 14 day course of antibiotics for patients and written discharge instructions, telephone follow-up at 24-48 hrs and 2 weeks.	Patients receiving appropriate medication, return for follow-up

\*N is the number of the population compared between intervention and control groups

### Description of individual studies

The interrupted time series study by Trent 2006(112) aimed to assess if using a multifaceted approach in a single academic paediatric outpatient setting improved the management of mild to moderate PID. The intervention included practitioners and their patients. Practitioners were provided with a PID treatment algorithm, clinical practice guidelines and training to follow the PID care protocol. The patients were given the initial empirical treatment at the site as well as the full 14 day course of antibiotics to take home. They were also given written discharge instructions and telephone follow-up at 24-48 hours and at 2 weeks. Data were extracted from medical records for 56 patients diagnosed with PID and treated as an outpatient before the intervention, and 71 patients following the intervention. Patients diagnosed before and after the intervention were of similar age and race, and had similar insurance status and positivity rates for Gonorrhoea and Chlamydia. Uptake of the intervention varied; 65% of practitioners used the clinical practice guidelines and 52% distributed the patient information sheet; 88% of patients received the 14 day course of antibiotics; 50% were contactable by telephone within 24-48 hours and 38% were contactable at 2 weeks. Comparing the management of PID before and after the intervention, testing for Gonorrhoea and Chlamydia were similarly high (98% versus 100%, respectively) but requesting wet-film microscopy of vaginal discharge increased (3% versus 38%). The proportion of patients receiving the

recommended antibiotics increased following the intervention (62% versus 91%) and so did the proportion who attended for follow-up within 72 hours (10% versus 43%).

The same author subsequently conducted a RCT of an educational video aimed at improving PID self-management in adolescents diagnosed with mild to moderate PID.(110) The researchers recruited 126 adolescents who presented to one of five clinical sites. All patients were managed using the multi-factorial approach described in Trent 2006 (i.e. practitioners were given the PID treatment algorithm, clinical practice guidelines and the treatment site provided patients with the full 14 day course of empirical antibiotics). In addition to routine management, the intervention involved watching a six minute video. The video aimed to have patients better acknowledge the barriers and benefits of PID self-care. The baseline characteristics of the study population were similar between groups. None of the outcomes examined at two week follow-up, including completing the course of antibiotics (intervention vs. control: 66% versus 66% respectively), follow-up visit within 72 hours (32% versus 16%), abstention from intercourse (78% vs. 89%), partner notification (88% vs. 92%) and partner treatment (71% vs. 53%) was found to differ statistically in the unadjusted analysis although the authors performed adjusted analyses and found that increased partner treatment became significant.

Balamuth 2010(111) conducted a RCT aimed at improving practitioner diagnosis and management of PID using an abbreviated PID treatment summary sheet versus the full 2006 CDC STD treatment guidelines. The study recruited 237 emergency paediatricians and asked them to complete an on-line multiple choice survey assessing their diagnosis and treatment of PID. To assist them with completing the survey, the practitioners had been randomised to either a web link to the 2006 CDC STD treatment guidelines or a one page PID treatment summary sheet that had been developed by the authors based on the most salient points from the CDC guidelines. The characteristics of practitioners were generally similar between comparison groups. More practitioners reported using the summary sheet than the web link (79% versus 50% respectively). Significant differences were also found between groups for the proportion of practitioners who chose the correct antibiotics (summary sheet versus web link: 97% vs. 61%) and who made the correct follow-up recommendations (76% versus 32%). The proportion making the correct diagnosis (45% versus 50%) and choosing the correct admission criteria (87% versus 90%) did not differ between groups.

### Methodological limitations

Two studies included in this review were RCTs and therefore of a higher quality for assessing interventions than the observational study. However all studies still had methodological issues that limit their interpretation or generalisability to the NSW and Australian setting. Overall the studies were relatively small, and conducted on adolescent patient groups and in hospital or outpatient settings. Due to the nature of the studies and the interventions, allocation of the intervention was not concealed to either participants or the outcome assessors.

Specifically, the RCT by Trent 2010, which did not find any benefit to PID management with the video intervention in the intention to treat analysis, was limited by the loss to follow-up. The outcomes of interest assessed at 2 week follow-up were missing for 39% of participants. The RCT by Balamuth 2010 was limited primarily by the hypothetical nature of the study outcome and the generalisability of the study findings. Rather than actual clinical diagnosis of PID and treatment of real patients, the outcomes were hypothetical responses to survey questions. Only 35% of physicians invited to complete the study were included and it is unknown if those who took part differed from those who did not take part. Also, randomisation to the intervention occurred before recruitment to the study (at the point of email invitation) and while baseline characteristics of study participants

were similar between groups, smaller numbers of study participants were allocated to the intervention group than the control (n=109 versus n=128). The 2006 study by Trent found a significant difference in some outcomes although the study design meant that differences between the populations measured before and after the intervention that could potentially bias the findings, could not be adequately accounted for. Also, while the absolute numbers of PID diagnoses made before and after the intervention (56 versus 71) could suggest that the intervention improved the diagnosis rate of PID, the lack of denominators and hence underlying rate of PID diagnosis at the study site meant that this kind of interpretation was not possible. Similarly, as the intervention was multifaceted, the contribution made by various aspects of the intervention to the improved patient antibiotic adherence and attendance at follow-up was not able to be disentangled.

## **Discussion**

### Generalisability of findings

Applying the findings from these three small US studies to the diagnosis and management of PID in NSW is difficult. In Australia, the majority of PID, especially mild to moderate disease, is managed in general practice by general practitioners rather than in hospital settings by specialists.(96) While Balamuth found that abbreviated summary PID clinical guidelines may improve practitioner treatment of PID, compared to the US CDC treatment guidelines,(101) the Australian guidelines for PID are already substantially shorter. Therefore any potential benefit from such a strategy may be limited although easily accessible PID guidelines may still be a worthwhile intervention. Trent's 2006 multifaceted intervention to improve PID diagnosis and management would be considered low level (Level III) evidence under the Australian National Health and Medical Research Council Guidelines for evaluation of scientific evidence.(113) Therefore while some components, such as the provision of the 14 day course of antibiotics at presentation and written discharge instructions, may be innovative and feasible in an Australian setting, they may also require further study in a NSW general practice setting using a more robust study design, and consider issues such as the socioeconomic status of the patient population before they could be recommended for widespread implementation.

### Future directions of research to improve PID diagnosis and management

While they were not included in this review because they did not assess improved compliance with diagnostic and management guidelines as an outcome, some recent RCTs of antibiotics for PID have compared simplified regimens such as once daily or once weekly dosing to more conventional treatments under the premise that simplified regimens will result in greater patient compliance with treatment (see Table 3.2). These studies have found that for uncomplicated PID management, simplified regimens have had similar or better clinical and microbial cure rates than the conventional treatment, however no studies examined longer term sequelae. Australian guidelines currently recommend empirical treatment for uncomplicated outpatient PID with 1g oral Azithromycin, plus 100 mg Doxycycline twice daily for 14 days, plus 400mg Metronidazole twice daily for 14 days, plus a single dose of ceftriaxone 500mg intramuscularly if gonorrhoea is suspected or proven.(86) A more simplified regimen whereby the Doxycycline may be substituted for a second dose of Azithromycin has also been suggested.(114) It is possible that future Australian trials could investigate the use of more simplified antibiotic regimens to maintain similar cure rates but with the intention to improve patient compliance.

**Table 3.2: Randomised controlled trials comparing simplified to more conventional antibiotic regimens for outpatient management of PID**

Study ID	Year/ Setting	n	Simplified regimen	Comparator regimen	Outcomes (intention to treat analyses)
Savaris 2007(115)	Single centre, Porte Alegre, Brazil	120	250mg iv ceftriaxone Plus 1g oral azithromycin per week for 2 weeks	250mg iv ceftriaxone Plus 100mg oral doxycycline BD for 2 weeks	Microbiological and clinical cure rates: 98.2% vs. 85.7% (p=0.02) (azithromycin vs. doxycycline)
Ross 2006(116)	Multi-centre Europe and Sth Africa	741	400mg oral moxifloxacin daily for 2 weeks	400mg oral ofloxacin BD plus 400mg oral Metronidazole BD	Clinical cure: 75.6% vs. 82.6% (moxifloxacin vs. ofloxacin plus Metronidazole)

In Australia, as part of a trial of screening for Chlamydia ([www.accept.org.au](http://www.accept.org.au)), an evaluation of a PID education package delivered to general practitioners is currently underway. The package involves reading materials, a DVD on PID diagnosis and management, and instructions on how to record PID diagnoses in the GP's medical record software. Practitioner diagnosis rates, antibiotic treatments prescribed and practitioner knowledge surveys measured before and after the intervention will be used to assess the effectiveness of the educational package. This data may inform future strategies to improve PID diagnosis and management in the Australian general practice setting. Improving the diagnosis of PID through better practitioner training or using diagnostic algorithms that begin with the setting of a woman presenting with lower abdominal pain should also be considered as a possible interventions to evaluate in the Australian setting.

Finally, as PID is an important and serious sequelae of genital Chlamydia infection in women, monitoring PID incidence rates is important in order to estimate changes in the diagnosis of the disease, changes in the true incidence of disease and to monitor the impact of interventions aimed at improving detection and management. Surveillance of PID in NSW and Australia would benefit from more standard case definitions of PID for practitioners to use, and more standard coding in medical records.

### Conclusions and recommendations

This review found that there is little research in the area of improving practitioner and patient adherence to PID diagnosis and management guidelines. Only three studies were identified, and because of the study settings and methodology, the relevance of their findings to the NSW and Australian health system is limited. Based on the general review of literature in this area, we suggest that for monitoring and surveillance purposes more uniform ways to diagnose PID and classify PID in medical records are required and to improve practitioner diagnosis of PID better training and education needs to be considered. Based on the systematic review of literature we also suggest that further studies in the NSW setting, that may employ any one of the following interventions should be investigated to determine if they improve the diagnosis and management of PID: abbreviated practitioner clinical management guidelines, provision of the 14 days of antibiotic treatment at presentation, simplified antibiotic regimens, written instructions for patients.

## Chapter 4: Effectiveness of chlamydia screening

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### Abstract

**Introduction:** Screening for chlamydia infection has been undertaken in various settings as a means of reducing the prevalence of chlamydia and its sequelae in populations. We undertook a systematic review of studies examining the effectiveness of chlamydia screening programs.

**Methods:** We extended a systematic review published by Gottlieb et al that covered the period January 1990 to March 2008. We searched several electronic databases until January 2011 and included studies examining the outcomes of pelvic inflammatory disease (PID), ectopic pregnancy, infertility, adverse pregnancy outcomes, neonatal infection, and chlamydia prevalence.

**Results:** We included eight studies in the review; seven were randomised trials, and one was a single population time trend study. Two studies had appeared since the last published review on this topic, and both within the last twelve months. In three studies the primary outcomes was PID, in another three it was chlamydia prevalence, in one it was both chlamydia prevalence and PID and another study reported PID, ectopic pregnancy, infertility, births and epididymitis in men. Three of the five studies included in the review with PID as the primary outcome showed significant reductions in rates of PID associated with increased screening, ranging from 35% to 56%. Of the four studies which focused on chlamydia prevalence as an outcome following screening, all showed significant reductions in chlamydia prevalence (three were in women, and one in men). No trials reported the outcomes of more than one round of screening.

**Conclusion:** There is some evidence that chlamydia screening reduces chlamydia prevalence and PID in young females. Methodological inadequacies could have overestimated the observed benefits in some of the trials.

## Introduction

*Chlamydia trachomatis* is a sexually transmitted infection that is the most common reportable communicable condition in the United States (US), Australia and other European countries.(117-118) Chlamydial infection is associated with adverse health outcomes, particularly for women, including pelvic inflammatory disease (PID), ectopic pregnancy, and tubal infertility.(119-120) In 2010, around 1.3 million new diagnoses were reported in the US(117) and 70,000 cases in Australia. (117-118), but these cases are a minority of those that actually occur, as most infections remain asymptomatic and undiagnosed.(119-120) Accordingly, clinical guidelines in various countries recommend regular testing of those considered most at risk. In Australia, the guidelines call for annual screening of all sexually active women aged 25 or less, and men who have sex with men.(121)

Systematic screening programs have also been established to detect asymptomatic cases, with the twin goals of reducing transmission and reproductive tract morbidity. A number of studies have assessed strategies for increasing testing rates in the population (Chapter 5 and 6). Although increasing the rates of testing appears to be feasible, the impact of this strategy applied at a population level on reducing chlamydia transmission rates and its complications has been challenged.(122-123)

Several reviews have been undertaken of the evidence base relating population screening to these outcomes. The most recent published review covered papers published until March 2008 (Gottlieb SL et al)(124), and an unpublished review covered studies to the end of 2009. With this being a fast moving field of research enquiry, we have again updated the reviews with studies published up to January 2011.

## Methods

### Review process

We searched the electronic databases Medline, EMBASE and the Cochrane Controlled Trials Register from January 1990 to January 2011. The reference lists of manuscripts found in the search were hand searched to identify additional relevant articles. There were no language restrictions. We used subject heading and free text terms that combined “*Chlamydia trachomatis* infections” or “PID” with terms for screening.

Studies were included if they examined an organised strategy for chlamydia screening in adult women or men and reported on any of the following outcomes: incidence or prevalence of chlamydia infection; PID, ectopic pregnancy, and infertility; adverse pregnancy outcome; neonatal morbidity or mortality; and male infertility.

We included randomised controlled trials, non-randomised comparative studies, and single population observational time trend studies if they included data from at least two time points before the introduction of the intervention.(125) Two reviewers screened titles and abstracts to identify potentially relevant articles. Full text manuscripts were then read independently. Discrepancies were resolved by discussion to reach consensus about the final list of reports to include. Two independent reviewers extracted data and discrepancies were resolved by discussion.

From studies which reported on the reproductive tract morbidity, we either abstracted or calculated the relative risk comparing rates of PID in the intervention and control groups, as the primary effect measure for the study. A Chi-square based Q statistic test was used to assess heterogeneity. Meta-analysis was performed in STATA 10 (StataCorp, College Station, TX, USA).

## Results

Our key word searches identified 2,980 unique references between 1990 and January 2011. We screened 428 abstract or full text manuscripts, and found a total of eight studies that met the review criteria. Of these studies, seven were randomised trials, and one was a time trend study within a single population. Two studies had appeared since the last published review on this topic, both within the last twelve months. In three studies the primary outcomes was PID(126-128); in another three it was chlamydia prevalence in men and women(129-131); in one it was used chlamydia prevalence and PID(132); and one study reported PID, ectopic pregnancy, infertility, births in women and epididymitis in men(133).

### Reproductive tract morbidity

Three of the five studies assessing PID as an outcome showed significant reductions in rates of PID following a single screen and treatment.

Giertz G et al (1987)(127) conducted a study in 487 Swedish women under 25 years of age, who underwent abortion between September 1983 and September 1984. The patients were randomly distributed into 2 groups. In Group A (n=288) specimens were taken from the cervix of the patients for culture and direct immunofluorescent staining for *C. Trachomatis*, and pre-operative treatment with doxycycline was given if they were found to be positive; and in Group B (n=259) a clinical examination was performed. Women in both groups were assessed for postoperative PID signs through a bimanual examination. *C. trachomatis* culturing was only conducted postoperatively when signs of infection were found. In group A, 41 of 288 women found to have chlamydia on screening received preoperative doxycycline treatment and none developed PID (0%). Among the remaining 247 women without *C. trachomatis* on testing, 14 developed PID which in the screened group gave an incidence of PID of 4.9%. In contrast, 25 of the 259 women in Group B (9.7%) developed PID, giving a relative risk of PID in the screened group about half that of women in the control group (risk ratio 0.50, 95% CI:0.27-0.95).

Scholes D et al (1996)(126) demonstrated through a randomised controlled trial that the risk of PID in women invited for screening was about half of that of the control group, one year after a single round of testing. Women at high risk were identified through a questionnaire mailed to all women aged 18-34 years enrolled in a health maintenance organization. Eligible respondents were randomly assigned to undergo testing for *C. trachomatis* or receive usual care; both groups were followed for one year. Possible cases of PID were identified through linkage to a variety of data bases and were confirmed by review of medical records. Of 2,607 eligible women, 1,009 were randomly assigned to screening and 1,598 to usual care. A total of 645 women in the screening group (64%) were tested for chlamydia and 7% tested positive and were treated. At the end of the follow-up period, there had been 9 verified cases of PID among women in the screening group and 33 cases among women receiving usual care, giving a relative risk of 0.44 (95% CI:0.20-0.90).

Østergaard L et al (2000)(132) compared the efficacy of a screening program for chlamydia based on home self-sampling with that of screening based on conventional swab sampling performed at a doctor's office as part of usual care. Participants were sexually active male and female students at 17 high schools in the county of Aarhus, Denmark. The study assessed the number of new infections and the number of subjects who reported being treated for PID at 1 year of follow-up. Follow up was completed on 443 (51.1%) of 867 women in the intervention group and 487 (58.5%) of 833 women in the control group. Nine (2.0%) women in the intervention group and 20 (4.1%) in the control group reported being treated for PID (p=0.045).

Two other studies assessing PID as an outcome found no significant reductions in rates of pelvic inflammatory disease associated with increased screening.

A trial in London(128) called the POPI (prevention of pelvic infection) trial (Oakeshott et al, 2010), measured the incidence of PID in female university students randomised to receive immediate testing and treatment for chlamydia, and compared this to the incidence in those for whom testing and treatment were deferred by 12 months through storage of samples. The investigators followed 2,529 women (mean age 21 years) with outcome data were available on 94%. PID diagnosis was made by two specialists (with a third as arbiter) who conducted a blind assessment of medical records against predefined criteria. Over 12 months, there were 38 cases of probable or possible PID, 1.3% (15/1191) in the intervention group and 1.9% (23/1186) in the control group (relative risk 0.65, 95%CI:0.34-1.22).

A randomised trial in Denmark (Andersen et al, 2010)(133) found that DNA amplification assay of non-invasive samples (first-void urine samples for men and a self-collected vaginal sampled for women) did not reduce the long-term risk of reproductive complications in women or of epididymitis in men. A random sample of 4,000 women and 5,000 men were contacted by mail in 1997 and offered the opportunity to be tested for *C. trachomatis* by means of a self-sample obtained at home and mailed directly to the laboratory. The other 11,459 women and 9,980 men not contacted received usual care and constituted the control population. Participants were followed for nine years through linkage with Danish health registers. Data were collected on diagnoses of PID, ectopic pregnancy and infertility, as well as in-vitro fertilisation (IVF) treatment and births in women, and on epididymitis in men. Among women, no differences were found between the intervention group and the control group: Calculated RR (95% CI) for PID 0.91 (0.64-1.31); ectopic pregnancy 1.02 (0.74-1.41); infertility 1.1 (0.96-1.29); IVF treatment 1.09 (0.85-1.41) and births 0.98 (0.92-1.04). In men, the calculated RR for epididymitis was 0.85 (0.85-1.29).

### Chlamydia prevalence

All four studies assessing chlamydia prevalence post-screening showed significant reductions associated with increased screening. In one of these studies a significant decrease in prevalence was only seen in males, and not females.

Cohen et al (1999)(16) assessed chlamydia prevalence at three high schools with over 2,000 students in the 9th through the 12th grade who were given the opportunity to be tested during three consecutive school years for chlamydia and gonorrhoea, using urine ligase chain reaction tests. Five comparable schools with 5,063 students enrolled served as wait-listed controls where students were tested only in the third year. In the three intervention schools, annually, 52% to 65% of all enrolled students participated; among those enrolled in schools for at least 2 years, 83.4% of students were tested at least once. In the control schools, 52.4% students were tested in the third year. At first test, in all eight schools, 286 (11.5%) of 2,497 girls and 143 (6.2%) of 2,308 boys were found to have chlamydia, and 48 (2.5%) of 1,883 girls and 19 (1.2%) of 1,628 boys had gonorrhoea. Over 90% of infections were asymptomatic. With repeat testing, chlamydia prevalence among boys decreased significantly to half the rate of comparison schools (3.2% vs. 6.4%). Among girls chlamydia prevalence declined only slightly (10.3% vs. 11.9% in comparison schools) and the decrease was not significant.

In Uppsala County, Sweden, between 1985 and 1993, examinations for chlamydia were performed in a central laboratory. A change in national legislation in 1988 encouraged screening, and its impact was assessed through an ecological study by Herrmann B et al (1995)(131). The analysis included 119,892 tests, representing 95.4% of all specimens taken during the study period. Eighty-six percent

of the samples were tested by culture and the remainder by enzyme immunoassay. Seventy-nine percent of specimens came from women. Rates of positivity declined from 107.2 per 1,000 tests in 1985 to 32.3 in 1993 in women and from 183.3 to 70.7 in men. Using multivariate logistic regression, establishment of the national legislation led to a reduction in chlamydia positivity with an adjusted odds ratio of 0.89 (95%CI:0.80-0.99) in females and 0.85 (95%CI:0.73-1.0) in males. Positivity rates were highest in clients of sexually transmitted infection clinics and youth clinics and lowest in private practices.

Hodgins S et al (2002)(129) invited all adults in six Inuit villages in Canada to provide urine specimens as part of an intensive sexual health education and promotion campaign. In the six comparison villages there was no campaign but opportunistic testing was available. The rate of chlamydial infection decreased from 37.1 per 1000 population (one year before the campaign) to 24.2 per 1000 population (one year after the campaign) (OR=0.65, 95%CI:0.52-0.81; p=0.0003). The rates of infection in the control villages were 28.1 per 1000 population before the campaign and 26.1 per 1000 after. In a subset of women who presented for pre-natal and PAP testing, the prevalence of chlamydial infection decreased from 12.3% (before) to 4.6% (after the campaign) in the intervention villages (p=0.0002). The corresponding prevalence in the control villages was 9.3% before and 8.2% after campaign.

Østergaard et al (2000)(132) found fewer diagnosed infections at follow up in 443 female students who had been invited to provide home-collected vaginal specimens compared with 487 controls who were told to visit their general practitioner, with 13 (2.9%) and 32 (6.6%) of new infections identified in the intervention group and the control group, respectively (p=0.026).

**Table 4.1: Reproductive health outcomes** from included studies

Author surname, year	Study design	Time frame	Outcome	Intervention			Control			RR (95% CI)
				Number women	Number of cases	%	Number women	Number of cases	%	
Østergaard L et al, 2000 (132)	Cluster RCT	1 year	PID	443	9	2.0%	487	20	4.1%	0.64* (0.37-1.11)
Scholes D et al, 1996 (126)	Individual RCT	1 year	PID	1009	9	0.9%*	1598	33	2.1%*	0.44 (0.20-0.90)
Oakeshott P, 2010 (128)	Individual RCT	1 year	PID	1191	15	1.3%	1186	23	1.9%	0.65 (0.34 - 1.22)
Giertz G et al, 1987 (127)	Individual RCT	4 wks post-op	PID	288	14	4.9%	259	25	9.7%	0.66* (0.43-1.02)
Anderson et al, 2010 (133)	Individual RCT	9 yrs	PID	4000	23	0.6%*	11459	74	0.6%*	0.91* (0.64-1.31)
			EP	4000	27	0.7%*	11459	75	0.7%*	1.02* (0.74-1.41)
			Infertility	4000	129	3.2%*	11459	322	2.8%*	1.1* (0.96-1.29)
			IVF treatment	4000	43	1.1%*	11459	109	1.0%*	1.09* (0.85-1.41)
			Births	4000	967	24.2%*	11459	2833	24.7%*	0.89* (0.92-1.04)
			Epididymitis	5000	16	0.3%*	9980	40	0.4%*	0.85* (0.56-1.29)

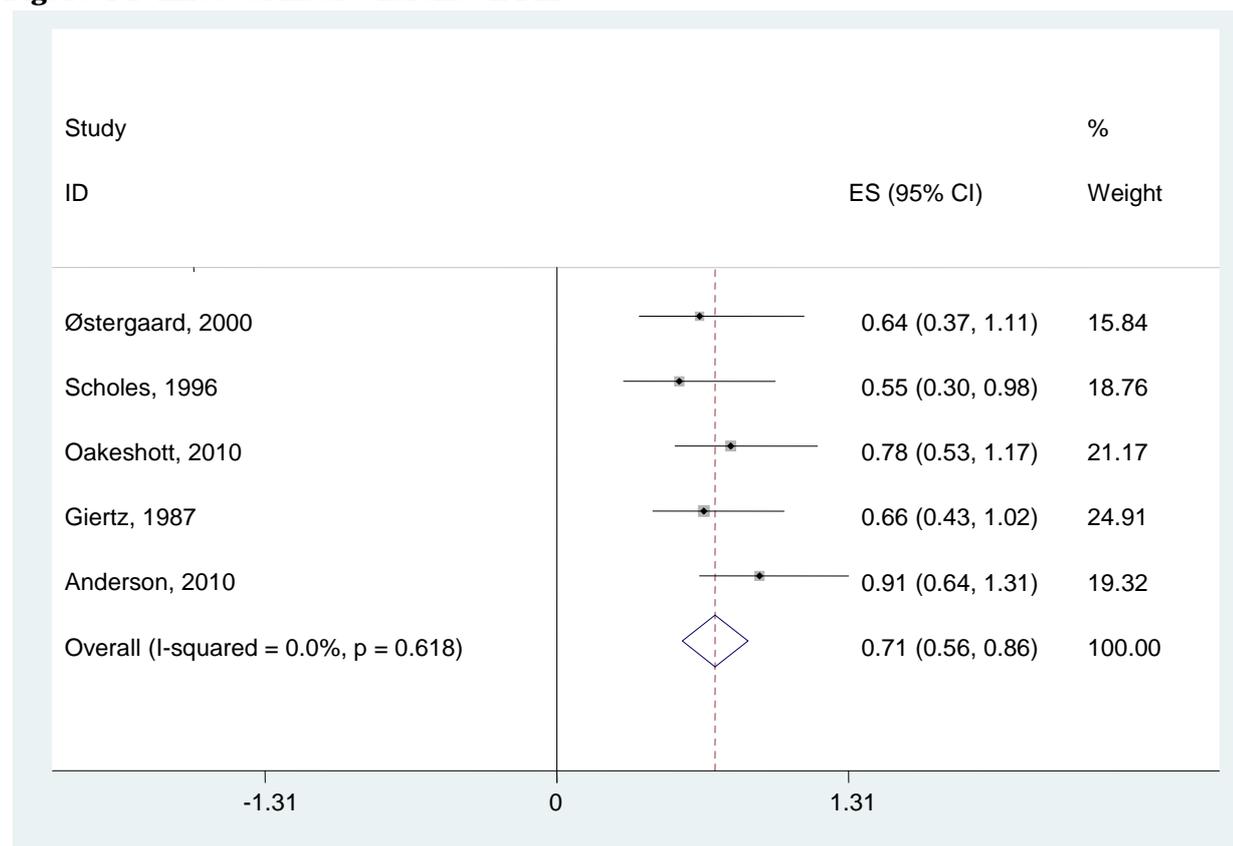
PID=pelvic inflammatory disease, RCT= randomised controlled trial, RR=relative risk

\* Calculated from available data

**Table 4.2: Chlamydia prevalence study results from included studies**

Author surname, year	Study design	Sex	Time period	Intervention			Time period	Control			Results (95% CI)	RR (95% CI)
				Tested (n)	Positive (n)	% positive		Tested (n)	Positive (n)	% positive		
Østergaard L et al, 2000 (132)	Cluster RCT	F	1 year	443	13	2.6%*	1 year	487	32	8.1%*	5.5% (0.95 - 10.0%)	0.59* (0.37-0.94)
Hodgins S et al, 2002 (129)	Cluster RCT	F	1 year	569	26*	4.6%	1 year	-	-	8.2%	intervention p=0.0002 control p=0.63	-
			Pre	1223	150*	12.3%	Pre	-	-	9.3%		
Cohen DA et al, 1999 (130)	Cluster RCT	F	3 years	562	58	10.3%	1 year	1411	168	11.9%	p>0.05	0.89* (0.7-1.12)
		M	3 years	588	19	3.2%	1 year	1242	79	6.4%	p<0.01	0.59* (0.39-0.89)
Herrmann B et al, 1995 (131)	Time trend study	F	1993	-	-	3.2%	1985	-	-	10.7%	aOR=0.89 (0.80 - 0.99)	-
		M	1993	-	-	7.1%	1985	-	-	18.3%	aOR=0.85 (0.73 - 1.0)	-

M=male, F=female, RCT= randomised controlled trial, OR=odds ratio, AOR=adjusted odds ratio  
\* Calculated from available data

**Figure 4.1: Effect of interventions on PID**

The black and grey square and horizontal line correspond to relative risk and 95% confidence interval for each study. The diamond represents the combined relative risk and 95% confidence interval.

## Discussion

Our systematic review assessed evidence for the effectiveness of chlamydia screening in reducing chlamydia and related morbidity. Three of the five studies that used PID as the primary outcome showed significant reductions in rates following increased screening, in the range 35% to 56%. All four studies which tracked chlamydia prevalence following screening found significant reductions (three studies in women, one in men).

## Methodological aspects of the studies

The studies included in the review had a number of weaknesses that could have biased their results. As *C. trachomatis* may be implicated in about 17-47% of PID (based on prevalence of chlamydia in young women in Australia, see Chapter 2 for details) even if screening and treatment prevented all cases due to chlamydia, an effect greater than halving of the overall risk of PID seems implausible. In many studies the weakness was in the procedures for diagnosis for PID, which may have led to under ascertainment, although it would be of equal magnitude in both groups. Many studies included women at high risk of chlamydia and thus results might not be generalisable to all young women. As trials of screening cannot be blinded, the invitation for screening may be associated with other interventions, such as behavioural counselling, which may have played a role in any differences observed between comparison groups. Differential rates of enrolment and loss to follow up might also have resulted in systematic differences between intervention and control groups. Only one study had sufficient long term follow up to assess the impact of screening on other important sequelae such as infertility. All studies which examined the impact of screening on chlamydia prevalence were based on single rounds of screening. This could have potentially biased the result in favour of the screened group, which includes incident infection; in contrast to the control group, which also includes prevalent infections that might have been present before the trial started.

### Does screening reduce PID?

The POPI trial had a robust design (high follow-up rates and blinded PID assessment) and thus the 35% reduction in the overall incidence of PID, although not statistically significant, may indicate the maximum benefit that can be achieved when an entire population has a one-off screen and the vast majority of positive cases are treated.(128) The reduction in PID among women who were positive chlamydia at baseline and were treated (1/63 in the intervention group vs. 7/74 in the control group, RR=0.17, 95%CI:0.03-1.01), provides further evidence that the trial's results are valid. The authors estimated that it was necessary to screen 147 women for chlamydia or to treat 13 women who tested positive for chlamydia to prevent one case of PID over 12 months.

The limitations of screening can be seen in the 10 reported cases of chlamydia-positive PID among women who were chlamydia-negative at baseline in the POPI trial, which could not have been prevented by the screening intervention.(128) These cases highlight the importance of ongoing chlamydia transmission through new relationships or re-infections within ongoing partnerships resulting from failed partner notification. Additional follow-up for chlamydia testing and genotyping would have provided valuable information about these issues.

A single screening test could only have a substantial direct effect if most infections detected were recently acquired and are treated before they can cause upper genital tract inflammation. This is unlikely because chlamydia can persist asymptomatically for up to five years after infection,(82) so most infections in a previously unscreened population would already have been present for some time and might already have caused tubal damage. On the other hand, higher levels of screening uptake and partner notification should interrupt community transmission and reduce exposure. The 33% screening uptake among Danish school students would probably not have reduced transmission substantially.(132) In another study involving health maintenance organisation members, community level transmission is unlikely to have been affected as the population was not geographically contiguous.(126) Neither trial reported partner treatment rates.(126, 132) In one trial that examined pre-abortion screening, only 10% of male partners of women with either chlamydia or gonorrhoea were treated.(134)

Mathematical models provide information about how chlamydia screening would prevent PID in the long term. In these models, the reduction in PID depends on reducing transmission at a population level by repeated yearly screening, treatment and partner notification to reduce the risk of exposure to chlamydia, and not to an individual effect of interruption of ascending infection.(135-136)

### Strengths and limitations of the review

We conducted comprehensive literature searches of multiple databases without language restrictions, and used rigorous methods to identify, appraise, and synthesise the evidence. It is unlikely that we excluded any important studies during the dates covered by the search. We did not combine effect estimates statistically for most comparisons because of the small numbers of studies, and differences in the interventions, populations or data reporting.

### Implications for chlamydia screening program design

As demonstrated in the POPI trial, most cases of PID over 12 months were not prevented by a single chlamydia screen and occurred in women who were negative for chlamydia at baseline. If PID follows soon after incident infection, then the latent period (i.e. the time between infection and symptomatic disease) in chlamydia may be much shorter than previously thought. If screening intervals are shortened, more incident cases will be detected and more chlamydial PID could be prevented, but costs of screening would increase for both the health service and the screening participant. A more efficient strategy could be to focus on more frequent testing of those at higher risk, such as women with a new sexual partner or a recent history of chlamydial infection. Another element of chlamydia control programs that could benefit from strengthening is the effective management of sex partners to prevent re-infection. Heijne et al (2011) described a pair compartmental model that explicitly incorporates sexual partnership duration and re-infection.(137) The results have implications for the design of chlamydia screening strategies. They found that ~30% of current sex partners need to be notified to counterbalance the effect of re-infection in a screening program.

### Implications for the evaluation of chlamydia screening

A reduction in chlamydia transmission following screening would provide good primary evidence of its effectiveness. The ideal screening design would be an intervention implemented in randomly assigned areas over two or more screening intervals. The ideal evaluation would involve conducting a prevalence study with high participation, follow up, treatment, and partner notification rates, thus prevalent infections would have been detected and treated.

PID is the most commonly used biological outcome because it is the most frequent complication of chlamydia.(138). However, its use as trial outcome is fraught with problems. Firstly, clinical diagnosis of PID can lack sensitivity and specificity.(139) Secondly, many PID case definitions include a positive chlamydia test as a requirement of diagnosis, so diagnosis of lower abdominal symptoms is likely to be influenced by the chlamydia screening status. Thirdly, practitioners usually cannot be blinded to the screening allocation in a trial, however reported symptoms should at least be recorded in a standard way and an independent blinded assessor should assess the final outcome, as done in the POPI trial.

Ectopic pregnancy and tubal infertility are more important consequences of chlamydial infection but difficult to measure as they are often too rare or delayed. Record linkage studies may be useful but would need to take into account the number of chlamydia tests undertaken in the screening arm.

Two new trials provide essential additional information about the effectiveness of chlamydia screening. Both involve multiple screening rounds and use chlamydia prevalence as an end point. The first, the Australian Chlamydia Control Effectiveness Pilot (ACCEPt, trial registration number ACTRN12610000297022), is a cluster randomised trial funded by the Australian government, which aims to determine whether increased repeated chlamydia screening among 16–29-year-old women and men attending general practices can reduce chlamydia prevalence in the surrounding population. The intervention will be randomised at the postcode (town) and all primary care clinics in each town will be invited to participate. To increase screening the trial will include a multifaceted package of prompts, recalls, continuing medical education modules, incentives, and regular feedback. The ACCEPt study aims to enrol around 54 towns and compare the prevalence of chlamydia before and after the intervention in around 3000 young people (men and women). Chlamydia prevalence will be estimated through consecutive sampling of young patients attending the intervention and control clinics for any reason. The incidence of PID will be a secondary outcome. The first prevalence studies were undertaken in early 2011. The second, is the Chlamydia Screening Implementation (CSI) project being conducted in three areas of The Netherlands where 16% of all invited individuals aged 16–29 years have been tested in the first round.(140)

## **Conclusion**

In conclusion, our review suggests that the effectiveness of chlamydia screening in improving health outcomes requires further evaluation in randomised trials over multiple screening rounds with primary biological endpoints. Trials currently under way should prioritise both screening and prevention of re-infection to maximise the impact on chlamydia transmission.

## Chapter 5: Interventions to increase chlamydia screening in primary care

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### Abstract

**Background:** As most genital chlamydia infections are asymptomatic, screening is the main way to detect and treat cases. We undertook a systematic review of studies assessing the efficacy of interventions for increasing the uptake of chlamydia screening in primary care.

**Methods:** We reviewed studies which compared chlamydia screening in the presence and the absence of an intervention. The primary endpoints were screening rate or total tests. Studies without a well-defined control group were excluded.

**Results:** We identified 15 reports describing 16 intervention strategies; ten were randomised controlled trials and six observational studies. Seven of the 16 interventions were associated with significant increases in screening rates at the 0.05 level. Strategies used were a multifaceted quality improvement program that included provision of a urine jar to patients at registration (65% in intervention group vs. 21% among female adolescents and 49% vs. 5% among male adolescents); doctors offering a test to all presenting young male clients, prior to consultation (29 vs. 4%); linking screening to routine Pap smears (6.9% vs. 4.5%), computer alerts for doctors (12.2% vs. 10.6% in young females); education workshops for clinic staff ( $p < 0.001$ , in young females); internet-based continuing medical education (15.5% vs. 12.4%, in young females); and free sexual health consultations (16.8% vs. 13.2% in females and 4.2% vs. 2.1% in males).

**Conclusions:** Interventions that effectively promoted the universal offer of chlamydia test in age groups at risk had the greatest impact on increasing screening in primary care.

## Introduction

Infection with *Chlamydia trachomatis* is a significant public health problem. In women it causes adverse health consequences such as pelvic inflammatory disease which in turn can lead to tubal factor infertility and ectopic pregnancy.(119-120) As over 80% of infections are asymptomatic, screening on the basis of epidemiological risk factors such as age and sexual history is the main way to detect cases.(119-120) Clinical guidelines in many countries recommend chlamydia screening in all sexually active young females.(121, 141-142)

Primary care clinics play an important role in the prevention and management of sexually transmissible infections (STIs). A large proportion of young people attend primary care clinics each year for one reason or another (46, 143), and most chlamydial infections are diagnosed in this setting.(143-144) However, despite the central role of primary care in chlamydia management, the proportion of young people attending these clinics who are offered screening at the time of their visit is generally under 10% in many developed countries including Australia(46), the United States (US)(145),the United Kingdom (UK)(146), and other European countries.(143)

A systematic review in 2006 identified four published trials of interventions to increase chlamydia screening in primary care and found that educational packages targeting primary care physicians, and the elimination of barriers to screening within clinic systems were effective at increasing screening.(147) Since then, a number of new publications have reported on the evaluation of interventions to increase chlamydia screening in primary care clinics. This systematic review aimed to provide an updated synthesis of studies examining the efficacy of these interventions.

## Methods

The systematic review was conducted according to the PRISMA statement.(148)

### Review strategy

A publication was considered for inclusion if it reported on the evaluation of an intervention to increase chlamydia screening rates in a primary care clinic, through a comparison with chlamydia screening rates (proportion of patients tested within a given time period) in a control group or control time period. A primary care clinic was defined as a health service that provides the first point of entry into the health care system, addresses the vast majority of patient concerns and needs, and is the ongoing focal point for all of a patient's health care requirements. This definition excluded more specialised services, such as sexual health clinics, family planning clinics, and pharmacies.

The electronic bibliographic databases Medline, PubMed, EMBASE, the Cochrane Controlled Trials Register and the Australian New Zealand Clinical Trial Registry were searched to the end of September 2010. Only English language publications were included. Reference lists of selected studies were also checked for other potentially relevant studies.

The following key terms were used in the searches:

1. Chlamydia infections, or Chlamydia, or Chlamydia trachomatis, AND
2. Testing or screening, AND
3. Intervention, or trial, or intervention studies AND
4. General practice or general practitioner or GP or primary care

The papers were reviewed and information was extracted by two authors independently. Disagreements were resolved by discussion and consensus.

Publications were excluded that did not incorporate a control group; reported on screening rates in the absence of a specific intervention; described chlamydia or STI screening programs in clinic or community settings other than primary care; described surveys of patients or providers about chlamydia screening; or did not report original data.

For each paper that met the inclusion criteria, information was extracted on the clinic location, the target population, the intervention strategy, the study design, the sample size, the statistical tests used and the outcomes of the evaluation including chlamydia screening rates or number of tests.

### Analysis

We conducted a frequency analysis of information related to the clinic (location, type), intervention type and evaluation methods (sample size, design, analytical techniques, time period of the evaluation and reported outcomes).

The primary outcome for each study was the screening rate, defined as the proportion of patients attending the clinic who were tested for chlamydia. For studies that did not report this proportion, we accepted the total number of tests done as an alternative.

If a paper presented data from males and females separately but did not present a combined result, we calculated the overall study effect estimate by summing the total numbers of patients seen and patients tested, and dividing the latter by the former.

From each study, we abstracted the odds ratio (OR) or relative risk (RR) indicating the proportion tested in the intervention group compared to controls. For studies which did not report a measure of this kind we calculated the outcomes using Stata statistical software(149), including 95% confidence intervals if the necessary figures were provided in the paper.

### **Results**

Using the search words 'chlamydia' and 'screening', 'intervention' and 'general practice', and variations of these terms, 96 articles were identified and the abstracts from these articles were reviewed (Figure 5.1). A total of 81 papers were excluded because they either described interventions to improve outcomes other than chlamydia screening (n=25); described chlamydia or STI screening programs in clinic or community settings other than primary care (n=15); were reviews or commentaries which did not contain original data (n=13); described surveys of patients or providers about chlamydia screening (n=5); described a cross sectional or cohort study which reported STI incidence or prevalence, screening rates or risk factors (n=4); described mathematical transmission models or cost-effectiveness analyses of the impact of chlamydia screening (n=4); described a study of non-genital chlamydia (n=5); described a chlamydia immunological study (n=1); was a case report (n=1); there was no control group (n=2); the paper did not contain any data (n=6).

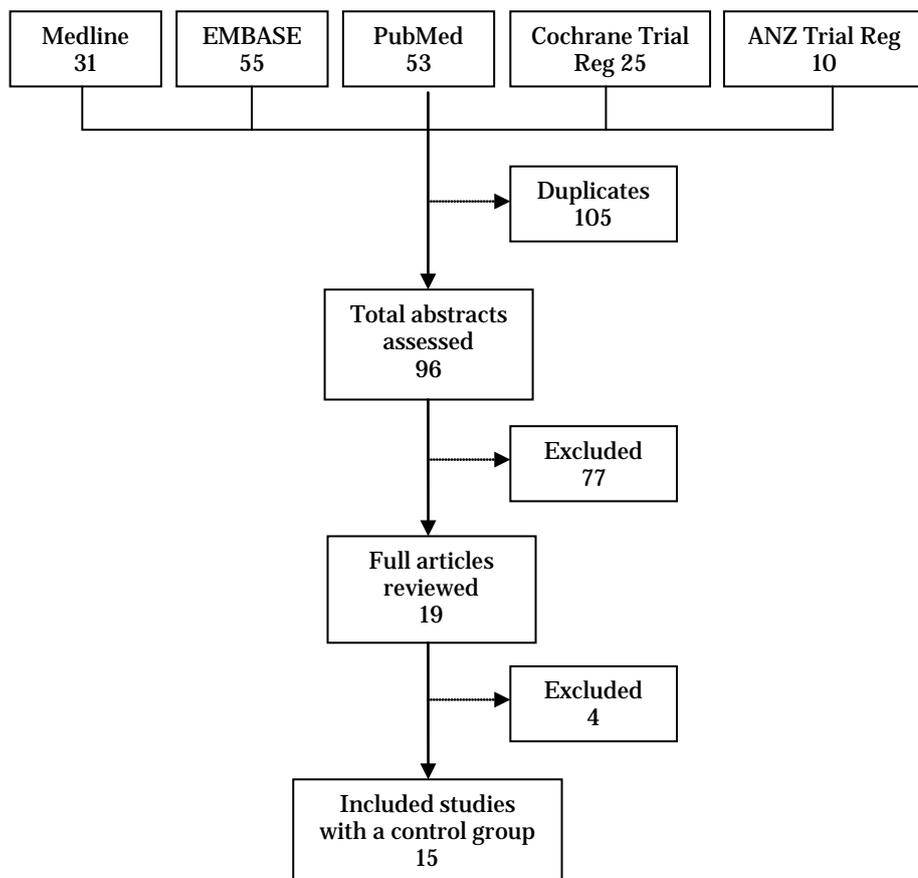
The remaining 15 papers (143, 145, 150-162) were included in the review. They were conducted in Australia (n=5), the US (n=5), the UK, Scotland, Belgium, Denmark and New Zealand (NZ) (1 each).

Two papers(155, 158) each reported on the evaluation of two distinct intervention strategies, and two papers reported on the evaluation of the same intervention strategies (one in females, one in males) (159-160) giving a total of 16 strategies evaluated across the 15 papers.

As shown in Table 5.1, we grouped the 16 strategies to increase chlamydia screening into six broad categories, based on the methodological descriptions provided in the reports: medical record prompts(155, 158, 162); clinician incentives (151, 157); alternative specimen collection approaches

(143, 153); clinician education (145, 150, 161); patient education(152); and quality improvement programs.(156, 158-160).

**Figure 5.1: Search results**



Of the 16 intervention strategies, eleven were described as having been evaluated using a randomized controlled trial (RCT) design(145, 151, 153, 155, 158-160, 162) while five reported using an observational design with control clinics or a control period.(143, 150, 152, 156-157, 161) One of the randomized designs only involved two clinics, so was reclassified for the purpose of the review as observational.(150) Of the other five observational evaluations, two involved non-random allocation of clinics to the intervention, with comparison being made to control clinics and to the pre-intervention period in the intervention clinics (143, 157), and the other three used a before and after design within the same group of clinics.(152, 156, 161)

The primary study outcomes reported were clinic screening rates (13 studies)(143, 145, 151-153, 155, 157-160, 162), total tests done (two studies)(150, 156), and mean number of tests per clinician (one study).(161) One of the studies that reported total tests also described the screening rate in four of six participating clinics.(156) In one study the primary outcome data was screening rates at the clinic level but only one doctor in each clinic participated in the intervention.(145) In the RCTs, the total number of participating clinics ranged from 12-191. In the observational studies, the range was 2-49. Three evaluations did not report statistical tests of the significance of the difference between intervention and control groups.(150, 156-157) None of the observational studies reported any form of adjustment in their analyses for differences in baseline characteristics, including chlamydia screening rates, between the intervention and control clinics, although there were such differences. For example in the NZ study, clients of intervention clinics were more likely to be of a lower socioeconomic status, Māori and rural population.(157)

Seven of the 16 intervention strategies were significantly associated with increased chlamydia screening at the 0.05 level (143, 145, 153, 155, 157, 159-160, 162) (Table 5.1, Figure 5.2) and of those that reported an odds ratio or relative risk, or where one could be calculated, the percent increase in screening increased from 15.1% (163) to 673% (143) (Table 5.1, Figure 5.2). The seven others that reported significance tests found no significant increase in screening rates (Table 5.1, Figure 5.2). (151-152, 154-155, 158, 161)

The greatest impact (673 % increase) in chlamydia screening was observed in a Danish study in which doctors were asked to test all 16-25 year old males whom they saw for any reason, by use of a first-catch urine sample. Control clinics comprised all other clinics in Denmark. Baseline screening in control and intervention clinics was 3.4% and 3.7% respectively and following the intervention the study found screening rates were 29% in the intervention clinics compared with 4% in the control clinics ( $p < 0.001$ ). (143)

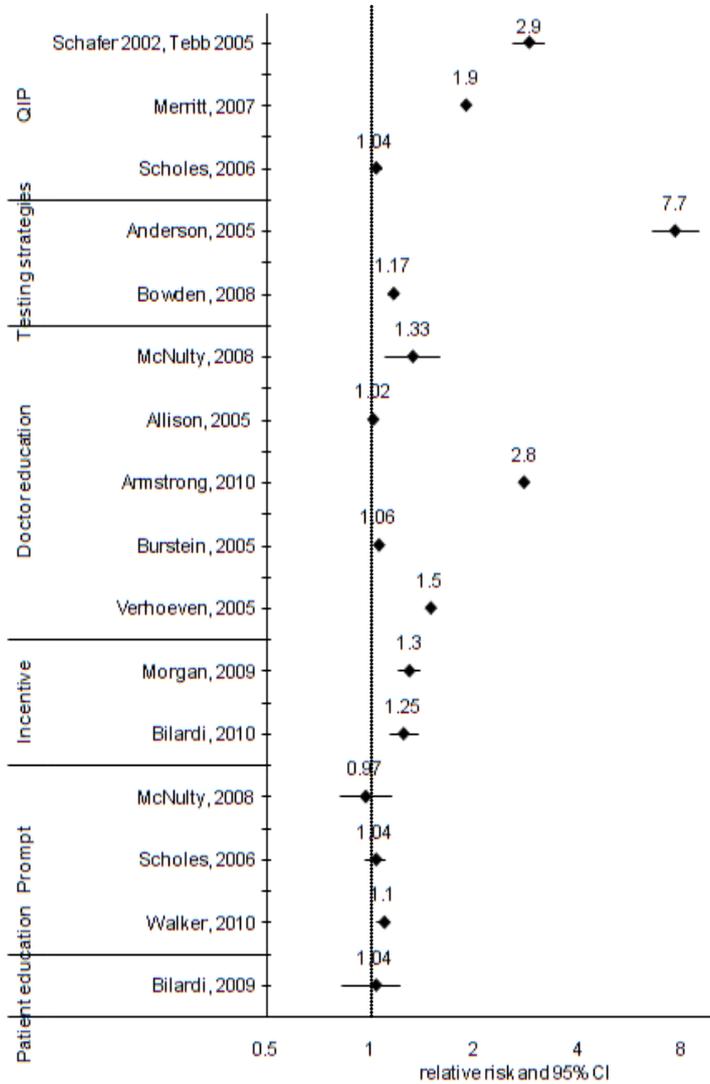
A large was also observed in a multifaceted quality improvement program targeting the screening of 14-18 year olds, in whom a screening rate of 65% was achieved in females by the end of the program compared to the 21% in the same time period at control clinics, and 49% in males compared to 5% in the control clinics ( $p < 0.001$ ). (159-160) Clinicians in the intervention group participated in a 4-stage clinical improvement initiative consisting of an baseline analysis of the gap between current and best screening practice in participating clinics, capacity building, developing a clinic flow chart and promotional material, monthly meetings of the team members to identify barriers to screening and strategies to overcome them, development of performance indicators, and introduction of universal urine specimen collection from all adolescents at registration, prior to examination.

Other strategies that were associated with significant but smaller increases in screening included linking chlamydia screening with a Pap smear in a RCT in Australia (153). In this study, about 25% of all chlamydia screening in both study groups were conducted among females aged 30-39 years with a very low chlamydia positivity obtained ( $< 1\%$ ). Integration of computer alerts within patient management systems based on age group (16-24) and female gender of clients in Australia, also demonstrated a small increase in screening. (163) An evaluation of the impact of provision of funding for free sexual health consultations for registered under-25 year olds in, New Zealand) reported a 10.4% screening rate in the intervention clinics, compared to 7.8% in the control clinics with no other statistical tests reported. (157) Small but significant increases in chlamydia screening were also reported due to an interactive educational workshop for clinic staff promoting screening in 16-24 year old females in the UK (155) and an internet-based education program for doctors, promoting screening in 16-24 year old females. (145)

Two intervention studies reported increases in screening but did not include any statistical analysis to demonstrate the increases were significantly different from control groups. (150, 156) One was a multi-faceted quality improvement program in Australia that introduced chlamydia screening during practice visits for other purposes. Doctors were trained to developed tactics for introducing the chlamydia test and had regular meetings to discuss progress. (156) However, the increase was not uniform or sustained. There was little change in screening levels at four practices, there was a transient increase in one and more sustained increase in a single practice. The other study was conducted in Scotland and introduced an external advisor at one clinic to raise awareness of chlamydia and train staff on guidelines, and compared chlamydia screening to another clinic without an advisor. (150) The number of chlamydia tests performed in a six month period before, increasing by 120% during the 6 month period when the advisor was present, with 70% of tests conducted by practice nurses. In the control clinics screening only increased by 11%.

Five studies targeted both males and females.(150, 152, 156-157, 159-160), and four of these found a greater increase in screening in males, compared with females (Table 5.2, Figure 5.3).(150, 152, 157, 159-160) while one which used the strategy of linking screening with women’s health-related consultations demonstrated a greater increase in screening in females (Table 5.2, Figure 5.3).(156)

**Figure 5.2: Crude relative risk of intervention studies to increase chlamydia screening, by intervention strategy type (n=16)**



CI=Confidence interval, QIP=quality improvement program

**Table 5.1: Findings of interventions to increase screening (n=16)**

Author surname, year	Country	Intervention type	Evaluation design	Clinics (n)	Target age group (yrs)	Sex	Intervention phase	Intervention group		Control group		Statistical findings reported	Crude RR (and 95% CI) calculated by reviewer
								Patients (n)	% tested	Patients (n)	% tested		
Walker(162) 2010	Aust	Prompt	RCT	66	16-24	F	During	12098	12.2%	12924	10.6%	OR=1.3 (95%CI:1.1-1.4) <sup>A</sup>	1.1 (1.04-1.12) <sup>F</sup>
			Before	11518	8.3%	11704	8.8%						
Scholes(158) 2006	US		RCT	23	14-20	F	During	1777	42.6%	1732	40.8	OR=1.03(95%CI:0.89-1.20) <sup>B</sup>	1.04 (0.97-1.10)
McNulty(155) 2008	UK		RCT	44	16-24	F	During	_*	_*	_*	_*	RR=0.97(95%CI:0.82, 1.15) <sup>C</sup>	0.97 (0.82-1.15) <sup>C</sup>
Bilardi(151) 2010	Aust	Incentive	RCT	12	16-24	F	During	1589	13.4%	1792	8.8%	OR=0.9 (95%CI:0.6-1.2) <sup>D</sup>	1.25 (1.14-1.38) <sup>F</sup>
			Before	2662	11.5%	2689	6.2%						
Morgan(157) 2009	NZ		Non-RCT	49	18-24	F, M	During	8208	10.4	17592	7.8	p=0.05 <sup>E</sup>	1.3 (1.2-1.4) <sup>F</sup>
		Roll out	10956	9.3	23457	8.1							
		Before	5509	8.3	11606	7.6							
Bowden(153) 2008	Aust	Alternative specimen collection	RCT	31	16-25	F	During	16082	6.9%	10794	4.5%	OR=2.1 (95%CI:1.3-3.4) <sup>G</sup>	1.17 (1.13-1.21) <sup>F</sup>
Anderson(143) 2005	Denmark		Non-RCT	3	16-25	M	During	617	29.4%	11204	3.8%		
			Before	607	3.7%	12007	3.4%	p<0.001 <sup>H</sup>	7.7 (6.6-9.0) <sup>F</sup>				
Verhoeven(161) 2005	Belgium	Doctor education	RCT	36	<35 yr	F	During	_*	7#	_*	4.72#	p=0.106 <sup>H</sup>	1.5 <sup>I</sup>
Burstein(154) 2005	US		Non-RCT	NS	15-26	F	During	_*	32%	_*	_*	NS	1.06 <sup>I</sup>
			Before	_*	30%	_*	_*						
Armstrong(150) 2010	Scotland		Non-RCT	2	15-24	F, M	During	_*	162^	_*	148^	NR	2.8 <sup>I,J</sup>
		Before	_*	57^	_*	121^							
Allison(145) 2005	US	Quality improvement program	RCT	191	16-26	F	After	_*	15.5%	_*	12.4%	p=0.044 <sup>K</sup>	1.02 <sup>I,K</sup>
			During	_*	13.3%	_*	13.0%						
			Before	_*	16.2%	_*	18.9%						
McNulty(155) 2008	UK		RCT	82	16-24	F	During	_*	_*	_*	_*	RR=1.33 (95%CI:1.10, 1.60) <sup>C</sup>	1.33 (1.10, 1.60) <sup>C</sup>
Bilardi(152) 2009	Aust	Patient education	Non-RCT	3	16-24	F, M	During	2997	5.3%	_*	_*	NS <sup>HM</sup>	1.04 (0.83-1.22)
		Before	2300	5.1%	_*	_*							
Schafer(159) 2002	US	Quality improvement program	RCT	10	14-18	F, M	During 16-18m	222	56.0%	237	14.6%	p<0.001 <sup>M</sup>	2.9 (2.6-3.2)
Tebb(160) 2005							During overall	2007	46.9%	2218	16.1%		
							Before	156	3.8%	147	11.1%		
Scholes(158) 2006	US		RCT	23	14-25	F	During	5650	42%	6105	40.1%	OR=1.01 (95%CI:0.92-1.12) <sup>B</sup>	1.04 (1.00-1.08) <sup>F</sup>
Merritt(156) 2007	Aust		RCT	6	15-24	F, M	Late-intervention	_*	442^	_*	_*	NR	1.9 <sup>I</sup>
		Before	_*	227^	_*	_*							

Aust=Australia, US=United States, UK=United Kingdom, NZ=New Zealand, RCT=Randomised controlled trial, OR=odds ratio, RR=relative risk, M=male F=female NR=not reported, NS=not significant. \*Information not reported, #mean tests per GP, ^Total tests

A=Mixed effect logistic regression with a 3-level hierarchy (patients, individual GPs and GP clinics)

B=Chi-square tests and logistic regression model

C=Multi-level model with aggregate baseline tests and positivity included as co-variables. Unit of analysis was GP practice

D=Mixed effect logistic regression with a 2-level hierarchy (patients, individual GPs)

E=t-test for differences in proportion of tests conducted in males and 16-24 year olds in the intervention practices compared to control practices

F=Screening rate in intervention clinic compared to control clinic during intervention period only

G=Logistic regression adjusted for clustering within general practices = number of female doctors per practices and number of doctors enrolled in the practice were included in the model

H= Test for equality in proportions

I=Insufficient information to calculate 95% CI

J= Total tests before intervention compared to during the intervention in intervention clinics only

K=An intention to treat analysis at the clinic level comparing mean post-intervention screening rates for the two groups. A general linear model adjusted for pre intervention done and intra intervention screening rates using repeated-measures analysis

L= F=Screening rate in intervention clinic compared to control clinic post intervention

M= only p values for male and females estimates provided in paper, both gave similar result, so summary provided

**Table 5.2: Findings of interventions to increase screening, by sex (n=5)**

Author surname, year	Intervention type	Sex	Intervention phase	Intervention group		Control group		Statistical findings reported	Crude RR (95% CI) calculated by reviewer
				Patients (n)	% tested	Patients (n)	% tested		
Morgan(157) 2009	Incentive	F	During	4018	16.8%	9068	13.2%	NR	1.3 (1.2-1.4)
			Roll out	5368	15.5%	12124	13.7%		
			Before	2676	13.9%	6077	13.0%		
		M	During	4190	4.2%	8524	2.1%	p=0.05 <sup>A</sup>	2.0 (1.6-2.5)
			Roll out	5588	3.4%	11333	2.1%		
			Before	2833	3.0%	5529	1.7%		
Merritt(156) 2007	Quality improvement program	F	Late-intervention	-*	10.2% <sup>C</sup>	-*	-*	NR	1.5 <sup>B</sup>
			Before	-*	6.7% <sup>C</sup>	-*	-*		
		M	Late-intervention	-*	6.3% <sup>C</sup>	-*	-*	NR	1.4 <sup>B</sup>
			Before	-*	4.5% <sup>C</sup>	-*	-*		
Armstrong(150) 2010	Doctor education	F	During	-*	146 <sup>^</sup>	-*	138 <sup>^</sup>	NR	2.8 <sup>B,D</sup>
			Before	-*	53 <sup>^</sup>	-*	113 <sup>^</sup>		
		M	During	-*	16 <sup>^</sup>	-*	10 <sup>^</sup>	NR	4.0 <sup>B,D</sup>
			Before	-*	4 <sup>^</sup>	-*	8 <sup>^</sup>		
Bilardi(152) 2009	Patient education	F	During	2002	6.4%	-*	-*	0.95 <sup>E</sup>	1.01 (0.78-1.30)
			Before	1548	6.3%	-*	-*		
		M	During	995	3.0%	-*	-*	0.77 <sup>E</sup>	1.13 (0.65-1.98)
			Before	752	2.7%	-*	-*		
Schafer(159) 2002, Tebb(160) 2005	Quality improvement program	F	During 16-18m	101	65%	109	21%	p<0.001 <sup>F</sup>	2.76 (2.40-3.18)
			During overall	1017	47%	1194	17%		
			Before	80	5%	86	14%		
		M	During 16-18m	121	48.5%	128	9.1%	p<0.01 <sup>G</sup>	3.08 (2.62-3.62)
			During overall	990	46.7%	1024	15.1%		
			Before	76	2.6%	61	7.0%		

OR=odds ratio, RR-relative risk, \* Information not reported, M=male F=female, NR=not reported  
<sup>^</sup>Total tests

A= t-test for differences in the proportion of tests conducted in males and 16-24 year olds in the intervention practices compared to control practices

B= Insufficient information to calculate 95% CI

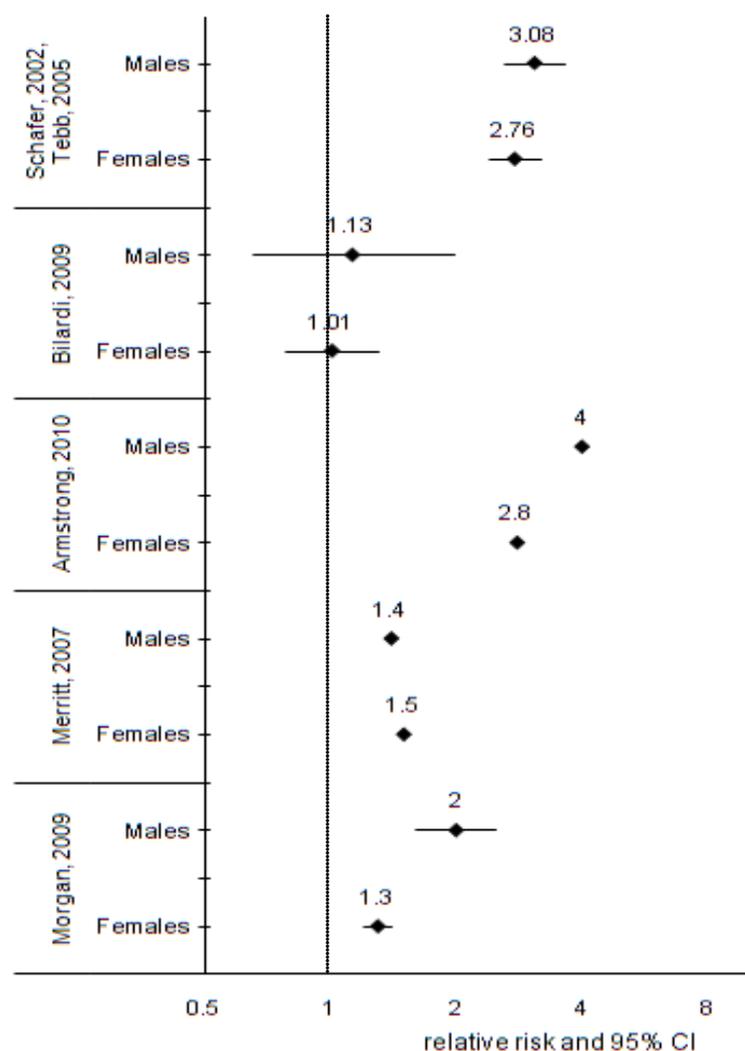
C= Screening rates based on 4 of the six clinics in the intervention clinics only

D=Screening rate in intervention clinic compared to control clinic during intervention period only

E= Test for equality in proportions

F=Assessed the statistical significance of the time by group effect using an F test

G=Adjusted for differences in ethnicity between study groups at baseline

**Figure 5.3: Relative risk of intervention studies to increase chlamydia screening, by sex (n=4)**

CI=Confidence interval

Armstrong(150), Merritt(156) only total tests reported and no statistical tests done, so relative risk calculated by reviewers (without 95% CIs)

The remaining eight intervention strategies that did not result in an increase in chlamydia screening were: a written chart prompt in the US;(158) an educational package (video and text) on communication skills for sexual history taking in Belgium(161); clinician referral of patients to an interactive website called “Youth Check Your Risk’ post-consultation in Australia(152); laboratory forms modified to include information about chlamydia screening in the UK(155); screening recommendations and provider training in the US(154); a \$5 (AUD) incentive in Australia (151); and a multifaceted quality improvement program in the US. (158) The quality improvement program included selecting ‘leaders’ within each clinic, an initial training session, regular feedback on screening performance, provision of guidelines, a prompt with Pap test, posters and chlamydia information. The control group received the standard chlamydia screening guideline – this was placed on each clinic’s intranet and all physicians were advised of its posting. The intervention did not significantly affect overall screening rates, but did lead to a significant increase in screening in women having a Pap test (74.6% versus 70.4%,  $p=0.04$ ) and a significant increase in screening in women undergoing a physical examination (64.4% versus 59.7%,  $p<0.01$ ).

## Discussion

In this review, we found that a variety of new approaches are being evaluated for their potential to increase uptake of Chlamydia screening among young people attending primary care clinics. A range

of potentially effective strategies were identified in these studies, with seven out of 16 finding statistically significant increases in screening rates and a further two reporting increases without a measure of statistical significance.

The two studies with greatest effect from the US and Denmark, involved systems change to enable all patients to be offered a chlamydia test. In contrast, the effect of the multi-faceted quality improvement programs by Scholes(158) and Merritt(156) which found no or limited increases in screening rates, may have been constrained because the interventions didn't cause sufficient systems change to results in the universal offer of screening, instead it was more opportunistic often linked with Pap smears. However in the study by Scholes(158) the lack of effect may also have been because the screening rates in the control population were very high (40.1%). This study placed standard chlamydia screening guidelines on each clinic's intranet in the intervention and control clinics, which in turn alerted all doctors of the need for screening and may have had a positive effect on screening rates.

The main limitation of linking chlamydia screening with Pap smears is that it is unlikely to capture young women (<20 years) ineligible for Pap smears in most developed countries, as demonstrated the study by Armstrong(150), where most of the increased screening occurred outside the target age range, and Bowden where 25% of chlamydia screening in both study groups were conducted among women aged 30-39 years.(153) Furthermore the extent of chlamydia screening would be reliant on recommended Pap smear screening frequency which does not necessarily coincide with recommended chlamydia annual screening frequency nor the recommended target age groups for chlamydia screening. The strength of this strategy is that screening could be conducted by practice nurses during women's health consultations, overcoming the barriers of insufficient time raised by clinicians(164-166), and concerns that discussing chlamydia in a consultation unrelated to a sexual health might upset patients.(164-165, 167)

Two doctor education strategies resulted in small but statistically significant increases in screening; interactive education workshops in general practice clinics in the UK(155), and internet-based Continuing Medical Education (CME), involving 4 modules released every 3 months to primary care physician offices in the US.(145) The interactive workshop is likely to require significant staff resources to roll out at a national level. The CME strategy may be cheaper but would be unlikely to reach all clinicians, with CME activities generally taken up by those clinicians interested in the area of sexual health.

Computer alerts were also shown in one study in Australia to achieve a small improvement in provider behaviour.(162) These findings are consistent with a Cochrane review on the effects of on-screen, point of care computer reminders on processes and outcomes of care, which found that computer reminders achieved a median improvement in process adherence of 3.8% (IQR: 0.4% to 16.3%) for test ordering.(168) In contrast, more passive prompts such as attaching a reminder sticker to medical records (155), and including chlamydia information on laboratory result forms(158), did not significantly increased chlamydia screening.

Although Bilardi demonstrated that a small incentive paid to practitioners did not increase chlamydia screening rates in Australia,(151) the study was limited by the fact that clinicians did not receive the payment until the conclusion of the trial and there was limited contact and ongoing communication from study investigators during the trial.(Personal communication - Hocking) The authors recommended future studies should include a higher incentive, and/or be associated with more regular feedback.(151) Merritt et al(156) also firmly concluded that an effective screening program will require significant incentives along the lines of the effective practice incentive

programs (PIP) for immunisation and Pap smears in Australia, and should be tied with good quality data to monitor performance and feed this back to practices. Incentive payments were used in the chlamydia screening pilots conducted in the UK. General practitioners were reimbursed up to £20 per eligible person screened, with screening acceptance rates within clinics of up to 81%.(169-170) However, once the chlamydia screening program was rolled out across the country, incentive payments were removed and screening participation rates within clinics fell to below 10%.(146) Incentive payments were offered to general practitioners to enrol patients for chlamydia screening in Amsterdam with 94% acceptance.(171) However, without RCT evidence, it is not possible to predict how well general practitioners would respond to an incentive payment to increase chlamydia screening rates.

None of the studies specifically explored the role practice nurses or other clinic staff could play in chlamydia screening in primary care, although in the study by Armstrong et al(82) practice nurses conducted 70% of screening by linking it with Pap smears, and in the study by Shafer(159) and Tebb(160) the urine jar was given to patients by reception staff at registration, prior to the examination. It is possible that practice nurses, and other generalist accredited health workers could play a greater role in chlamydia screening in primary care clinics.

This review has some methodological limitations. First, we did not search the grey literature so it is possible that some evaluations were not identified, particularly those with a negative outcome. Second, it is possible that there could have been participation bias in the observational studies. Third, the populations and health care systems in the study settings also varied, so the extent to which the findings would apply to other settings is uncertain. For example, the multi-faceted quality improvement intervention reported by Shafer(159) and Tebb(160) was conducted in paediatric clinics whereas as a number of other studies were in general practice clinics. Fourth, due to the heterogeneity of the interventions and outcomes we were unable to pool the outcomes to determine a summary effect.

To maximise the value of future evaluations, attention should be paid to methodological issues, including conducting statistical tests for significance, taking into account the pre-intervention screening rates or difference in other baseline characteristics into the analysis, and reporting screening rates rather than total tests done. The lack of reporting of screening rate in some studies is likely to be related to the need to obtain the number of unique patients from general practice patient management systems, which can be facilitated through data extraction software.(172)

The question remains as to which of these strategies should be employed in primary care to increase chlamydia screening. It is not clear which would be the most cost-effective due to absence of costing data for all the strategies to enable comparison of impact per unit cost. While the effect of the intervention seen in the study by Shafer(159) and Tebb(160) appeared to be relatively large, the intensity and complexity of the strategies employed would be most likely too difficult to implement universally. By contrast, the computer alert evaluated by Walker and colleagues(162) would be easier to disseminate with little impact on a general practitioner's time but would not achieve coverage levels of sufficient magnitude to have an impact on population prevalence as demonstrated in mathematical modelling.(173)

In the review we also did not identify any studies which assessed the impact of the intervention on annual testing. However the Australian Chlamydia Control Effectiveness Pilot (ACCEPt) is currently underway in Victoria, NSW and Queensland and plans to address this question. The ACCEPt study, led by Hocking et al(174), aims to assess the effectiveness of a multifaceted intervention to increase annual chlamydia testing in the target age group (men and women aged 16-29 year olds) who attend primary care services. The trial uses a cluster RCT design. The intervention will be randomised at the postcode level and all GP clinics and ACCHSs in each postcode (estimated at 2-3 clinics on average) will be invited to participate. Overall, about 80% of postcodes will be selected from rural/regional areas. The fundamental premise of this trial is that increased levels of testing can be achieved by providing a supportive intervention and that once levels of testing are increased high enough (more than 30%), the prevalence of chlamydia will fall. Clinics are currently being recruited and once randomized the intervention will be in place for up to 4 years. There will be approximately 160 general practice clinics and 10 Aboriginal Community Controlled Health Services recruited into the trial. GPs or practice nurses, where appropriate, will be requested to opportunistically offer a chlamydia test to all eligible 16 to 29 year old patients when they present for a consultation for any reason. Clinics will receive an evidence based multifaceted support package that will facilitate chlamydia testing. The control clinics will be asked to continue their usual practice and will be advised to offer chlamydia testing to eligible patients according to the professional guidelines and will receive a PID education package at enrolment and a chlamydia education package at conclusion

**Box 5.1: ACCEPt intervention strategies**

1. Identifying a 'practice champion' within each clinic
2. Development of a patient reminder system that will enable clinic staff to recall tested patients for follow up testing
3. Incentive payments to the GP for each test conducted. These payments will range from \$5 (AUD) per eligible test for up to 20% coverage to \$8 (AUD) per test for over 40% coverage
4. A computer alert in the medical records software prompting staff to discuss chlamydia testing;
5. Partner notification strategies including websites which contain information and strategies to help health care staff and patients undertake partner notification;
6. Provision of quarterly chlamydia testing reports to each GP and clinic;
7. Chlamydia and PID education package for GPs and other clinic staff including strategies for introducing chlamydia testing during a consultation.

Additional strategy in Victorian clinics

8. Practice nurses will receive sexual health training and the clinic will receive a \$10 incentive for every test conducted by the practice nurse

of the trial (Box 1).

In the same intervention, Hocking et al will assess the effectiveness of practice-nurse led testing in the Victorian clinics participating in the study. Practice nurses at intervention clinics will receive sexual health training and the clinic will receive a \$10 incentive for every test conducted by the practice nurse, consistent with practice nurse Medicare rebates for other preventative health procedures, such as immunisations, conducted by practice nurses (Box 1).

In 2011-2013, the Aboriginal and Torres Strait Islander Health Program, of the Kirby Institute will assess the effectiveness of a quality improvement program in four Aboriginal Community Controlled

Health Services in NSW to improve STI and blood borne virus (BBV) testing and management. The intervention is funded by NSW Health. The program titled SHIMMER will be evaluated using a before and after design. Clinics will be recruited from regional/rural areas. ACCHSs have already been consulted and have signed participation agreements. Clinics will receive an multifaceted quality improvement program including: (i) identifying a 'practice champion' within each clinic who will receive support and be encouraged to ensure that feedback and information are given to clinic staff; (ii) establishing best practice targets in STI and BBV testing and management; (iii) conducting a baseline site assessments to identify barriers to achieving 'best practice'; (iv) six monthly system assessments to monitor progress in achieving 'best practice'; (iv) provision of training and education materials for staff here required; (v) installation of software on the clinic's patient management system to enable population health level data to be collected and reports prepared; (vi) development of a tailored sexual health action plan; and (vii) health promotion initiatives to encourage increased attendance at the clinic. The intervention will commence in early 2011 and run for two years, with an interim analysis at 12 months.

Despite the limitations to the studies published, it appears that interventions that provide easy and systematic means of offering a chlamydia test to all eligible clients had the greatest impact on increasing screening in primary care.

## Chapter 6: Interventions to increase re-screening for chlamydial infections

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### Abstract

**Background:** Repeat infection with *Chlamydia trachomatis* following treatment is common and increases the risk of sequelae. Despite clinical guidelines recommending re-screening within 3 months of treatment, re-screening rates remains low. We undertook a systematic review to identify studies which compared rates of re-screening for repeat chlamydial infection between patients receiving and not receiving an intervention.

**Methods:** We searched Medline, EMBASE and conference websites from 2000 to September 2010 using variations of the terms "chlamydia" and "re-screening" and "intervention". We used meta-analysis methods to calculate the overall relative risk effect on re-screening rates by study design and strategy type.

**Results:** We identified eight randomized controlled trials (RCTs) and four controlled observational studies, all conducted in the United States. Four RCTs assessed mailed screening kits +/- reminders, with an average effect estimate of 1.3 (95%CI:1.1-1.5); two RCTs assessed motivational interviewing +/- reminders with a summary effect of 2.1 (95%CI:0.9-3.4); one RCT evaluated the effect of reminders with a relative risk (RR) of 9.7 (95%CI:1.3-71.3); and another RCT assessed the effect of a \$20 patient incentive with a RR of 1.2 (95%CI:0.6-2.2). Three controlled observational studies assessed reminder strategies with RRs of 1.97 (95%CI:1.76-2.21), 1.01 (95%CI:0.66-1.55), and 1.88 (95%CI:1.58-2.24) - a summary effect was not calculated due to significant heterogeneity; and one controlled observational study assessed the promotion of clinical guidelines with a RR of 1.4 (95%CI:0.96-1.9).

**Conclusion:** The review suggests that the use of mailed screening kits is an important strategy to increase re-screening and reminder systems are promising.

## **Introduction**

*Chlamydia trachomatis* is the most common reportable infection in the United States (US), Australia and other European countries.(117-118) In 2010, around 1.3 million new diagnoses were reported in the US.(117) Chlamydial infection is associated with adverse health outcomes including pelvic inflammatory disease (PID), ectopic pregnancy, and tubal infertility.(119-120) Repeat infections are associated with an increased risk of reproductive health complications.(120) As chlamydia is most commonly asymptomatic, screening is required for detection of infections.

Repeat chlamydial infections are common. The repeat infection rate following treatment in women in US cohorts was 15.5% at six months(175) and 22% at 12 months in an Australian study.(176) In men, the repeat infection rate was 10.9% at 4 months.(177) People treated successfully for chlamydia are at risk of re-infections due to sex with new partners or sex with previous partners who have not yet been treated. (178) Batteiger et al (2009) found that of the repeat infections identified among young women participating in a longitudinal cohort; 84.2% had evidence of re-infection, based on the presence of different genotypes, while 13.7% appeared to be treatment failures.(179) Although re-infection rates can be reduced by improved partner treatment rates of chlamydia re-infection are still high (>10%) among women whose partners received treatment.(180-181)

Since 2002 clinical guidelines in the US, Australia, and many European countries have recommended that any person diagnosed with chlamydia should be re-tested within 3 months of treatment.(142, 182-184) Despite this recommendation, re-screening for repeat chlamydial infection rates remains low in many clinical settings.(185-187) Over the past five years, a number of initiatives to increase re-screening for repeat chlamydial infection have been undertaken and evaluated. In this paper, we systematically review the evidence for the impact of those interventions.

## **Methods**

This systematic review was conducted according to the PRISMA statement.(188)

### Definitions

Re-screening was defined as a test occurring subsequent to an index episode of chlamydial infection. Repeat infection was defined as a positive chlamydia test after the index chlamydial infection, regardless whether the infection was due to new exposure following treatment, treatment failure or lack of initial treatment.

### Review strategy

The electronic bibliographic database Medline, EMBASE, the Cochrane Controlled Trials Register and the Australian New Zealand Clinical Trial Registry were searched to the end of September 2010. Only English language papers were included. Reference lists of selected studies were also checked for other potentially relevant studies. Websites and conference proceedings of the following conferences were also reviewed to identify potential unpublished studies including: the National STD prevention conference, Centres for Disease Control and Prevention, US; The International Society for Sexually Transmitted Diseases Research Meetings; the Australasian Sexual Health Conference; and the British Association of Sexual Health and HIV Meetings. Conference presentations were included if the corresponding full report was not available. If the required information was not available in the report or conference presentation, authors were contacted for unpublished data. Studies published from 2000 onwards only were included.

The following terms were used in the searches:

1. 'Re-screening' or 'repeat screening' or 're-testing' or 'repeat testing' or 're-infection' or 'repeat infection' or 'test for re-infection' or 'test of re-infection' or 'recurrent' or 'persistent' or 'test of cure' or 'treatment failure'
2. 'Chlamydia infections', or 'chlamydia', or 'Chlamydia trachomatis'
3. 'Intervention' or 'trial' or 'intervention studies'

The papers were reviewed and information was extracted by two authors independently. Disagreements were resolved by discussion and consensus.

A report was considered for inclusion in the review if it described the rate of re-screening for repeat chlamydial infection following an intervention aimed at increasing re-screening rates, and compared it with re-screening rates in a control group which did not receive the intervention, or a comparison period in the same population.

Publications were excluded if they did not include a comparison group or comparison period; reported on re-screening rates or repeat infection in the absence of a specific intervention; described surveys of patients or providers about re-screening for repeat chlamydial infection but did not measure re-screening rates; or if original data were not reported.

For each study that met inclusion criteria, information was extracted on the clinic location, the target population, the intervention strategy, the study design, the sample size, the statistical tests used, the outcomes of the evaluation including re-screening for repeat chlamydial infection rates and repeat infection rates.

From each study, we either abstracted or calculated the relative risk comparing re-screening rates in the intervention and control groups, as the primary effect measure for the study.

To examine evidence for publication and small study biases we drew funnel plots of log risk ratios against trial size (measured by standard error of the log risk ratio).

Where appropriate we pooled data using meta-analysis. We used the  $I^2$  test to estimate the approximate proportion of total variability in point estimates that can be attributed to heterogeneity other than that due to chance.(189) We used the following strategy to pool data, depending on the level of between study heterogeneity:

- $I^2 < 25\%$ , fixed effects meta-analysis to estimate the common RR (95% CI), assuming that all or most between trial variability is due to chance;
- $I^2 25-75\%$ , random effects meta-analysis(190) to estimate the average RR. We present both 95% CI, which express uncertainty around the average effect, which is assumed to be normally distributed, and the 95% prediction interval (PI), which takes into account the whole distribution of the effects(191);
- $I^2 > 75\%$ , heterogeneity too great for summary estimate to be calculated.

We explored possible reasons for heterogeneity by stratifying study results by study design (randomised versus non-randomised studies), and type of intervention.

Meta-analysis was performed in STATA 10 (StataCorp, College Station, TX, USA).

## Results

There were 243 articles identified in the search and the abstracts from these articles were reviewed (Figure 6.1). A total of 235 were excluded because they either described a study of diseases

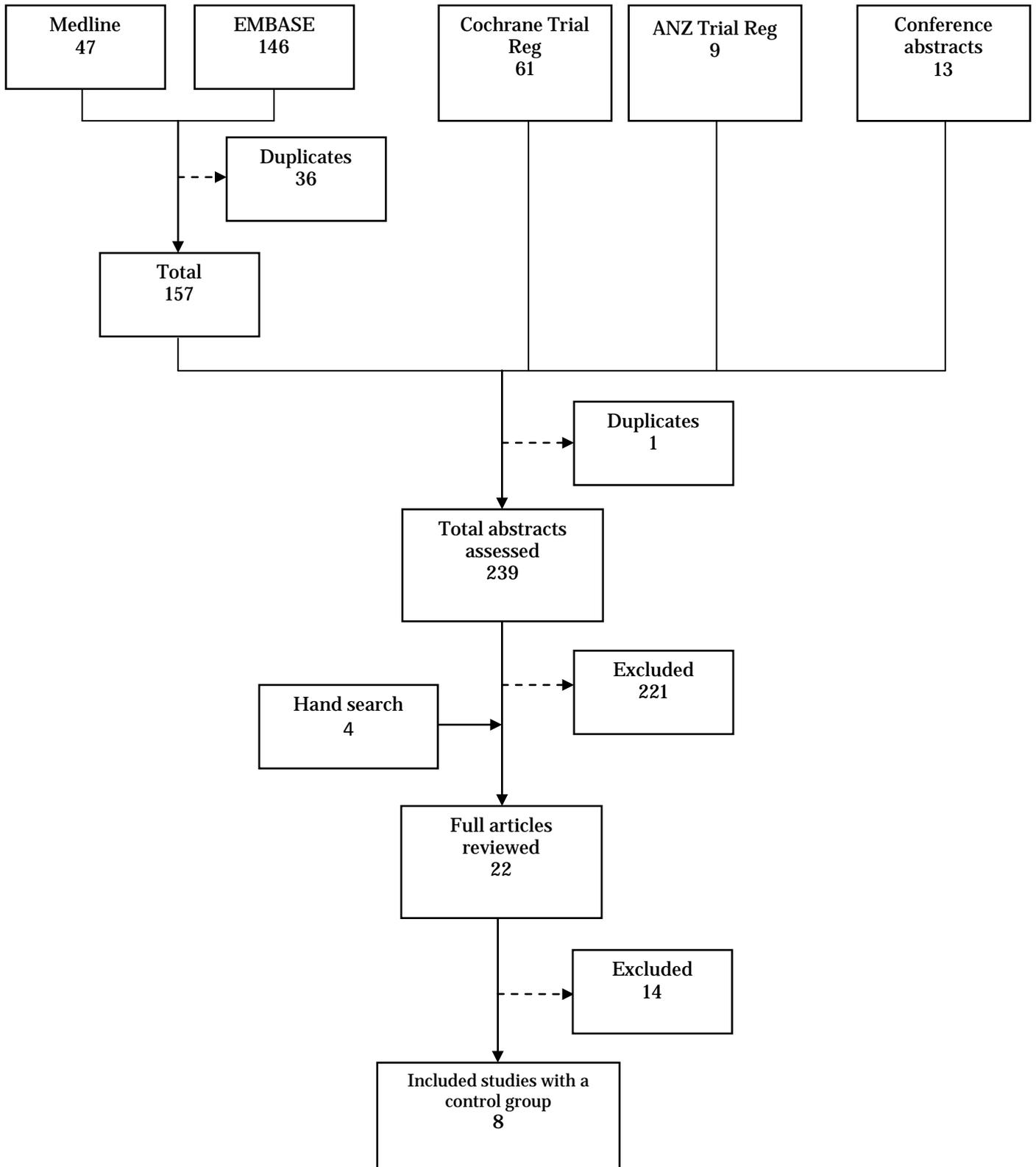
(including STIs) other than genital chlamydia (n=170); interventions to improve outcomes other than re-screening for repeat chlamydial infection (n=53); described a cross sectional or cohort study which reported re-screening for repeat chlamydial infection or repeat infection rate (n=5); described a cost-effectiveness analyses of the impact of re-screening for repeat chlamydial infection but no new empirical data comparing re-screening in intervention and control populations (n=1); there was no control group (n=3); were reviews or commentaries which did not contain original data (n=2); or described surveys of patients or providers about re-screening for repeat chlamydial infection but did not refer to an intervention (n=1) (Figure 6.1).

The remaining eight studies were included in the review.(192-199) The studies were all conducted in the US with four evaluated with a randomized controlled trial (RCT) design, and four others with a controlled observational design (Table 6.1). The eight studies evaluated 12 separate interventions aimed at increasing re-screening rates. One paper evaluated four distinct strategies(192) and another evaluated the intervention in two different clinical settings.(198)

Eight of the 12 strategies were based in sexual transmitted disease clinics,(192-195, 198) two in family planning clinics(197-198), and two in a variety of primary care clinics (including Infertility Prevention Project Clinics).(196, 199) The follow-up period for assessing whether re-screening had occurred varied across studies (Table 6.1). The sample size in the RCTs ranged from 102 to 808, and in the controlled observational studies ranged from 173 to 10,432.

The approaches taken to increase re-screening for repeat chlamydial infection could be grouped into five broad categories: single or combinations of reminders (phone, email, letter and postcard)(192-194, 196); mailed screening kits with or without reminders(195, 198-199); patient incentives(192); motivational interviewing for patients with or without reminders(192), and promotion of re-screening guidelines to clinicians(197) (Table 6.1).

**Figure 6.1: Search results**



**Table 6.1: Interventions aimed at improving chlamydial re-screening, overall finding (n=12)**

Author, year	Intervention type	Intervention strategy	Design	Sex	Target age groups (yrs)	Clinics (n), type	Re-test outcome time period	Intervention on phase	Intervention group		Control group		OR 95% CI , p value as reported in paper	Crude relative risk (95%CI) calculated by reviewers
									Patients (n)	Re-tested (%)	Patients (n)	Re-tested (%)		
Gindi(197) 2004	Promotion of guidelines	Promotion of guidelines	Before-After	F	NR	13 FPCs	3-4m	During	916	5.4%	-	-	NR	1.35 (0.96-1.90)
								Before	2120	3.96%	-	-		
							1-6m	During	861	22.8%	-	-	NR	1.15 (0.94-1.41)
								Before	622	19.77%	-	-		
Malotte(192) 2004 Study 2	Motivational interviewing +/- reminder	Motivational interviewing	RCT	F, M	14-30	1 SHC	≤3 m	During	25	12.0%	29	3.4%	OR=2.5 (95%CI:0.2-28.0) <sup>A</sup>	3.48 (0.39- 31.38)
Malotte(192) 2004 Study 1		Motivational interviewing plus telephone or letter reminder	RCT	F, M	14-30	2 SHCs	≤3 m	During	136	23.9%	141	11.4%	OR=2.5 (95%CI:1.3-4.8) <sup>A</sup>	2.14 (1.24- 3.70)
Malotte(192) 2004 Study 1	Incentive	\$20 patient incentive	RCT	F, M	14-30	2 SHCs	≤3 m	During	144	13.2%	141	11.4%	OR=1.2 (95%CI:0.6-2.4) <sup>A</sup>	1.16 (0.62- 2.17)
Gudgel(196) 2006	Reminder	Phone, letter or email reminder in 2/3 clinics	Before-After	F, M	NR	55 PCCs	2.5-6m	During	5863	16.0%			NR <sup>B</sup>	1.97 (1.76-2.21)
Before								4569	8.1%					
Kohn(193) 2010		Phone reminder plus letter reminder for non-attenders	Before-After	F	NR	1 SHC	1-5m	During	65	36.9%			NS <sup>C</sup>	1.01 (0.66-1.55)
								Before	88	36.4%				
Malotte(192) 2004 Study 2		Phone reminder	RCT	F, M	14-30	1 SHC	≤3 m	During	27	33.3%	29	3.4%	OR=12.3 (95%CI:1.4-112.0) <sup>A</sup>	9.67 (1.31-71.31)
Paneth-Pollak(194) 2010	Postcard reminder	Controlled observational	F, M	NR	10 SHCs	2.5-4m	During	1267	14.1%	3861	7.5%	p<0.0001 <sup>C</sup>	1.88 (1.58-2.24)	
							Before	-	-	1092	8.6%	p<0.0001 <sup>C</sup>	-	
Cook(199) 2007	Mailed screening kit	Mailed screening kit	RCT	F	15-24	11 PCCs	Average tests per person per yr	During	~99	2.38	~99	2.02	Rate ratio=1.18 (95%CI: 1.03-1.35) <sup>D</sup>	1.18 (1.03-1.35)
Sparks(195) 2004		Option of mailed screening kit or clinic re-screening	RCT	F, M	>14	1 SHCs	28 days	During	60	45%	62	32%	OR=1.7 (95%CI:0.8-3.8) <sup>E</sup>	1.39 (0.88-2.20)
Xu(198) 2008		Mailed screening kit plus subset received telephone reminder before scheduled re-screening (STD clinics)	RCT	F	>15	3 SHCs	≤3 m	During	407	31.9%	401	25.4%	p=0.04 <sup>E</sup>	1.26 (1.01-1.56)
		Mailed screening kit plus subset received telephone reminder before scheduled re-screening (FPCs)	RCT	F	>15	FPCs	11-15 weeks	During	407	21.3%	401	15.5%	p=0.04 <sup>E</sup>	1.38 (1.02-1.86)
							≤3 m	During	~202	48%	~202	28%	p<0.001 <sup>E</sup>	1.70 (1.31-2.21)
11-15 weeks	During	~202	27%	~202	20%	p=0.1 <sup>E</sup>	1.38 (0.96-1.97)							

SHC=Sexual health clinic, FPC=Family Planning Clinic, IFC=Infertility clinic, PCC=Primary care clinic, RCT=Randomized controlled trial, m=month, yr=year, M=male, F=female, NR=not reported, NS=not significant

~total sample size given in RCT, but not sample size in each arm, thus the total was divided by 2

A= Intention-to-treat analysis. Multiple logistic regression analysis controlled for age, sex, race/ethnicity, education, employment status, and study location, B=Chi-square test conducted on females rates only (p<0.0001)

C=The statistical test used was not reported, D=Intention-to-treat analysis, E= Chi-square test or t-test for equality of proportions

Re-screening rates

As shown in Table 6.1, the seven strategies that significantly increase in re-screening were: phone, letter or email reminder(196); phone reminder(192); postcard reminder(194); mailed screening kit(199); mailed screening kit plus subset received telephone reminder before scheduled re-screening at sexual transmitted disease clinics(198); mailed screening kit plus subset received telephone reminder before scheduled re-screening at family planning clinics(198); and motivational interviewing plus telephone or letter reminder. (192)

The five strategies that produced no significant increase in re-screening were the distribution of re-screening clinical guidelines by email or memo and conferences to clinicians(197); motivational interviewing to patients at the initial visit to encourage return for screening(192); a \$20 incentive (cash or supermarket voucher) given to patients when they returned for re-screening(192); a reminder by phone, and letter for non-attenders(193); and an option of mailed screening kit or clinic re-screening, compared to the control group who were recommended to return to the clinic for re-screening. (195)

Among those studies which presented re-screening rates for both males and females, the re-screening rates in males were generally lower than females in the control group, and in some studies and settings the intervention increased re-screening preferentially in females, and in others it increased more markedly in males (Table 6.2). (192, 194, 196)

**Table 6.2: Interventions aimed at improving re-screening for repeat chlamydial infection, by sex (n=4)**

Author, year	Intervention (comparison strategy)	Re-test time period	Clinic	Target group	Intervention phase	Intervention group		Control group		p value reported in paper
						Patients (n)	Re-tested (%)	Patients (n)	Re-tested (%)	
Malotte(192) 2004 Study 1	\$20 incentive	<=3 m	Clinic 1	F	During	-	6.9%	-	13.8%	NR
				M	During	-	23.3%	-	17.7%	NR
			Clinic 2	F	During	-	9.1%	-	17.6%	NR
				M	During	-	13.5%	-	7.7%	NR
Malotte(192) 2004 Study 1	Motivational interviewing plus telephone or letter reminder	<=3 m	Clinic 1	F	During	-	28.6%	-	13.8%	NR
				M	During	-	17.9%	-	17.7%	NR
			Clinic 2	F	During	-	29.0%	-	17.6%	NR
				M	During	-	22.4%	-	7.7%	NR
Paneth-Pollak(194) 2010	Postcard reminder	2.5-4m	All	F	During	480	17.5%	1203	10.0%	Women more likely to be re-tested than men in all groups: Intervention (p0.0071) Before (0.0261) non-intervention (p<0.0001)
					Before	-	-	396	11.1%	
				M	During	787	12.1%	2658	6.3%	
					Before	-	-	696	7.2%	
Gudgel(196) 2006	Phone, letter or email reminder	2.5-6m	All	F	During	4500	19.0%	-	-	p<0.0001
					Before	3268	9.0%	-	-	
				M	During	1363	6.0%	-	-	NR
					Before	1301	6.0%	-	-	

m=month, M=male, F=female, NR=not reported

## Meta-analysis

We calculated a crude RR for each paper. The use of any strategy to increase re-screening was associated with an  $I^2$  of 77% ( $p=0.001$ ) demonstrating significant heterogeneity thus we didn't calculate a summary effect estimate. Stratification by study design show that the heterogeneity was largely due to the observational studies. The use of any strategy to increase re-screening among observational studies was associated with an  $I^2$  of 83% ( $p=0.001$ ) and the use of any strategy evaluated by an RCT to increase re-screening was associated with an  $I^2$  of 1.5% ( $p=0.418$ ). On this basis, the meta-analysis was stratified by study design – RCT versus observational design.

The funnel plot for RCTs (Figure 6.2) showed there may be some publication bias. Two studies which appear on the lower right quadrant of the figure were both small sample size studies from the same trial by Malotte et al (2004) and only evaluated to disentangle significant effect observed in the initial study which had a much larger sample size. (192)

**Figure 6.2: Funnel plot for studies on effect of interventions on re-screening, RCTs only (n=8)**

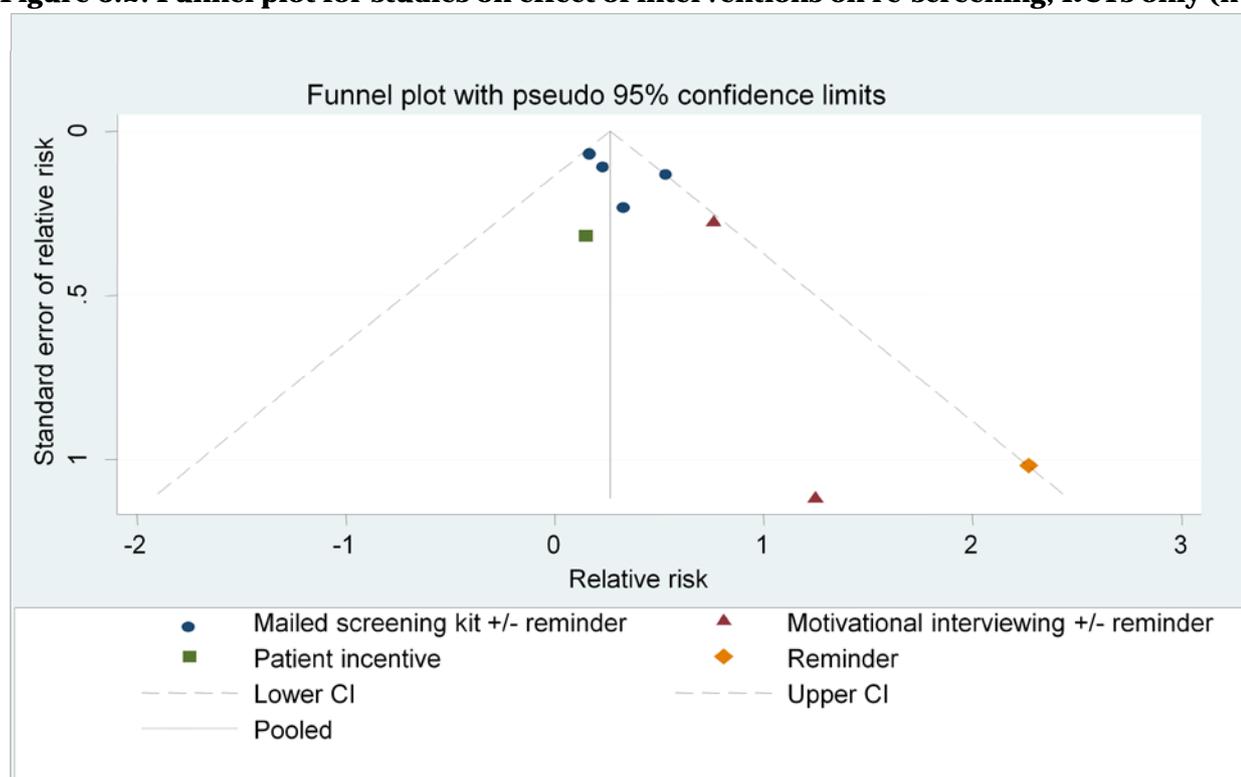
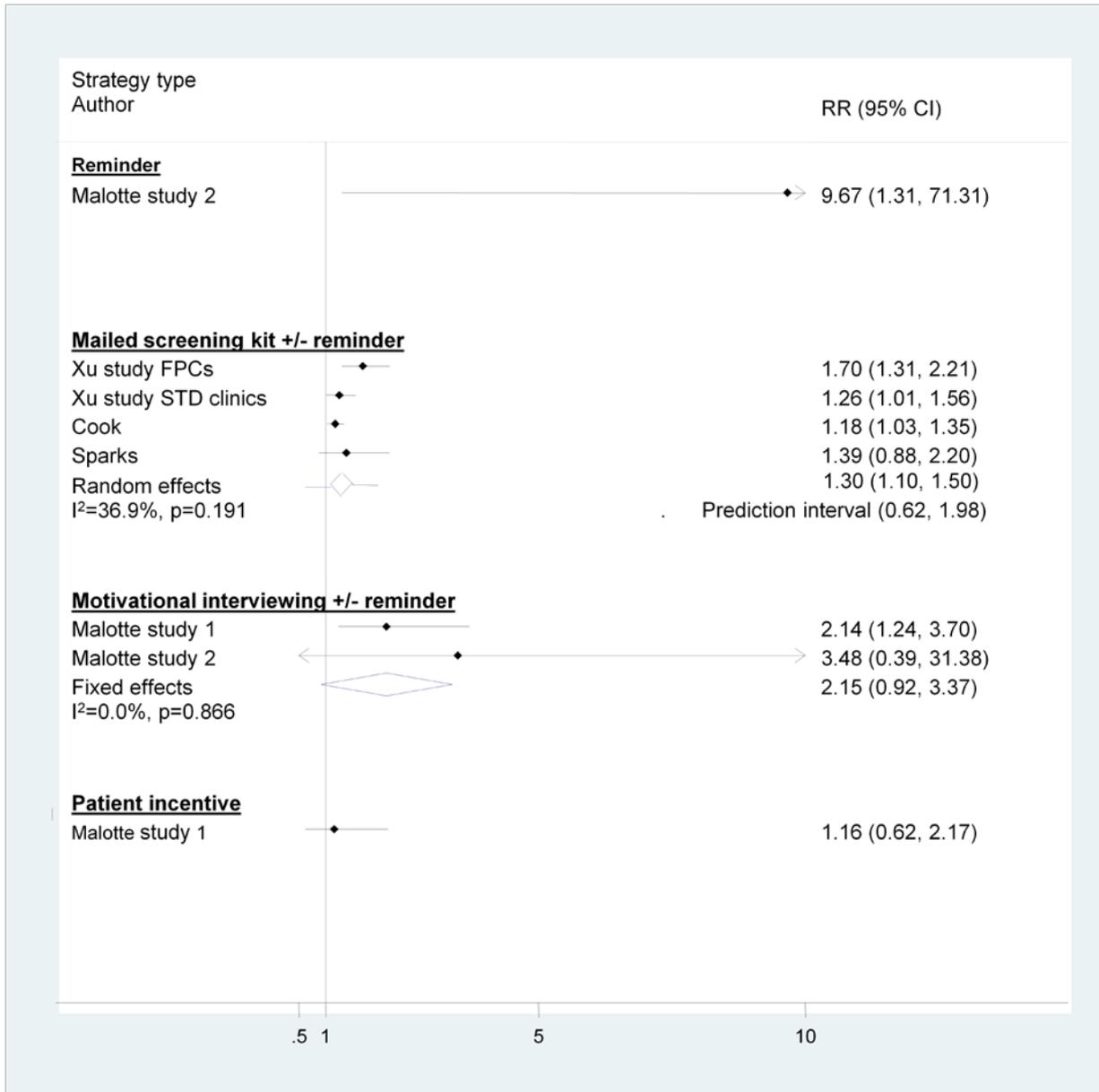


Figure 6.3a shows the effect of RCT interventions on re-screening by strategy type. There were four RCTs assessing mailed screening kits with or without reminders, with an  $I^2$  of 36.9% ( $p=0.191$ ). The random effects model showed the average effect was 1.3 (95%CI: 1.1-1.5) and the 95% prediction interval was 0.62- 1.98. There were two RCTs assessing motivational interviewing with or without reminders with an  $I^2$  of 0.0% ( $p=0.866$ ), thus a fixed effects model was used giving a summary effect of 2.1 (95%CI: 0.9-3.4). Only one RCT assessed the effect of reminders with a RR of 9.7 (95%CI:1.3-71.3), another RCT assessed the effect of patient incentives with a RR of 1.2 (95%CI:0.6-2.2).

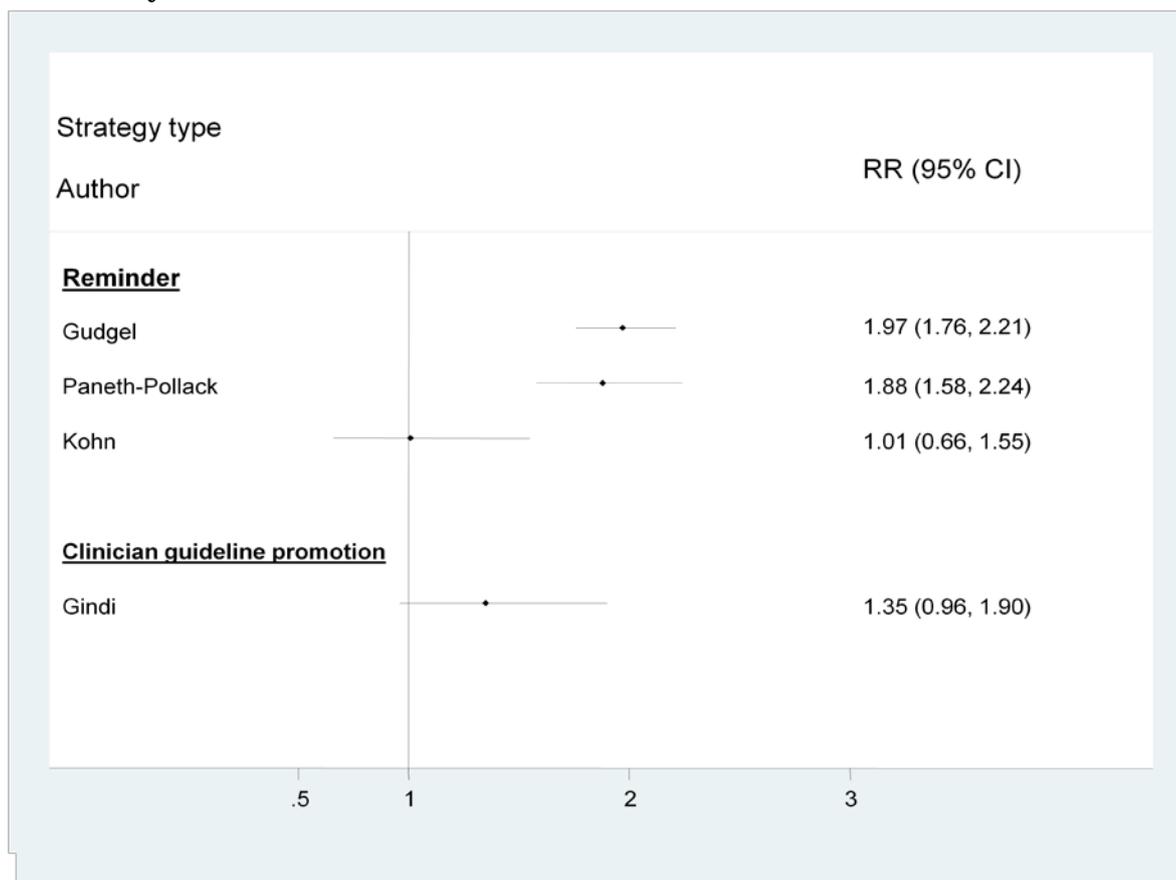
Figure 6.3b shows the effect of interventions on re-screening by strategy type evaluated using an observational studies design. Three studies assessed reminder strategies with RRs of 1.97 (95%CI:1.76-2.21), 1.01 (95%CI:0.66-1.55), and 1.88 (95%CI:1.58-2.24) - a summary effect was not calculated due to significant heterogeneity ( $I^2$  of 86%,  $p=0.001$ ). One other observational study assessed the effect of promotion of clinical guidelines with a RR of 1.4 (95%CI:0.96-1.9).

**Figure 6.3a: Effect of interventions on re-screening by strategy type , RCTs only (n=8)**



The diamond represents the combined relative risk and 95% confidence interval.

**Figure 6.3b: Effect of interventions on re-screening by strategy type, controlled observational studies only (n=4)**



\* The three reminder strategies gave an I-squared of 86% (p=0.001) demonstrating that heterogeneity was too great for a pooled estimate to be calculated

***Repeat infection rates***

The four studies that reported on repeat infections all found that among those re-tested, the repeat infection rate was lower in the intervention group compared to the control group (Table 6.3).(193-194, 198-199)

**Table 6.3: Repeat infection rate in interventions aimed at improving re-screening for repeat chlamydial infection (n=4)**

Author, year	Intervention (comparison strategy)	Target group	Re-test outcome time period	Intervention phase	Intervention group		Control group		OR 95% CI, p value reported in paper
					Re-tests (n)	Repeat infection (%)	Re-tests (n)	Repeat infection (%)	
Cook(1999) 2007	Mailed screening kit	Females 15-24 yrs	18 months	During	2.38 <sup>A</sup>	20.4 <sup>B</sup>	2.02 <sup>A</sup>	24.1	NS
Kohn(1939) 2010	Phone reminder plus letter reminder for non-attenders	Females	1-5m	During	24	12.5%	32	18.8%	NS
Paneth-Pollak(1994) 2010	Postcard reminder	Males and females	2.5-4m	During	179	12.3%	288	20.1%	p=0.05
				Before	-	-	94	25.5%	p=0.015
Xu(1989) 2008	Mailed screening kit plus subset received telephone reminder before scheduled re-screening (SHCs)	Females >15 yrs	11-15 weeks	During	82	14.6%	58	17.2%	p=0.68
	Mailed screening kit plus subset received telephone reminder before scheduled re-screening (FPCs)	Females >15 yrs	11-15 weeks	During	97	14.0%	56	12.0%	p=0.8

m=month, yr=year, A= Average CT/NG tests per person per yr, B=per 100 women years, NS=not significant

## Discussion

We identified eight studies and found that a variety of strategies can increase re-screening for repeat chlamydial infection in primary care. We found that mailed screening kits, reminders, and combinations of both approaches were the most effective at increasing re-screening.

Three studies were evaluated using a before-after design and it is possible that the intervention group patients may have had characteristics which facilitated re-screening irrespective of receiving the intervention. Some studies may also have underestimated re-screening rates, as a proportion of patients may have undergone screening at other health services. Most studies were conducted in sexual health clinics, raising the question of generalisability to other healthcare settings. It is possible that the primary care setting includes a group of patients who differ in terms of re-screening characteristics from those attending sexual health clinics. For example in the study by Xu (2008)(198) considerably higher re-screening rates were achieved in family planning clinics in the US compared with sexual health clinic.

The studies of mailed screening kits for self-collection of samples resulted in a significant increase in re-screening rates and with the meta-analysis random effects model showing an average effect of 1.3 (95%CI: 1.1-1.5) and  $I^2$  of 36.9% ( $p=0.191$ ) suggesting 37% of the variability in effect estimates is due to real study differences (heterogeneity) and 63% due to chance. The prediction interval of 0.62-1.98 contained one meaning that mailed screening kits with or without reminders may not increase re-screening when applied in some individual study settings. However in some of the mailed screening kit studies,(198-199) a reminder system was used in both the intervention and control group, potentially reducing the apparent benefit of the mailed screening kit. The mailed screening kit strategy reported by Xu et al (2008)(198) was found to have a cost benefit compared to returning to the clinic for re-screening; \$54 per self-collected test compared to \$118 if the specimen was taken in clinic.(200) Self-collected samples have been used in a variety of clinical and non-clinical settings to expand access to chlamydia screening in young women.(201-202) Self-collected urine or vaginal swabs for *C. trachomatis* can be tested with nucleic acid amplification tests, and thus should not result in any loss of accuracy compared to clinic-derived specimens.(203) Self-collected urine and vaginal specimens are both acceptable in men and women.(204)

Of the four reminder strategies identified in the review, one was evaluated using an RCT and showed a significant increase in re-screening; the other three were observational studies and could not be pooled due to substantial heterogeneity between studies, but two showed a significant increase in re-screening. Three of the four reminder strategies involved phone calls (+/- letters), and two of these three studies significantly increased re-screening. Phone reminder calls have been found to be useful in other contexts. A meta-analysis of 23 randomized trials found that phone reminders were effective in reducing missed appointments.(205) and a Cochrane review showed that postcards, letters, and telephone calls were all effective in improving vaccination rates in patients, with phone reminders being most effective but most expensive.(206) Phone reminders have been shown to be cost-effective in increasing re-screening(207) but phone reminder systems are resource-intensive because of the need for multiple attempts, often outside typical business hours. As demonstrated by Xu et al (2008) the reach can be low, with only 50% of women successfully reached by the phone call in this trial, however among those reached the re-screening rates increased to 55.4% in the intervention group, compared with 31.9% in the intervention group with a subset only receiving the reminder.(198) One study in our review assessed the impact of postcard reminders on increasing re-screening, and found it to be a successful strategy to increase re-screening for repeat chlamydial infection. This finding is consistent with research in other areas of health. For example, low-cost

self-addressed postcards have been successfully used to improve clinic attendance in dental care (208) and paediatrics(209-210)

Two reminder strategies that did not appear in our review was the use of text messaging and electronic medical record alerts. Text messaging has been found to have similar efficacy to letters and phone calls at encouraging behavior change, but is much cheaper.(211) Text message reminders also have the advantage of convenience and immediacy. Acceptability of text message reminders has been specifically demonstrated in the sexual health context.(212) Medical alerts which prompt clinicians to consider an outstanding medical procedure/test or vaccination when a patients attends for their next consultation are used in primary care for various purposes and could be particularly effective for re-screening reminders among clinicians in settings such as general practice where many patients attend the clinic on at least an annual basis.(213)

An internet-based survey of clinicians at family planning clinics in California found only 44% of clinicians reported using active reminder strategies for re-screening, 50% utilized low-intensity strategies (written materials, wall posters, verbal motivational interviewing, or unknown strategy), and 6% used no strategies. Of the active reminder strategies, 33% made follow-up appointments or gave appointment cards to patients; 29% used phone calls, 17% used letter reminders, 17% used chart-based reminders, 1% used e-mail reminders and no provider used text messaging as a strategy.(214) The most common barrier to re-screening was patients not returning to be re-tested.(214)

Motivational interviewing remains a potential strategy to be used to increase re-screening, however further empirical evidence is needed. Both studies included in the review were from the same trial by Malotte et al (2004) and motivational interviewing alone was only evaluated to disentangle the significant effect observed for motivational interviewing combined with a reminder, and thus was based on a small sample size.(192) Motivational interviewing have been demonstrated to be effective at encouraging other health behavior change such as smoking cessation, but the effect is generally modest and the strategy is resource intensive.(215-216)

The lack of effect seen for the patient incentives in the review study may be the result of the long time period between the initial visit and the re-screening visit. Malotte et al (2004)(217) suggested a combination of incentives and a reminder may have been more effective than either strategy alone by making the availability of the incentives more apparent to the participants closer to time of the re-screening visit.

A number of studies identified in the review, demonstrated that patients may choose different strategies depending on their personal circumstances and it is important for programs to provide different options. In the intervention group of the study by Sparks et al, 30% of participants selected the self-collected mailed screening kit strategy and 70% chose to attend the clinic for re-screening(195). The study by Cooks et al (2007), reported that although most women (179) received their home kit in the mail, 18 (9%) picked it up from the clinic.(199) A recent analysis of young women recruited from a music festival in Australia who were mailed a screening kit, showed those living with their parents were less likely to post back the screening kit.(218) These findings suggest that interventions need to be tailored to the needs and preferences of males and female, adolescent and adult patients.

Our review also showed that of the four studies which reported repeat infections rates, the rate was lower in the intervention arm compared with the control arm. As the studies in this review did not collect treatment data or detailed sexual behavior data we were unable to distinguish between re-infection, new infections and treatment failures. If we accept that most are re-infections based on

the study by Batteiger et al (2009),(179) this suggests that the interventions to encourage re-screening are reaching patients at lower-risk of chlamydial re-infection. For example in the RCT by Xu et al (2008)(198) although a similar number patients were enrolled in each arms of the study (around 400) and the re-screening rate increased to 31.9% in the intervention arms compared to the 25.4% in the control arm, there was a similar yield of positive tests at re-test (12 in the intervention arms vs. 10 in the control arm). Similarly in the postcard reminder intervention study described by Panetta Pollack et al (2010)(194) the proportion of persons returning for re-screening increased in the postcard group, but there was no change in the number of infections detected at re-screening. However strategies which are able to increase re-screening rates to 50% or above may find the numbers of infections detected are much greater. This raises the issue of whether trials are needed to assess whether re-screening can lead to a reduction in the complications associated with chlamydia such as PID.

This review has some methodological limitations. Although we searched multiple electronic bibliographic database and conference websites it is still possible that some evaluations were not identified, particular those with a negative outcomes. Also, due to the heterogeneity of the interventions we were unable to pool all interventions, and some types of interventions to determine a summary effect.

Based on our review of the literature, although chlamydia re-infection is an important health issue for women, we only identified eight published interventions studies, representing 12 strategies, to ensure re-screening 3 months after treatment. The review suggests that the use of mailed screening kits is an important strategy to increase re-screening and phone reminder systems are promising. Text message may be useful as a reminder strategy but has not yet been formally evaluated in this context.

## Chapter 7: Effectiveness of home-based screening using self-collected mail-in specimens at increasing testing uptake

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### Introduction

Most chlamydial infections are asymptomatic and thus regular screening is important to detect and treat infections, and also prevent onward transmission. (128, 219-220) To increase opportunities for testing, and reduce barriers associated with clinic visits, home-based screening programs using self-collected mail-in specimens have been implemented in many countries across the world. Recently, Shih et al (2011) published a review to assess if home-based screening using self-collected mail-in specimens resulted in more testing compared to conventional clinic testing (221). We summarize the findings of this review in this chapter.

### Methodology

Shih et al (2011) searched PubMed/Medline, from January 2007 to August 2010 using the following search terms:

*Sexually transmitted infections; chlamydia trachomatis; chlamydial infections; neisseria gonorrhoeae; mass screening; home care services; self care; self-examination; postal service; specimen handling; reagent kits; diagnostic*

Seven RCTs and two observational studies were short-listed by Shih et al (Table 7.1).

### Results

#### RCTs

Seven RCTs which compared home-based screening using self-collected mail-in specimens (here after referred to as *home-based sampling*) with clinic-based screening were identified by Shih et al. Out of these, two focused on home-based methods for contact tracing instead of STI screening, and were thus excluded from the review. Shih et al, divided the RCT in two categories, based on the country resources.

#### RCTs conducted in the US:

Graseck et al, (2010) compared the uptake of chlamydia testing in women who were posted kits to self-collect samples in the home compared to women who were encouraged to have a test for chlamydia at the clinic and any related clinic expenses were reimbursed by the study. (222) The study found that 56.3% of women in the home-based sampling group had a chlamydia test compared to 32.9% in the clinic group and this difference was statistically significant (RR=1.7, 95%CI:1.4-2.0). As part of the same study, a survey was conducted on testing satisfaction and all women who participated in the survey (n=122) said that self-vaginal swabs were easy to use, 70% said that vaginal self-sampling was extremely easy, 83% of home-testers preferred home sampling in the future, whereas only 49% of clinic-testers preferred clinic testing in the future (p<0.001).

Scholes et al, (2007) conducted a trial among men, comparing usual clinic testing to two different interventions: invitation letter to test with a test-request card that could be mailed back to receive a testing kit; or an invitation letter with a home testing kit. (223) More men completed testing when they were sent an invitation letter with a request card (3.6%, RR=5.6, 95%CI:3.6-7.8) or invitation

letter with a testing kit (7.8%, RR=11.1, 95%CI: 7.3-16.9) compared to usual clinic care (0.8%). However, more men completed testing when they actually received the testing kit compared to those who received a request card (RR=2.3, 95%CI:1.8-2.9).

Cook et al, (2007) reported on the Detection Acceptability Intervention for STDs in Young Women (DAISY) study, to show if testing rates increased by offering repeated home-based sampling at 6, 12 and 18 months.(224) Women in the clinic group also received a post-card at 6, 12 and 18 months encouraging them to test at a clinic. Overall, women in the home sampling group had more tests than women in the clinic group overall (RR=1.38, 95%CI:1.23-1.55).

### RCTs conducted in the resource-poor communities:

Two similar trials were conducted in South Africa and Brazil, comparing the effectiveness of home-based sampling with clinic-based screening. In both trials, women in the clinic-group were encouraged to get tested. Jones et al, (2007) found that more women in the home-based group were tested (60%) compared to clinic group (42%, RR=1.4, 95%CI:1.2-1.7).(225) Similarly, Lippman et al, (2007) found that more women tested in the home-based sampling group (93%) compared to the clinic group (89%, RR=1.04, 95%CI:1.00-1.09).(226) However, participants in home sampling group in this study were asked to drop their samples to the clinic, instead of mailing them, which reduces the benefit of home-sampling and could account for the lesser difference between the two groups. Both studies also reported findings of surveys conducted among participants and found that participants considered self-collection of vaginal samples to be easy and were comfortable doing self-collection. Jones et al, reported that self-collection at home was preferred by 58% of home group and self-collection at clinic was preferred by 66% of clinic group. Similarly, Lippman et al reported that self collection at home was preferred by 61% of home group; however, in this study only 26% of clinic group preferred self-collection at clinic.

**Table 7.1: RCTs comparing home based with clinic-based screening**

Author, publication year	Year of study	Country	Age group (years)	Sample size	Intervention	Sex	Intervention group		Control group		RR (95% CI)
							Sample	% screened	Sample	% screened	
<i>RCTs</i>											
Graseck et al, 2010 (222)	2009	US	-	558	Home-based screening	F	268	56.3%	280	32.9%	1.7 (1.4-2.0)
Scholes et al, 2007(223)	2001-2002	USA	21-25	8820	Invitation letter for screening plus test-request card	M	2940	3.6%	2940	0.8%	5.6 (3.6-8.7)
							2940	7.8%	2940	0.8%	11.1 (7.3-16.9)
Cook et al, 2007(224)	2000-2003	US	14-25	403	Home-based screening	F	197	-	191	-	1.38 (1.23-1.55)
Jones et al, 2007(225)	2003-2004	South Africa	14-25	626	Home-based screening	F	313	60%	313	42%	1.4 (1.2-1.7)
Lippman et al, 2007(226)	2004	Brazil	18-40		Home-based screening	F	410	93%	408	89%	1.04 (1.00-1.09)
<i>Observational studies</i>											
Graseck et al, 2010(227)	2008	US	-	462	Home-based screening	F	-	64.6%	-	31.6%	2.04 (1.51-2.76)
Williamson et al, 2007(228)	2001-2004	UK	13-25	4475	Home-based screening	F	-	46.1%	-	48.1%	-
						M	-	80.2%	-	-	-

RCT=Randomized Controlled Trial; RR=Relative Risk; CI=Confidence Interval

### **Observational studies**

Two observational studies were included by Shih et al. The first was conducted by Graseck et al (2010) and found that 75.5% women who participated in the study chose home-based sampling,

16.1% chose family planning clinics and 8.2% chose their own providers to get tested(227) and women in the home-based sampling group were more likely to be tested (64.6%) than those in the clinic group (31.6%, RR=2.04, 95%CI:1.51-2.76). The second study by Williamson et al (2007) offered home testing kits at commercial settings (e.g. record stores and pharmacies) and clinic-based testing at sexual health clinics or on college campuses.(228) Overall, 51.3% participants completed testing, with 51.3% of the testing at home (after obtaining the kits from commercial venues), 42% testing at clinic and 6.7% at college campus; 80.2% men used home testing compared to 46.1% women.

### **Economic and cost analysis**

Shih et al, found two studies which discussed the cost effectiveness of home-based STI sampling. However, one study was excluded as its objective was to evaluate a systematic population-level STI screening program compared to opportunistic screening, rather than comparing home-based and clinic-based screening. The study by Smith et al (2007) conducted in US, compared costs associated with STI screening in home vs. clinic setting, using data gathered from the DAISY trial.(229) They reported that home-based sampling was cost saving; clinic testing was calculated to be \$111 per test with \$49 in direct and \$62 in indirect costs, compared to \$25 per test in home testing. However, home sampling was not cost-effective when participants were recruited from surrounding neighbourhoods.

### **Discussion**

The review by Shih et al demonstrated that in almost all studies there were higher chlamydia testing rates achieved with home-based sampling compared to clinic-based testing. Studies included in the review also reported that home-based sampling is well-accepted among young people and often preferred compared to clinic testing. These findings suggest that home-based sampling using self-collected mail-in specimens, may be a good option for increasing testing in young, high-risk individuals, particularly those with less access to clinical services.

However, there are a number of factors to consider when interpreting these findings. First, a number of studies included in the review did not report the positivity rates to assess if there was a difference in chlamydia detection rates among young people who attend clinics versus the home-based sampling group. It is possible that young people who posted back their specimens were at lower risk than young people who attended the clinic. Often young people with new partners attend clinics for contraceptive advice and having a new partner is one of the strongest risk factors for chlamydia.

Second, a number of real world screening programs involving home-based sampling have reported lower chlamydia testing rates than the trials in this study. For example, in a population based mail out in the Netherlands, 34% (n=6,877) out of 20,495 young people, who received the home-testing kit, sent a urine sample for testing after the first mail out.(230) Similarly, in another population based study in France, 4,957 people were invited to receive home testing kit, out of which 3,780 accepted; and 29% (n=1,102) sent a sample after receiving the initial testing kit.(231) In both these studies, the testing rates increased when reminders were sent to those who didn't send a sample after the initial mail-out. To implement home-screening on a population basis, would require large scale registries like cervical cancer which are not cheap, and also mechanisms to provide treatment and offer partner notification for those testing positive.

## **Chapter 8: Health promotion interventions to improve STI knowledge, reduce risk behaviours and chlamydia or other STIs in young people**

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### **Abstract**

**Introduction:** The risk of acquiring chlamydia is directly related to an individual's sexual behaviour. Some sexual behaviours increase the chance of acquiring sexually transmissible infections (STIs) including chlamydia, whereas others have protective effects. To inform future planning for sexual health promotion in Australia, we conducted a review of reviews describing the effectiveness of health promotion strategies aimed at modifying STI risk factors and/or STI incidence in young people in developed countries.

**Methods:** This chapter summarises five reviews including two meta-analyses and three systematic reviews. We categorised studies into nine broad categories: school curriculum-based health promotion programs; curriculum-based abstinence programs; other school-based programs; clinic-based programs; school-based and school-linked clinic programs; multi-component programs; information technology-based programs; social marketing campaigns; and alcohol and drug use programs.

**Results:** School curriculum-based programs that support use of condoms and contraceptives with or without abstinence are associated with effective and consistent decrease in various sexual risk factors and increase in protective factors. However, abstinence-only curriculum based-programs programs are not associated with any change in sexual risk behaviour. Availability of condoms and contraceptives in schools does increase their uptake but whether this leads to an actual increase in use has not been confirmed. Clinic-based programs are associated with an increase in the use of condoms and contraceptives and also a decrease in incidence of STIs; however, the decrease in STI incidence is only seen mid- to long-term. Multi-component programs report beneficial effect on more than one behavioural outcome; they are associated with a delay in the initiation of sex, an increase in condom use, and a reduction in number of sexual partners and pregnancies. Information-technology based programs are inexpensive, acceptable, and easy to replicate, and report positive effects on more than one sexual behaviours. Programs that combine risk factors like alcohol and drug use with sexual risk factors do not report a significant effect on the sexual behaviour.

**Conclusion:** There are a number of different strategies that can be used to modify sexual risk behaviour associated with STIs in young people. Some strategies are able to modify a number of important behaviours, including condom use and number of sex partners, whereas others only modify one of these.

## **Introduction**

Chlamydia is the most commonly reported notifiable disease in Australia(11) and left untreated can lead to pelvic inflammatory disease (PID), and in turn infertility, ectopic pregnancy, and chronic pelvic pain(8-10). Over the past decade chlamydia notifications have increased by 240% in NSW, from 4,399 in 2000 to 14,948 in 2009 and the highest notification rates are observed in young people aged 20-24 years, followed by young people aged 15-19 years and 25-29 years.(13, 232-233)

The risk of acquiring chlamydia is directly related to an individual's sexual behaviour. Some sexual behaviours increase the chance of acquiring sexually transmissible infections (STIs) including chlamydia, whereas others have protective effects. Abstaining from sex and being in a long-term mutually monogamous relationship are protective factors. However, repeated behavioural surveys conducted nationwide in secondary schools show that fewer young people are abstaining from sex, with 39.9% of Australian secondary school students reporting ever having sexual intercourse in 2008, compared to 34.7% in 2002.(21). In addition, assuming mutual monogamy is dependent on a partner's truthful report about his or her sexual behaviour, which can be a risk in itself.

Individuals who have multiple sexual partners have an increased risk of encountering a person who is infected with an STI and their risk of acquiring an STI rises as the number of partners increase, especially if the sexual partnerships are concurrent.(234-235) In Australia, the percentage of young people surveyed from national secondary schools reporting more than three sexual partners in the past 12 months has increased from 19.9% in 2002 to 29.7% in 2008.(21) While having multiple sexual partners affects an individual's risk of STI exposure, inconsistent condom use can increase a young person's chance of becoming infected. Despite clear benefits of using condoms, about half of young people in Australia do not use them. The national secondary school survey shows that in 2008 50.5% of young people reported always used condoms in the past 12 months; compared to 52.1% in 2002.(21)

Drug and alcohol use, are not direct risk factors for STIs but may increase an individual's risk taking behaviour.(236). Poor knowledge of what STIs are, how they're transmitted, and their consequences, can also lead to young people engaging in behaviours that may put them at risk of infection. The 2008 national secondary school survey showed that about 90% of students knew that both men and women can pass on an STI; 76% knew that always using condoms does not offer complete protection from all STIs; and 60% knew that apart from HIV not all STIs are curable. However, there were some important gaps in knowledge such as only 47% of young people knew that both men and women can suffer from chlamydia, and only 55% knew that chlamydia can lead to infertility in women.(21)

In light of increasing chlamydia notifications each year and increasing sexual risky behaviour in young people in Australia, primary prevention of chlamydial infection must remain a top priority for public health in the 21<sup>st</sup> century. To inform future planning related to sexual health promotion in Australia, we conducted a summary of reviews describing the effectiveness of health promotion strategies aimed at modifying STI risk factors and/or STI incidence in young people in developed countries.

## **Methods**

This chapter summarises systematic or meta-analytic reviews that were identified by experts in the field and published since 2007. These reviews describe the effectiveness of health promotion interventions to improve STI knowledge, reduce behavioural risk factors and/or STI incidence in young people in developed countries. Health promotion was defined as "the process of enabling

people to increase control over their health and its determinants, and thereby improve their health".(237)

We categorised the programs into nine broad categories. These categories include the following types of studies:

- School curriculum-based health promotion programs: includes programs that are part of a sex education curriculum on use of condoms and other contraceptives, and may include abstinence.
- Curriculum-based abstinence programs: similar to above, however the educational content focuses only on sexual abstinence.
- Other school-based programs: refer to programs based in educational settings but not as part of the curriculum, run by peers, teachers or invited community members and includes classroom and/or external activities.
- Clinic-based programs: includes education/counselling initiatives delivered to patients within a clinical setting.
- School-based and school-linked clinic programs: includes non curriculum-based programs (such as condom vending machines) in school health clinics or schools, or program outside of schools that are run by the schools (such as programs at school-linked community based health clinics).
- Information-technology-based programs: involves delivering sexual health promotion through various information-technology mediums like internet, videos, email and Short Messaging Service (SMS).
- Social marketing campaigns: includes media campaigns aiming to reduce sexual risk behaviour.
- Multi-component programs: cover interventions including more than one of the strategies above.
- Alcohol and drug use programs: includes strategies aiming to reduce alcohol, drug use, violence, and sexual risk behaviour.

## Results

Five reviews including two meta-analyses and three systematic reviews were identified by key experts. Three of the reviews included studies conducted in the US only. Table 8.1 summarises the design of the five reviews including type, target population, setting, number of studies included, and details of the intervention. Table 8.2 summarises the effect of various programs on behavioural outcomes and table 8.3 summarises the effect of various programs on knowledge outcomes. Figure 8.1 and figure 8.2 show the percentage of programs that have a significant effect on reducing the number of sexual partners or increasing condom use; and also show the number of studies that report on the respective outcome.

**Table 8.1: Characteristics of included reviews**

Review, Year	Type of review	Target age group (years)	Country	Years	Design of studies included	Total Studies (n)	Primary outcome	Broad intervention category	Studies included (n)	Intervention details
Kirby, 2007 (238)	Systematic	12-18	US	1997-2007	Experimental or quasi-experimental design • Measured behaviour for sufficient time length • Sample size of 100 • Appropriate statistical analysis used	115	Teenage pregnancy and STIs	Curriculum-based abstinence only programs	8	Encouraged young people to remain abstinent
								Curriculum-based comprehensive programs	48	Support both abstinence and condom and contraceptive use
								Clinic-based programs	12	Protocols of clinic appointments, provision of emergency contraception
								School-based and school-linked clinics programs	4	Counselling, physical examination, pregnancy testing, STI diagnosis and treatment and provision of condoms and contraceptives
								Multi-component programs	8	Community activities like workshops and discussions, sex education, training, distribution of education material and condoms, involving various stakeholders and media campaigns
								Information technology	3	Videos, computer-based programs
								Alcohol and drug use programs	7	Character education, identity mentoring, abstinence, social development and school-community linkages
Shepherd et al, 2010 (239)	Systematic and meta-analysis	13-19	All countries	1995-2008	RCTs	12	STIs	School-based programs	12	Education/information provision, skills training, professional training, provision of resources and services, mass media and incentives
Kang et al, 2010 (240)	Systematic	15-25*	Aus	2000-2009	Experimental or quasi-experimental design	42	HIV and STIs	School-based programs	1	HIV positive speakers deliver AIDS education
								Clinic-based programs	1	Young people provided information on safe sex and condom use and given resources by GPs
								Multi-component programs	2	Peer educator training, sexual health education material development and distribution, workshops and information stalls
								Social marketing campaigns	2	Advertisements in print, radio and email, poster displays, use of SMS, interactive websites
								Information technology	2	Email and SMS to send health messages
Blank et al, 2010 (241)	Systematic	<19	US	1995-2008	Conducted on educational premises (schools, further education colleges, higher education, pupil referral units)	29	Teenage pregnancy, contraceptive use, sexual behaviour	Curriculum-based programs	4	Class-room based sexual health education combined with community volunteering or virtual world environment
								School-based clinics and condom provision in schools	6	Services included provision of condoms or contraceptives, education, counselling, pregnancy tests, health assessments
								Multi-component programs	4	School environment, staff development, after school instructions, parent education, school community linkages and services at school health centres
Scott-Sheldon et al, 2010 (242)	Meta-analysis	All	US	1991-2009	RCT or quasi-experimental design • Provided information needed to calculate size effect	32	Condom use, number of sexual partners, STIs (incl. HIV)	Clinic-based programs	32	Clinical setting (STI clinics) - STI education, counselling and testing, skills training (condom use and communication), and motivational components (risk awareness, risk feedback, attitude towards condom use or number of sexual partners)

\*some studies up to 30 years

RCT=Randomized Controlled Trial; STI=Sexually Transmissible Infections

**Table 8.2: Results of reviews – sexual behaviour outcomes**

Intervention category	Author surname, year	Delayed the initiation of sex		Reduced frequency of sex		Reduced number of sexual partners		Increased condom use		Increased contraceptive use		Reduced sexual risk taking		Reduced pregnancy (self report)		Reduced STIs (self report)	
		Outcome reported (n)	Significant change (%)	Outcome reported (n)	Significant change (%)	Outcome reported (n)	Significant change (%)	Outcome reported (n)	Significant change (%)	Outcome reported (n)	Significant change (%)	Outcome reported (n)	Significant change (%)	Outcome reported (n)	Significant change (%)	Outcome reported (n)	Significant change (%)
Curriculum-based abstinence programs	Kirby, 2007 (238)	8	13%	6	33%	5	20%	5	0%	4	0%	3	0%	4	0%	4	0%
Curriculum-based programs	Kirby, 2007 (238)	32	47%	21	29%	24	46%	32	47%	9	44%	24	63%	6	33%	2	0%
	Blank et al, 2010 (241)	1	100%	1	100%	0	-	0	-	0	-	0	-	2	100%	0	-
Other school-based programs	Shepherd et al, 2010 (239)	7	29%	4	50%	6	17%	7	43%	4	25%	0	-	2	0%	0	-
Clinic-based programs	Kirby, 2007 (238)	1	0%	3	33%	2	50%	4	75%	2	50%	2	100%	2	50%	4	0%
	Kang et al, 2010 (240)	0	-	0	-	0	-	1	0%	0	-	0	-	0	-	0	-
	Scott-Sheldon et al, 2010 (242)	0	-	0	-	15	Sig*	20	Sig*	0	-	0	-	0	-	22	Sig*
School-based and school-linked clinics and condom provision in schools	Kirby, 2007 (238)	2	50%	1	0%	0	-	0	-	2	50%	0	-	2	50%	0	-
	Blank et al, 2010 (241)	0	-	3	67%	0	-	1	100%	0	-	0	-	2	0%	0	-
Multi-component programs	Kirby, 2007 (238)	4	75%	2	0%	1	100%	2	50%	1	0%	0	-	1	0%	0	-
	Blank et al, 2010 (241)	0	-	1	0%	0	-	4	100%	2	100%	0	-	0	-	0	-
Information technology-based programs	Kirby, 2007 (238)	0	-	3	67%	2	50%	3	0%	0	-	1	0%	0	-	1	100%
	Kang et al, 2010 (240)	0	-	0	-	0	-	1	100%	0	-	0	-	0	-	0	-
Social marketing campaigns	Kang et al, 2010 (240)	0	-	0	-	0	-	1	0%	0	-	0	-	0	-	0	-
Alcohol and drug use programs	Kirby, 2007 (238)	2	50%	5	40%	0	-	2	50%	0	-	2	50%	0	-	0	-

n =Number of studies which reported the outcome

% =Percentage of studies which reported a significant change in the outcome

\* Meta-analysis shows that the outcome is significant; Number of individual studies which report significant outcome not given

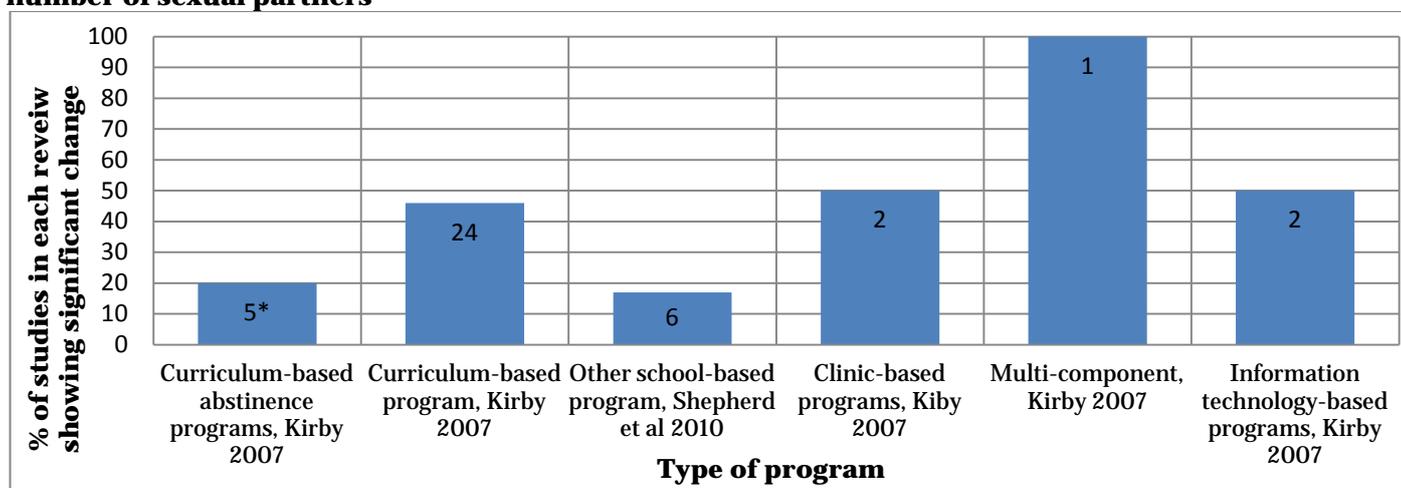
**Table 8.3: Results of reviews – knowledge outcomes (reported in the reviews)**

Intervention category	Author surname, year	Improved knowledge of STIs		Improved knowledge of HIV/AIDS		Improved knowledge of sexual health	
		Outcome reported (n)	Significant change (%)	Outcome reported (n)	Significant change (%)	Outcome reported (n)	Significant change (%)
Curriculum-based program	Kirby, 2007 (238)	8	100%	19	90%	3	100%
	Blank et al, 2010 (241)	0	-	0	-	1	100%
Other school-based programs	Shepherd et al, 2010 (239)	2	100%	5	80%	1	100%
Clinic-based programs	Kang et al, 2010 (240)	1	100%	0	-	0	-
Multi-component program	Blank et al, 2010 (241)	2	100%	0	-	0	-
Information technology-based programs	Kang et al, 2010 (240)	2	50%	0	-	0	-
Social marketing campaigns	Kang et al, 2010 (240)	1	0%	0	-	0	-

n =Number of studies which reported the outcome

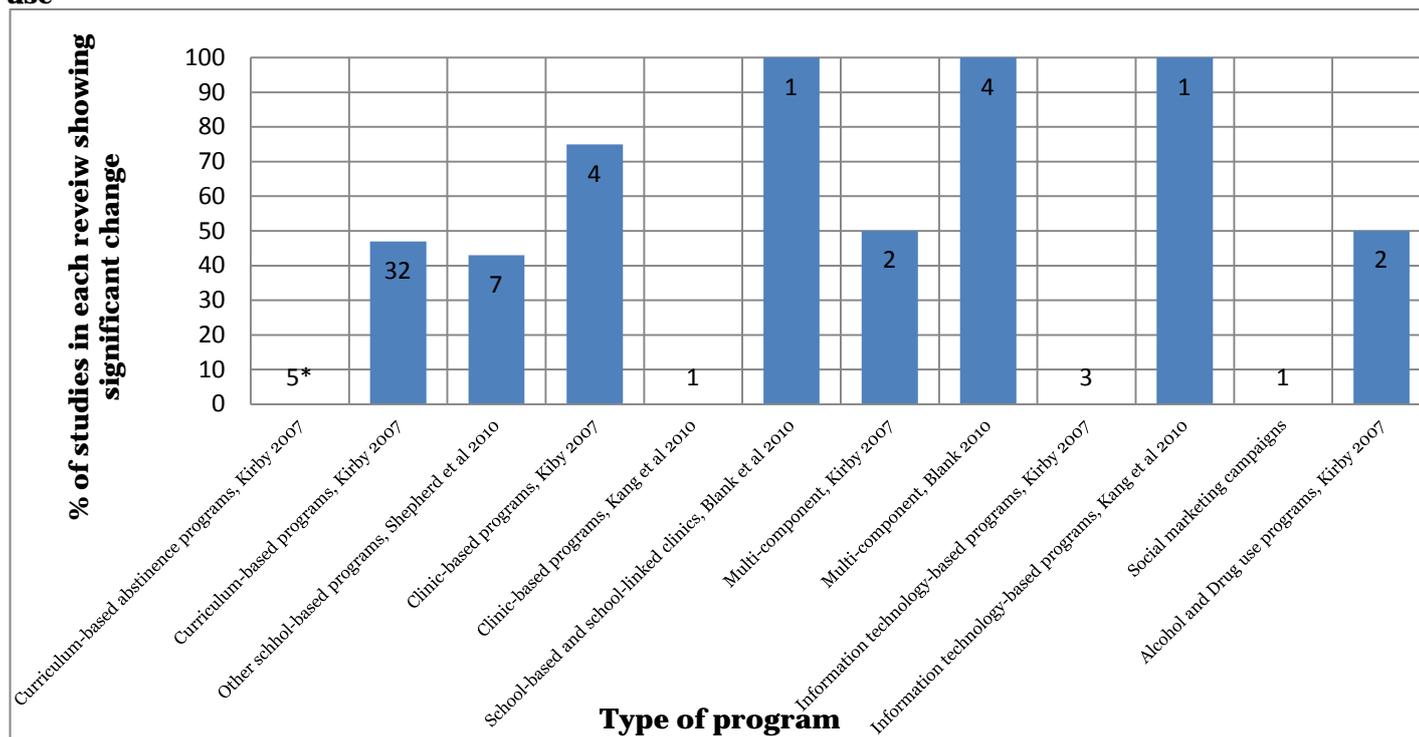
% =Percentage of studies which reported a significant change in the outcome

**Figure 8.1: Number and percentage of programs that had a significant effect on the reduction in number of sexual partners<sup>#</sup>**



\* Number of studies reporting outcome

# Only programs that reported on reduced number of sexual partners have been included

**Figure 8.2: Number and percentage of programs that had a significant effect on increasing condom use#**

\* Number of studies reporting condom use

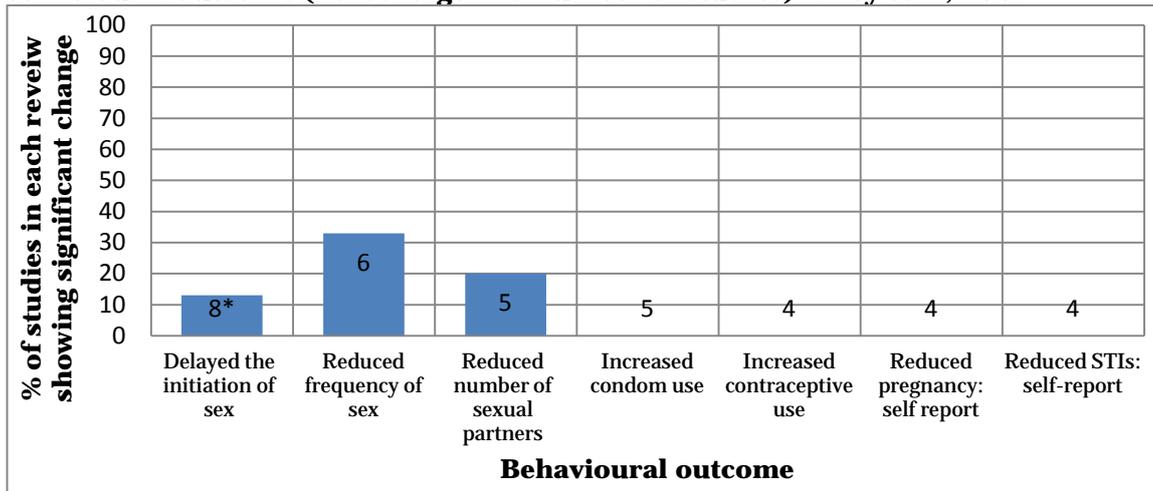
# Only programs that reported on increase in condom use have been included

### Curriculum-based programs

A systematic review by Kirby (2007)(238) identified 56 evaluations that measured the impact of curriculum-based sex and STI/HIV education programs. The review did not give any quantitative data about the effect of an intervention on an outcome; rather it described the number of studies that report a significant impact on an outcome. A variety of sexual behaviour outcomes were reported in the evaluations; with delay in the initiation of sex, and increase in condom use being the most common outcome. Biological outcomes such as reducing teen pregnancy and preventing STIs were reported in less than half of the studies (Table 8.2). The review divided the 56 programs into two categories: curriculum-based abstinence only programs; and comprehensive programs that supported both abstinence and use of condoms and contraceptives.

Eight curriculum-based abstinence only programs, considered by Kirby to have rigorous study designs, were included in the review. These programs were found to improve values about abstinence; however, only two of the eight programs showed moderately encouraging results on sexual behaviour. One delayed the initiation of sex and the other reduced the frequency and number of sexual partners. No studies reported increased condom and contraceptive use, or reduced pregnancy or STIs or sexual risk-taking (Figure 8.3).

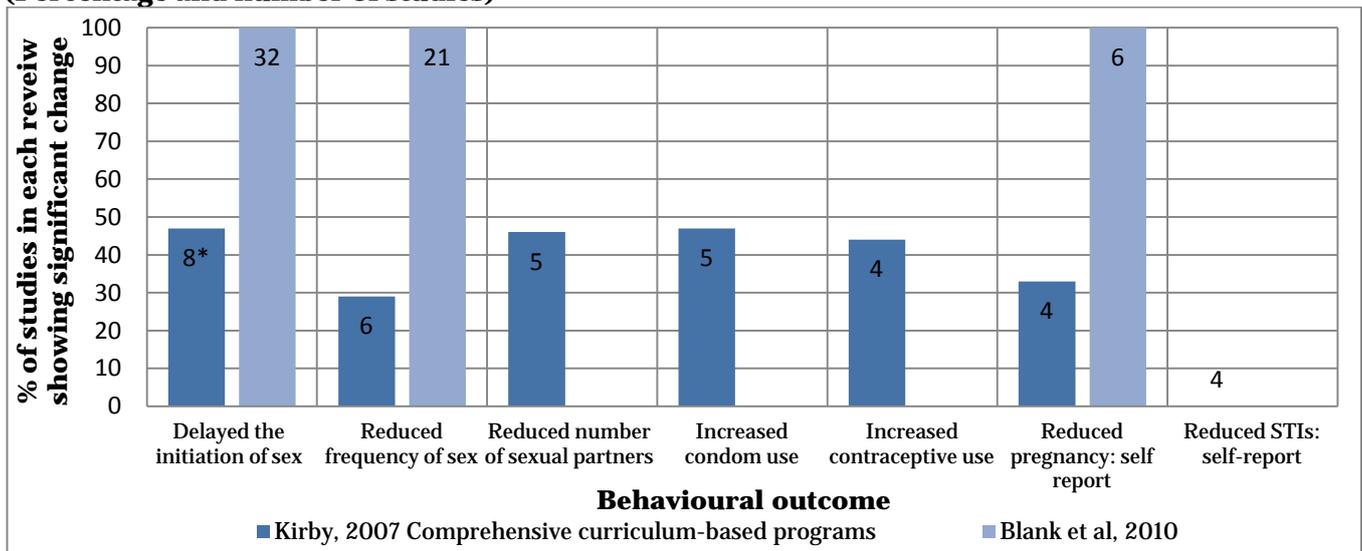
**Figure 8.3: Curriculum-based abstinence only programs reporting significant change in a behavioural outcome (Percentage and number of studies) Kirby et al, 2007**



\* Total number of studies reporting outcome

The Kirby (2007) (238) review also included 48 curriculum-based comprehensive sex and STI/HIV education programs which support abstinence and use of condoms and contraceptives. Two-thirds of the 48 programs resulted in statistically significant changes in delaying the initiation of sex, increasing condom and contraceptive use, reducing the frequency of sex, reducing number of sexual partners, and reducing sexual risk through changes in types of behaviour (Table 8.2, Figure 8.4). Around 40% of the 48 studies had significant changes on more than one of these behavioural outcomes. An in-depth analysis of programs (Table 8.4) revealed a number of program characteristics (related to development, content and implementation) that were consistently associated with effective programs, compared to programs that did not modify sexual risk behaviour or other outcomes.

**Figure 8.4: Curriculum-based programs reporting significant change in a behavioural outcome (Percentage and number of studies)**



\* Total number of studies reporting outcome

**Table 8.4: Characteristics of effective curriculum-based programs (238)**

<b>Development</b>	<b>Contents</b>	<b>Implementation</b>
<ul style="list-style-type: none"> <li>○ Include multiple experts in different areas</li> <li>○ Assessment of needs and assets of target group</li> <li>○ Use of logic model approach</li> <li>○ Consistency of activities with community values and available resources</li> <li>○ Pilot-testing</li> </ul>	<ul style="list-style-type: none"> <li>○ Focus on clear health goals</li> <li>○ Focus on specific type of behaviour leading to health goals</li> <li>○ Focus on sexual psychosocial risk and protective factors that affect sexual behaviour</li> <li>○ Creating safe environment</li> <li>○ Include multiple activities</li> <li>○ Use of sound teaching methods</li> <li>○ Appropriateness of activities according to culture, age and sexual experiences of the target group</li> <li>○ Logical sequence of topic</li> </ul>	<ul style="list-style-type: none"> <li>○ Support from appropriate authorities</li> <li>○ Selection of educators with desired characteristics and training them</li> <li>○ Activities to recruit and retain participants</li> <li>○ Implementation of activities with fidelity</li> </ul>

A review by Blank et al (2010), included four controlled before and after studies that reported on large interventions focused on class-room based sexual health education lessons.(241) Three studies looked at interventions that combined class-room sexual health education (including classroom based discussions, tailored computer based activities and peer videos) with community-volunteering (providing service in community settings like nursing homes, senior centres etc).(243-245) These interventions prevented both pregnancy and risky behaviour. The fourth intervention combined class-room sexual health education with an additional computerized element based on a 'virtual world environment'.(246) Findings from this study suggest that a virtual world intervention could be effective when combined with a curriculum based intervention to change sexual risk behaviour. The intervention group had significantly better understanding than the control group of how reproduction works, consequences of sex, and the importance of limiting sexual experiences.

### **Other school based programs**

The review by Shepherd et al (2010),(239) examined the effectiveness of school-based programs through a meta-analysis and cost-effectiveness analysis of teacher-and peer-led interventions compared with standard sexual health education. A total of 12 RCTs, considered methodologically sound by the Shepherd et al, were included in the review; all of which were conducted in a school/college and all included skills training and education/information provision. Other components included: professional training, provision of resources and services, mass media and incentives. The interventions were provided by peers, teachers, or health care, community or social workers. The length of interventions ranged from a single 5-hour session to 2-year 20 session interventions and focused on risk reduction and delay in sexual initiation. All aimed to increase knowledge of HIV and STIs. Most studies involved condom promotion, covered negotiation/communication skills and enhanced self efficacy. Meta-analysis showed there was no significant difference between the intervention and the control group for sexual initiation and overall condom use. There was a significant difference between the intervention and the control groups for number of sexual partners; contraception use; condom use self-efficacy; abstinence self-efficacy; condom-negotiation self efficacy; and knowledge about HIV/AIDS, STIs, and sexual health. There was no significant difference between the intervention and the control groups for sex refusal self efficacy; communication self efficacy; attitude towards sexual intercourse; attitude towards condom use; and intention to have sex.

A review by Kang et al (2010),(240) focusing on HIV/STI interventions in Australia, identified one educational intervention delivered in secondary schools. The study was a matched control study, that aimed to change the attitude of the students towards people living with HIV/AIDS.(247) HIV positive speakers delivered AIDS education to the students and disclosed their personal perspective of living with HIV. The outcome (change in attitude of the students) in schools that utilized such

speakers was compared with schools that did not. The study found a significant improvement in attitudes of students towards HIV positive people and safe sex after the intervention, and the effect of the intervention was sustained over 3 months. However, the effect was seen in female students only; male students had little change in attitude even immediately after the intervention. Kang et al, comment that this could have been because most of the HIV positive invited speakers were females or gay males.

### **Clinic-based programs**

A meta-analysis by Scott-Sheldon et al (2010) assessed the efficacy of behavioural interventions to reduce sexual risk behaviour and incident STIs (including HIV) among patients attending STI clinics (all age groups). The review included 32 studies, representing 48 separate interventions targeting a total of 67,538 patients (all age groups). The success of interventions was measured with four outcomes: condom use (reported in 20 studies), number of sexual partners (reported in 15 studies), incidence of STIs (reported in 22 studies) and incidence of HIV (reported in 5 studies). Many interventions were individually tailored to a patient (42%) and 31% were tailored to a group. Most interventions occurred during the clinic visit (62.5%) and were conducted in one session (56%; range 1-7). The time of session was between 15 min to 90 mins for individual interventions and 12.5 mins to 180 mins for group interventions, when the intervention was conducted in one session only. Interventions included STI counselling and testing (98%), education (85%), skill training (condom use - 75% and communication skills - 58%), and motivational components (risk awareness - 60%, risk feedback - 33%, and attitudes towards condom use and/or reducing number of sexual partners - 31%). Interventions were delivered one on one, in groups and through videos; and were delivered by either professionals or paraprofessionals. Only 40% of the interventions actually provided condoms to the patients. Incentives were given to the patients in 22 out of 32 studies. Types of incentives were: cash (US \$5 - \$75), food, gifts, child care, and free medication. In the short term (4-13 weeks), participants' self-reported condom use increased and the number of sexual partners decreased, but there was no effect on the incidence of STIs (table 8.5). In the medium term (22 -39 weeks), participants' condom use increased and there was a significant decrease in the incidence of STIs, but there was no effect on the number of sexual partners (table 8.5). In the long term ( $\geq 52$  weeks), there was no effect on overall participants' (of all age groups) condom use and number of sexual partners, but the incidence of STIs and HIV both were significantly reduced. However, among young people there was a significant increase in condom use and decrease number of sexual partners in the long term.

**Table 8.5. Effect of behavioural interventions in clinical setting (242)**

<b>Outcome</b>	<b>Short-term</b> (4-13 weeks)	<b>Medium-term</b> (22 -39 weeks)	<b>Long-term</b> ( $\geq 52$ weeks)
Condom use	Significant increase	Significant increase	No effect in general population (Significant increase in young population)
Number of sex partners	Significant decrease	No effect	No effect in general population (Significant increase in young population)
Incidence of STIs	No effect	Significant decrease	Significant decrease
Incidence of HIV	Not enough studies	Not enough studies	Significant decrease

The review by Kirby (2007) demonstrated that programs based at reproductive health/family planning clinics were found to improve knowledge and skills of the teenagers. A total of 12 studies were identified; six studies looked at the effect of protocols for clinic appointments (what happens

during a clinic visit: consultation and counselling, and materials and activities), four looked at the effect of providing emergency contraception to young women in advance so they can use it if they have unprotected sex, and two looked at the effect of other clinic programs such as initiatives to improve family planning services and inviting parents to follow-up visits. Self-reported condom and contraceptive use was demonstrated to increase significantly when clinic programs provide young people with written information about abstinence, condoms, contraception; engaged them in one-on-one discussions; and provided them with condoms and contraceptives. However, the long-term effects of these services on sexual behaviour were not estimated.

In the review by Kang et al only one study was identified that focused on health promotion for young people in a clinical setting. (248) This RCT was based in general practices in Sydney, Australia, and clinicians were recruited to provide information on safe sex and condom use and hand out safe sex resources to patients randomly allocated to intervention or control groups. All participants filled a self-administered questionnaire before seeing the GP and a follow-up questionnaire three months after the consultation. The outcome measures were changes in knowledge, self-reported risk perception, and self-reported condom use. Patients exposed to the information package showed no increase in knowledge or reduction in risk behaviour including condom use after three months compared to patients who did not.

### **School-based and school-linked clinics and condom provision in schools**

The review by Kirby (2007) included four studies looking at the effect of school-based clinics and a fifth study looking at the effect of a school-linked health reproductive health clinic on sexual behaviour of students in US schools. The clinics provided one or more of the following services: counselling, physical examination, pregnancy testing, STI diagnosis and treatment, and provision of condoms and contraceptives. Three studies included three or more schools, and two included only one school. Two evaluations assessed delayed initiation of sex, two assessed increased use of contraceptives, and another two assessed reduced number of self reported pregnancy; only one evaluation out of two in each group resulted in a significant change in these outcomes. Three studies evaluated the impact of the program on childbirth, and two of these reported no significant reduction. Only one of the five studies included condom provision as part of their program (condoms available in baskets in schools), and compared this to programs that didn't provide condoms. There was no significant difference in sexual initiation, frequency of sex, condom use and sexual risk taking between the programs. However, the evaluation did find a non-statistically significant but consistent change over time in increased condom use and reduced sexual activity at the schools that provided condoms.

A review by Blank et al (2010) demonstrated that, in the US, school-based reproductive health/family planning clinics were found to improve knowledge and skills of teenagers. Six interventions (four controlled before and after studies and two interrupted time series studies) were identified. Services included provision of condoms and contraceptives, health education, counselling, pregnancy tests, health assessments, group work and referral. Four out of six studies reported that provision of contraceptives on site at school based health centres increase their uptake. However, whether this increased uptake actually leads to an increase in use was not clear. Evidence from the remaining two studies showed that school-based health centres that only offer health care assessments or counselling do not produce any beneficial behavioural effects. The review shows that school-based health centres appear to have more effect on sexual behaviour when contraceptives are available on the site, either comprehensively or as condom availability programs, compared to interventions that only offer only health assessments or counselling.

## **Multi-component programs**

In the review by Kirby (2007), eight studies were identified that described six different multi-component community-wide programs. Three studies reported on one program that was replicated. The programs included a variety of community activities such as: workshops for young people and/or their parents (run in schools or in the community), discussions, communication skills-building, presentations at community events, inclusion or upgrading of sex education in schools, trainings of teachers, administrators, community leaders, and peer counsellors, distribution of educational materials, provision of condoms, hiring health educators, and involving school administrators and faith communities. Some programs also used mass media campaigns like paid TV and radio advertisements, billboards, posters, and websites. Three out of four programs delayed initiation of sex; two out of three reduced pregnancies; one out of two increased condom use; and one reduced the number of partners. Two studies that reported on frequency of sex did not demonstrate a reduction; one study that reported on contraceptive use did not demonstrate an increase; and one study each that reported on pregnancy and childbirth did not demonstrate reductions.

The systematic review by Blank et al (2010) identified four multi-component intervention studies. These interventions included components like: school organization, staff development, peer resources, school environment, after school instructions, parent education, school community linkages, and facilities at school-based health centres. Three of these studies were RCTs and one was a controlled before and after study. The outcomes of the studies were both pregnancy and sexual health measures. The three RCTs showed that a theory based multi-component HIV, STI and pregnancy prevention program called “Safer Choices” was effective in changing knowledge and behaviour.(249-251) This program resulted in increased condom use and contraception, reduced numbers of unprotected sexual encounters and unprotected sexual partners, and reduced reports of STIs. The fourth study described a peer-education program(252) and showed that a peer-education program improved knowledge and changed some behaviours like an increase in condom use.

The review by Kang et al (2010) identified two studies that looked at multi-component interventions. One study looked at the effect of peer educator training, and development and dissemination of sexual health educational material (including comic books, stickers, and posters) among young Aboriginal and Torres Strait Islander people attending a range of community services. The outcome measure was the perceived change in knowledge and skills regarding sexual health. The results of the study show that there was self-reported improvement in confidence, knowledge and skills of the participants and trainers. The other study looked at a range of sexual health information and discussion sessions targeting international students at a university in Queensland, Australia.(253) The intervention included distribution of print material, information stalls at orientation week, and intermittent workshops for students and professionals working with students. The intervention was only evaluated for acceptability rather than knowledge or behaviours. Thus, further evaluation of strategies is required.

## **Information technology-based programs (computers, videos, email, SMS)**

The review by Kirby (2007) showed that only three studies have measured the impact of videos, interactive videos and computer-based programs on behaviour. The first study measured the impact of a 14-minute, non-interactive video in a STI clinic compared with standard clinic care (without a counselling component). The second measured the impact of a stand-alone interactive video in healthcare sites, and the third measured the impact of a computerized program offering instruction

in small groups in schools. Two out of the three programs reduced the frequency of sex, one out of two reduced the number of partners, and one reduced self-reported STIs. None of the programs increased condom use. These programs were considered to be inexpensive, acceptable and easily replicated. Their impact may remain for possibly as long as six months.

A review by Kang et al, focusing on HIV/STI interventions in Australia, identified two studies (both RCTs) looking at the use of email and SMS to send health promotion messages to young people. The first RCT recruited young people attending a music festival in Melbourne: SMS and email was used to send health messages, with follow-up over 12 months.(254) The outcome measures were changes in STI knowledge, self-reported discussion with a clinician about sexual health, and self-reported STI testing in last six months. The study showed that use of SMS and email can improve knowledge in young people and can improve health seeking behaviour in young women. The other RCT used personalised emails from a sexual health nurse or a doctor with anonymous discussion about chlamydia risk and testing, delivered to young people accessing a chlamydia website.(255) The outcome measure was change in knowledge and attitudes, use of condoms, and self-reported chlamydia testing in past six months. The study showed that use of email increased the use of condoms, changed some attitudes, increased chlamydia testing rates but did not change knowledge much.

### **Social marketing campaigns**

A review by Kang et al (2010) focusing on HIV/STI interventions in Australia identified two mass media social marketing campaigns aimed at increasing knowledge and testing rates. Interventions that only focused on increasing testing rates without targeting knowledge or behaviour were not included. One was a multi-media campaign that included radio advertisements, posters in public places and educational institutions, print advertisements, email advertisements, use of SMS, and an interactive website in Western Australia.(256) The outcome measure was qualitative data on awareness and recall of campaign, acceptability of SMS, use of campaign materials by GPs, quantitative data on website traffic and chlamydia testing rates. The study showed that SMS and email are seen as good marketing strategies by young people for communicating sexual health information; targeted media increases awareness; and there was a significant increase in chlamydia testing and notifications (from baseline to during campaign) that was likely due to the media campaign. The campaign recall was 63%. Another evaluation reported as an abstract only assessed the impact of a state-wide social marketing campaign in Victoria, Australia.(257) The study showed that there was no significant change observed in chlamydia tests per month, no change in STI knowledge or condom use between those who recalled and did not recall the campaign. Campaign recall rate was only 37%. Since this review by Kang et al, the Victorian evaluation was published in *Sexual Health* and the authors showed that there was an increase in condom use and chlamydia testing during the campaign. However, the trend in testing had commenced before the campaign was rolled out, and a regression analysis demonstrated the increase observed during the campaign was not associated with the campaign. Also the change in condom use was not specific to those who had recalled the campaign. The same authors also commented on the evaluation of the WA campaigns and noted that the evaluators did not conduct a regression analysis, and thus the increase reported in chlamydia testing observed in the intervention period could have simply been due to a broader increase in testing among GPs in WA that had also been observed in other states.

## **Alcohol, drug use and violence programs**

The review by Kirby (2007) identified seven programs that aimed to modify several types of risky behaviours including alcohol and drug use, violence, and sexual risk behaviours. The type of programs included: character education program (designed to reduce drug use, violent behaviour, and risky sexual behaviour), identity mentoring program (use of small groups and role models to encourage norms), abstinence program (targeting sex, smoking, drinking and drug use), social development program (including competence skills used manage situations), and school-community programs (included parental support, community linkages, and school-wide activities). Two of five programs were associated with a reduction in the reported frequency of sex, two did not have any significant effect and one actually increased the frequency. One out of two programs delayed the initiation of sex. One program out of two, each, increased condom use and reduced sexual risk taking; whereas the other respective program had no significant effect on these behaviours. Only two out of seven programs significantly reduced smoking, drug use and violence; one did not have an impact on drug use or violence; and four did not report on this outcome measure. Overall, these programs were demonstrated not to have a positive effect on sexual behaviour.

## **Discussion**

This summary of reviews has shown that curriculum-based programs that support use of condoms and contraceptives with or without abstinence are associated with effective and consistent decrease in various sexual risk factors and increase in protective factors. However, abstinence-only curriculum based-programs are not associated with any change in sexual risk behaviour. Availability of condoms and contraceptives in schools does increase their uptake but whether this leads to an actual increase in use has not been confirmed. Clinic-based programs are associated with an increase in the use of condoms and contraceptives and also a decrease in incidence of STIs; however, the decrease in STI incidence is only seen mid- to long-term. Multi-component programs report beneficial effect on more than one behavioural outcome; they are associated with a delay in the initiation of sex, an increase in condom use, and a reduction in number of sexual partners and pregnancies. Information-technology based programs are inexpensive, acceptable, and easy to replicate, and report positive effects on more than one sexual behaviours. Programs that combine risk factors like alcohol and drug use with sexual risk factors do not report a significant effect on the sexual behaviour.

Programs that promote in-school interventions to increase the knowledge and skills of young people are particularly promising as a long-term investment as they will help to provide the background level of knowledge that may influence the general population attitudes related to sexual risk and HIV. The curriculum based education programs which were most effective had common elements including: use of a logic model approach, focus on clear health goals, use of multiple activities and sound teaching methods, support from appropriate authorities, and inclusion of activities to recruit and retain participants. These programs have been evaluated and shown to be successful on multiple occasions in a variety of communities (low to middle income; rural and urban) without major changes. The review of cost effectiveness studies by Shepherd et al (2010) shows that school-based interventions are more cost-effective when they are teacher-led rather than peer-led. Peers need to be trained every year because of turnover whereas teachers only require retraining every few years. The review of cost effectiveness studies also shows that school-based behavioural interventions for young people may become more cost-effective as the target population grows older; since favourable behaviour change may occur as they become more sexually active.

Condom uptake remains low in most countries, including Australia, with only about 50% of school students reporting always using condoms in the last year.(21) More strenuous efforts need to be made to both promote their use and to make them more available. As demonstrated in the review by Kirby (2007), the evidence about the impact of condoms availability programs in schools is limited and not conclusive. However there were no studies that focused on condom provision in other settings.

Comprehensive health promotion programs that are community-based and have multiple components were also shown to be consistently more effective at changing the sexual behaviour of young people. They have been demonstrated to produce multiple desired effects like increased knowledge and skills, delay in first sex, increased use of condoms and contraceptives, and reduced numbers of sexual partners. These programs are probably successful as they pay attention to the social and sexual norms of the population among whom the particular target group (such as young people or groups most at risk) live and interact. This includes people who influence their behaviours such as their parents, role models and influential people in the community, and external influences such as radio, films, television, and songs.

Similarly, health promotion interventions based at sexual and reproductive health services deserve consideration, as demonstrated by Scott-Sheldon et al (2010). They have been shown to be capable of success in regards to both changes in behaviour in the short-term followed by reduction in STI incidence in the long-term. The impacts of these interventions are more favourable when promoted to specific sub-groups who may be more at risk.

Mass media advertising can be useful in increasing public awareness and as a health promotion tool. However, advertising alone is not sufficient to bring about any population-wide changes in behaviour; thus broader set of interventions need to be used as part of social marketing campaigns to promote health.

Health promotion using text messages also appears promising. Acceptability of SMS as a marketing tool among young people was assessed in an evaluation of a mass media social marketing campaign in Western Australia.(256) The evaluation showed that 58% young people reported SMS to be a good method of communication, and thus a useful marketing strategy. A randomised controlled trial looked at the effects of text messages (containing sexual health information) on knowledge and health seeking behaviour of young people attending a music festival in Victoria, Australia.(254) Sexual health related text messages and emails were sent to the participants over a period of 12 months. Results from the RCT show that both knowledge and health-seeking behaviour improved in young women. Thus, health authorities should consider using SMS as a health promotion tool, especially when targeting young people is the aim.

Many studies included in the five reviews were not designed to evaluate the effectiveness of behavioural interventions on STI incidence as an outcome. Out of a total 156 studies included from the 5 reviews; only 33 studies assessed the incidence of STIs, and only 26 studies assessed pregnancy (both self-reported and lab-reported) as an outcome. Such studies need to be large and are thus expensive, but are important to be able to provide the defining evidence that governments need to fund large scale programs. Behaviour change interventions may take several years to have a major impact on incidence as demonstrated by Scott-Sheldon et al (2010) and many studies in the reviews had short follow-up periods. It is essential that if interventions are to be recommended because of their effectiveness for STI prevention, then trials must include STI incidence and, wherever possible, other biological outcomes such as pregnancy.

In conclusion, this summary of reviews has demonstrated that there are a number of different strategies that can be used to modify sexual risk behaviour associated with STIs in young people. Some strategies are able to modify important behaviours such as condom use and number of partners, and others only modify one of these. If a health department is considering spending money on reducing risk, it is now possible to estimate the likelihood of success of the program versus the likely costs involved. This statement should be qualified by the fact that many of the studies did not assess STI incidence as an outcome, and it is also possible that the change observed in behaviour may not be of sufficient magnitude to result in a population level change in STI incidence.

## Chapter 9: Modelling chlamydia prevention interventions to reduce chlamydia prevalence/incidence

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### Abstract

**Introduction:** Mathematical models of chlamydia transmission can help inform public health decision making on chlamydia prevention strategies.

**Methods:** We summarised the findings of mathematical modelling studies parameterised with data from young people in Australia, which explored coverage levels and target groups required for screening, contact tracing or condom use to reduce chlamydia prevalence in the population. The studies were identified by key experts.

**Results:** Only one mathematical modelling study met the inclusion criteria. This study was conducted in Australia and showed that if 40% of men and women <25 years were screened annually, the prevalence of chlamydial infection would decrease rapidly over 10 years in all age groups, with >50% of the reduction being achieved during the first 4 years. A 50% reduction in the overall prevalence of chlamydia infection in the population within 10 years could also be achieved by a variety of combinations of coverage levels and target groups; annually screening ~80% of females <20 years old, 30% of females <25 years old, 20%–30% of females <30 years old, 60% of males and females <20 years old, 20% of males and females <25 years old, or <20% of males and females <30 years old. This was a population based deterministic model rather than an individual based model, and it wasn't able to take contact tracing into consideration.

**Conclusion:** This model predicted that introduction of extensive screening of young people in Australia can reduce chlamydia transmission. The model wasn't able to take contact tracing into consideration which is a key factor that is likely to have an impact on subsequent re-infection. A recent study showed that the impact of the screening was reduced if re-infections were not treated, suggesting that any screening should be coupled with enhanced contact tracing to minimise re-infection and reduce costs of the screening program. No local studies were identified which explored coverage levels of condom use or partner notifications strategies required to impact of population chlamydia prevalence. Modelling which compares a range of prevention strategies (condom use, partner notification, screening), combinations of these strategies, and a variety of methods and targets groups within these strategies using Australian data, would be important to more accurately inform public health decision making in Australia.

## Introduction

Infection with *Chlamydia trachomatis* is a significant health problem in Australia and New South Wales (NSW). Over the past decade 92,672 chlamydia notifications have been reported in NSW alone, and the number of chlamydia notifications in NSW have increased steadily each year, from 4,399 notifications in 2000 to 14,948 in 2009. The number of notifications among men has also been steadily increasing each year.(11) Although young women aged 15–24 years bear the greatest burden of chlamydial infection, with more than two-thirds of notifications for women occurring in this age group,(13) this is an artefact of testing, and studies demonstrate the prevalence of chlamydia infection is similar in young women and men.(55, 258-259) The rise in chlamydia notifications is concerning because of the morbidity which results from untreated chlamydia, such as pelvic inflammatory disease, and infertility, particularly in women.(120)

Because up to 80% of chlamydia infections of women and men are asymptomatic(260), screening is needed to detect and treat the majority of cases. Non-invasive testing (first-pass urine samples) and single-dose antibiotic treatment now make widespread screening feasible. Screening programs for chlamydia are being adopted in many parts of the developed world.(140, 169-170) Contact tracing - or partner notification is considered an essential component in the control of these infections. Many different methods to undertake contact tracing have been utilised including patient-delivered-partner therapy, provider initiated contract tracing, public health initiated contract tracing, and referral letters.(261) Contact tracing and screening aims to detect and treat asymptomatic infections, reduce the morbidity of sequelae in infected females, as well as interrupting transmission and thereby reducing chlamydia incidence/prevalence.

Health promotion strategies which focus on increasing condom use and reducing other sexual risk behaviour have also been widely implemented in many countries including social marketing campaigns, school based education programs, and community-based programs.(238) These strategies seek to minimize transmission.

Mathematical models of chlamydia transmission, can help inform the level of coverage of prevention strategies (screening, condom use, partner notification) likely to be needed to reduce chlamydia transmission, and thus can help inform public health decision making about feasibility and priority setting.

## Methods

We summarised the findings of mathematical modelling studies parameterised with data from young people in Australia, which explored coverage levels and target groups required for screening, contact tracing or condom use, to reduce chlamydia prevalence in the population. The studies were identified by key experts.

It is important to note that models should be carefully appraised and any strengths and limitations in the model design, the assumptions made and the data used to parameterise the models should be identified and taken into consideration when interpreting the results. There is usually considerable uncertainty about the data used to parameterise a model. For example, there is no strong evidence available on the duration of infection in men, although evidence is available for women. Secondly, it is uncertain whether infection with chlamydia confers any short term immunity to an individual – allowing for immunity post chlamydia infection, can have a considerable impact on chlamydia transmission within a mathematical model.

## Results

Only one mathematical modelling study by Regan et al (2008)(173) met the inclusion criteria. This study reported the screening coverage required to reduce chlamydia prevalence in Australia.

The authors developed a dynamic deterministic transmission model of the chlamydia epidemic parameterized with Australian sexual behaviour and epidemiology data. A range of screening strategies and coverage rates were evaluated targeting various groups based on age and sex. Rigorous uncertainty and sensitivity analyses were undertaken.

The model predicted that if 40% of men and women under the age of 25 years were screened annually, the prevalence of chlamydia infection would decrease rapidly over 10 years in all age groups, and >50% of the decline would be achieved during the first four years (Figure 9.1).

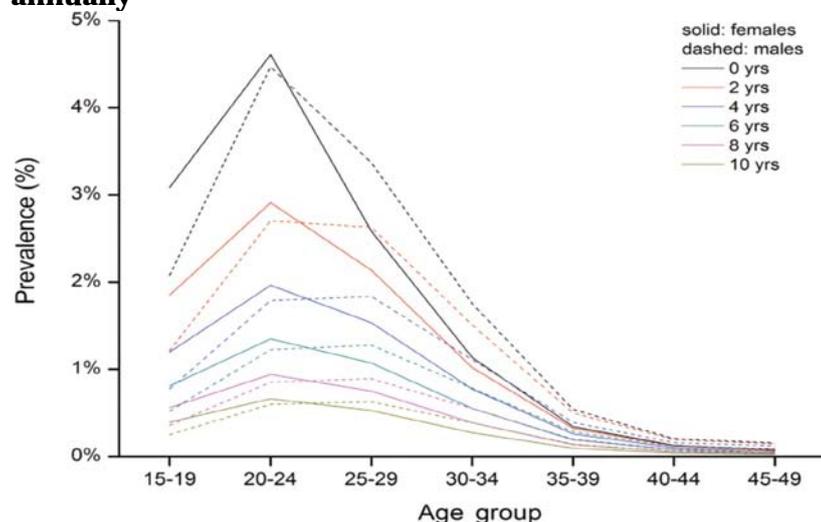
Targeting 20–24-year-olds had a two-fold greater impact on prevalence compared with targeting 15–19-year-olds or 25–29-year-olds and targeting 15–19-year-olds was slightly more effective at reducing prevalence than targeting 25–29-year-olds.

Targeting only men for screening and treatment resulted in approximately the same overall reduction in prevalence in women as the reduction observed in men. However targeting only women for screening and treatment resulted in slightly greater reductions in prevalence in women than in men.

A 50% reduction in the overall prevalence of chlamydia infection in the population within 10 years was therefore achieved by a variety of combinations of coverage levels and target groups:

- a. annually screening ~80% of females <20 years old
- b. 30% of females <25 years old
- c. 20%–30% of females <30 years old
- d. 60% of males and females <20 years old
- e. 20% of males and females <25 years old, or
- f. <20% of males and females <30 years old.

**Figure 9.1: Age-specific prevalence in males (dashed lines) and females (solid lines) at 0, 2, 4, 6, 8, and 10 years after the introduction of screening, when 40% of both males and females are screened annually**



As this was a population based deterministic model rather than an individual based model, it wasn't possible to take contact tracing into consideration— a key factor that is likely to have an impact on subsequent re-infection.

## Discussion

These modelling study by Regan et al (2008)(173) predicted that introduction of extensive screening of young people in Australia can reduce chlamydia transmission and prevalence. The coverage required for this strategy to lead to a substantial reduction in prevalence varied according to age groups and if both sexes were included. We did not identify any modelling studies relevant to Australia which explored the level of condom use, and partner notification required to have a population impact of chlamydia transmission.

In designing a screening strategy, decisions have to be made about gender, age, and other characteristics of the subgroup to be targeted. Regan et al (2008)(173) found many other screening scenarios that gave equivalent reductions to screening <25 year olds such as screening a low proportion of males and females (20%) but a broader age groups (<30 years old). (173) The limitation of the model by Regan et al (2008)(173) was that it didn't include contact tracing and thus may have overestimated benefit of the different coverage levels on reducing community prevalence. Heijne et al (2011)(137) established a simple model to illustrate the potential importance of partner notification. This model was not designed for quantitatively assessment of the impact of screening/treatment interventions, and thus was not included in this review. Heijne et al (2011)(137) found that after five years of chlamydia screening, there was a greater reduction in chlamydia prevalence in a model based on instantaneous partnerships where re-infection cannot occur (standard model) compared with a model (pair model) that accounts for subsequent partnerships and thus re-infection. The biggest difference in predicted impact on chlamydia prevalence between the two models was observed for screening coverage rates between 10 and 40%. As the screening rate increased above 40%, the impact of partner notification became less important. The point of when the impact became equal in the pair and standard model was when ~30% of current partners were notified and treated.

The results by Heijne et al (2011)(137) have implications for the design of chlamydia screening strategies. They found that ~30% of current sex partners need to be notified to counterbalance the effect of re-infection in a screening program. Although 30% sounds modest, it requires the partner to be identified and informed of their contact with the index case, treatment to be given and taken by both index case and partner, and the index case and potentially the partner/s to abstain from sexual intercourse until infection has cleared. A systematic review by Hogben et al (2008) showed that in the US although 48% to 79% of partners of men were notified, a much smaller proportion was treated (30%-61%). Higher rates of notification and treatment were associated with patients being offered medications to give to their partners (patient-delivered-partner therapy).(261) A recent cost analysis demonstrated that not only does contact tracing reduce the cost per positive case identified compared with increasing screening coverage alone, but it also improves sex equity in access to treatment for those infected.(262) Additional modelling efforts should focus on understanding the most promising partner notification strategies.

No models parameterised with Australian data have quantitatively assessing the impact of increasing condom use/partner notification, in fact there have been very few worldwide and most were conducted during times when less information was known about chlamydia biology and thus their findings are probably not relevant any more. For example, Kretzschmar et al (1996)(263)

modelled the spread of chlamydial infection in an age-structured heterosexual population in the Netherlands with a highly sexually active core group using an individual based model. Contact tracing strategies, screening of various subgroups, and the effect of condom use were compared. The prevalence in the population without any of the prevention strategies (reference scenario) was assumed to 4.1% based on epidemiological data. The model showed, contact tracing strategies were highly efficient in reducing prevalence. Treatment of 25% of partners reduced prevalence to 1.1%, and treatment of 50% reduced the prevalence to a very low level (0.3%). Increasing condom use resulted in a large reduction of chlamydia prevalence. Consistent condom use by 15% of the core group and 6% of non-core of the population resulted in chlamydia prevalence decreasing from 4.1 to 1.8%, and if 47% of core and 21 % of non-core use condoms consistently the chlamydia prevalence dropped to 0.08%. However the model assumed that only 25% of infections in men are asymptomatic, and 70% in women. Evidence today suggests that this may be as high as 80% for men.(260) Also two optimistic assumptions were made in this model: the first being that young people who used condoms were consistent in their behaviour by always using condoms in all their partnerships; the second and more influential, was that in a partnership between a person who used condom and a person who didn't use condoms, the behaviour of the person who used condoms was dominant, i.e., condoms were always used. These behaviours obviously do not reflect the realities of sexual behaviour among young people, and thus may have lead to unrealistic levels of condom use being assumed in the model. Modelling based on more realistic parameters based on Australian data is warranted.

This review has also highlighted that when policy makers are utilizing such models to inform decision makers, the parameters used in the models need to be carefully considered, and the model should be assessed to see if the inputs accurately reflect the sexual behaviour and disease transmission scenarios in the populations the potential strategies are being considered for. For example, even the Australian model by Regan et al (2008) reflects chlamydia prevalence in young urban young people(173), but does not reflect the epidemic in some remote Aboriginal communities.

In conclusion, these models predict that increasing introducing extensive screening in young people, coupled with contact tracing of 30% of partners is likely to substantially reduce chlamydia prevalence in young people. The question therefore remains what coverage is needed? Although this review has given some information to inform public health decision making in Australia, ideally modelling which compares a range of prevention strategies (condom use, partner notification, screening), combinations of these strategies, and a variety of methods and targets groups within these strategies using Australian data, would be important to more accurately inform public health decision making in Australia. In 2012-2013, the results of the Australian Chlamydia Control Effectiveness Pilot (ACCEPt) (as described in Chapter 4) will be used to develop an individual based model that will explore the impact of actual screening rates on population transmission and pelvic inflammatory disease.

## **Chapter 10: Conclusions**

### **Implications for government**

The potential for future ill-health resulting from undiagnosed chlamydia is what provides the rationale for funding chlamydia prevention programs. Older evidence probably overestimated the proportion of infected people who develop long-term complications from infection. However, the most recent study may have more precisely determined the correct scale of the problem. Taking into account the 3.7% prevalence of chlamydia in young women in Australia, and the relative risk of PID (6.5-25) as estimated from the POPI trial; we can estimate that 17%-47% PID in Australian women is attributable to a chlamydial infection.

Chlamydia notifications are increasing each year in NSW and the greatest burden of chlamydia infection is among young adults. There were no NSW chlamydia notification data available in Aboriginal and Torres Strait Islander people. While much of the increase in notifications reflects increased testing (the more you test, the more you diagnose), analysis of sentinel surveillance data shows a different picture – an increase in the prevalence of chlamydia in those tested at sexual health services, of 28% in females and 11.9% in males.

Behavioural surveys (2002 and 2008) show the median age of first sexual intercourse in Australian secondary school students has decreased and the number of sexual partners has increased, meaning a larger number of young people are potentially exposed to chlamydia. Despite this, an unacceptably low proportion of young people are being tested for chlamydia in general practice.

Because the incidence is high (~4% per year in young women) and re-infection rates are high (22%), regular chlamydia screening and re-screening after a chlamydial infection is vital. Evidence shows that in primary care clinics, interventions that provide easy and systematic means of offering a chlamydia test have the greatest impact on increasing testing. Evidence also shows mailed screening kits and reminder systems in clinical settings increase re-testing within 3 months of the initial infection. Text message may be useful as a reminder strategy but has not yet been formally evaluated in this context. Trials overseas have found that higher chlamydia testing rates can be achieved with home-based sampling compared to clinic-based testing, and home-based sampling was well-accepted among young people and often preferred compared to clinic testing. However, a number of population based screening programs involving home-based sampling have reported lower chlamydia testing rates than the trials above. Home-screening program on a population basis require costly large scale registries like cervical cancer screening, and mechanisms to provide treatment and offer partner notification for those testing positive.

One Australian mathematical modelling study explored the coverage levels and target groups required for screening. The modelling predicted that the introduction of extensive screening of young people in Australia can reduce chlamydia transmission and prevalence. The coverage required to lead to a substantial reduction in prevalence varied according to age group and whether both sexes were included. If 40% of men and women <25 years were screened annually, the prevalence of chlamydial infection would decrease rapidly over 10 years in all age groups, with >50% of the reduction being achieved during the first 4 years. No Australian modelling study has explored the potential impact of partner notification, or condom use. Modelling studies in other countries have highlighted that screening should be coupled with enhanced partner management to minimise re-infection and to reduce the cost of the screening program.

In our search of the literature, we did not identify any studies assessing the impact of the following strategies to increase testing in primary care: cash incentives (>\$5 associated with each test), multi-faceted intervention to increase annual testing in general practice clinics, SMS reminder systems to increase re-testing, target-based incentive schemes similar to the immunisation program, practice-nurse led interventions, or controlled testing interventions in Aboriginal populations. However, two large-scale trials are underway in NSW primary care clinics - ACCEPt and SHIMMER - that are multi-faceted testing interventions aimed at increasing chlamydia testing.

Timely diagnosis and treatment of PID is important to prevent long term reproductive sequelae. However, research suggests that adherence to PID management guidelines by practitioners and patients is poor, although NSW and Australian data are limited. To improve the diagnosis and management of PID, potential strategies that require further evaluation in the NSW setting include: sensitive diagnostic algorithms and abbreviated management guidelines, provision of the 14 days of antibiotic treatment at diagnosis, simplified antibiotic regimens, and written instructions for patients.

An effective and widely used intervention to increase knowledge and reduce sexual risk behaviour in young people is school-based curriculum education programs. Comprehensive health promotion programs that are community-based and include multiple components are also effective in changing the sexual behaviour of young people. Clinic-based counselling and education programs have been shown to increase the use of condoms and contraceptives and in addition have been demonstrated to decrease the incidence of STIs.

Determining whether these interventions are successful or need to be adjusted will require comprehensive surveillance programs. There are many gaps in available data which need to be addressed to inform the planning of prevention programs. The notification data does give some idea of the numbers, but it under-estimates the true burden of disease since most patients who have chlamydia are asymptomatic. Based on chlamydia prevalence studies, it is likely the true number of infections in 2009 in NSW was closer to 60,000 rather than the 14,948 reported, meaning that 45,000 infections in one year were not diagnosed and treated. There is a need to improve the notification data collection system to improve the reporting of Aboriginal and Torres Strait status. We also have no ongoing funded surveillance systems to assess chlamydia incidence and PID and infertility outcomes.

## **Recommendations**

1. Screening programs should employ strategies that result in system changes to increase chlamydia testing rates in primary care, as a very high proportion of young people do attend their general practitioner or primary care clinic at least once a year.
2. Home-based screening should be considered for young people who don't access health services regularly.
3. Any screening program in the future should be coupled with enhanced contact tracing to minimise re-infection and ongoing transmission.
4. Before embarking on large scale national chlamydia screening programs it would be prudent to wait for the results of the ACCEPt and SHIMMER studies.
5. Interventions that reduce sexual risk-taking behaviour of young people need to be considered
6. Enhancing curriculum based educations programs should be considered, with a similar content and duration to overseas programs demonstrated to consistently decrease sexual risk factors.

7. Comprehensive health promotion programs that are community-based and have multiple components should be considered.
8. Clinic-based motivational interviewing should also be considered.
9. More uniform ways to diagnose PID and catalogue PID in medical records is required for monitoring and surveillance purposes.
10. Data collections systems need to be enhanced; to be able to evaluate future strategies, particularly improved recording of Aboriginal and Torres Strait Islander status in NSW notification data. Systems are also needed to monitor chlamydia incidence and potential sequelae.
11. Modelling that compares a range of prevention strategies (condom use, partner notification, and screening), combinations of these strategies, and a variety of methods and targets groups within these strategies using Australian data, should be considered to more accurately inform public health decision making in Australia.

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## **Appendix**

### **Scope**

In October 2009 the NSW Ministerial Advisory Committee on HIV and Sexually Transmissible Infections (CAS) Health Promotion Sub-Committee decided to review the NSW response to chlamydia. A summary of research and projects on prior Chlamydia health promotion in NSW informed the discussion. A Chlamydia Working Group was established to review the literature and to provide advice and planning support for the creation of Chlamydia strategy in NSW.

The goals identified for the working group included:

- Greater knowledge by young people about Chlamydia, other STIs, and preventive behaviours.
- An increased rate of Chlamydia testing.
- A reinvigorated and re-focussed health promotion response to Chlamydia.
- Convene a Chlamydia Think Tank with specific questions to be answered by researchers and others:
  - What is the current evidence for Chlamydia interventions?
  - How can reduction of undiagnosed Chlamydia be achieved?
  - How can the goal of chlamydia control be achieved (for example, reduction of infertility caused by Chlamydia/STIs)?
- Support for the role of the Department of Education and Training in the implementation of the sexual health curriculum.

#### Chlamydia Working Group

To ensure chlamydia control strategies were evidence-based, the working group requested a review of the Chlamydia literature be answered in the following way:

1. What evidence is agreed upon or has consensus?
2. What evidence is inconsistent or contradictory?
3. What evidence is missing?

The NCHECR agreed to assist the CAS Health Promotion Sub-Committee Chlamydia working group activities by providing a review of international literature and reports (grey literature) to answer the following questions about ano-genital chlamydia:

1. What are the demographic, socioeconomic and behavioural characteristics of the populations that are most at risk of chlamydia and/or chlamydia sequelae in NSW?
2. What is the strength of evidence of association between chlamydia infection and PID and PID and infertility and ectopic pregnancy?
3. Are there co-morbidities or associated factors that increase the risk of chlamydia sequelae (such as re-infection or co-infection with other STIs)?
4. What interventions effectively increase testing for chlamydia?
5. What interventions improve practitioner diagnosis and management of chlamydia sequelae?
6. What interventions effectively increase partner notification (including patient-delivery partner therapy) for chlamydia or other STIs?
7. What interventions effectively increase re-testing for chlamydia?

8. What interventions effectively decrease the prevalence or incidence of chlamydia and/or chlamydia sequelae?
9. What interventions effectively decrease the sexual risk behaviour associated with chlamydia infection and other STIs?
10. For any interventions above, what is the level of coverage (and target populations) required to make an impact (include any modelling data showing the impact of using various coverage scenarios)?