**RATES AND RISK FACTORS OF CHLAMYDIA AND GONORRHEA REINFECTION AMONG ADOLESCENTS: A LITERATURE REVIEW**

by

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 **RATES AND RISK FACTORS OF CHLAMYDIA AND GONORRHEA REINFECTION**

**AMONG ADOLESCENTS: A LITERATURE REVIEW**

 Janine Talis, MPH

University of Pittsburgh, 2016

**ABSTRACT**

Adolescents have the second highest rates of gonorrhea and chlamydia infections. Understanding reinfection risk factors and rates among adolescents will significantly impact the development of prevention strategies, such as screening practices and sexual health education. The primary objective of this literature review was to assess the current gap in knowledge on gonorrhea and chlamydia reinfection risk factors and rates among adolescents. A literature review on reinfection rates and related risk factors of gonorrhea and chlamydia in adolescents was conducted through the PubMed database between 10/6/2015-10/10/2015, yielding 21 articles that met inclusion criteria. Each article was reviewed for adherence to topic, method, results, and limitations. There was little agreement on case definition for reinfection, which was defined by only 11 of the reviewed studies. Among adolescents (age range: 11-21), the overall prevalence rate of reinfection was 20.4%, while the overall incidence rate of reinfection was 23.6%. Reinfection rates were more frequently reported among females. Lack of data on male populations limited comparisons between the genders. Sexual and personal adolescent-specific risk factors associated with greater odds of reinfection include: lack of condom use, female gender, and history of abuse. In conclusion, this literature review highlights the public health significance of gonorrhea and chlamydia reinfections and the need for more research on reinfection rates and risk factors for reinfection in males, minority populations, and sexual minority adolescents to improve intervention measures that can be developed and implemented within these at-risk groups.

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preface

I would like to thank my friends and family for their unending support, especially my parents. I know I have not always been easy and I appreciate their patience. I would also like to thank my advisor Dr. Samar El Khoudary for being a member of my essay committee and for always being calm in the face of my anxiety. I would like to thank Dr. Nancy Glynn for acting as my guide through public health as well as for being a member of my committee. Finally, I'd like to thank Dr. Elizabeth Miller for being a committee member, and for helping me find the path I wish to walk along in my public health career.

# Introduction

## WHAT ARE GONORRHEA AND CHLAMYDIA AND WHY ARE THESE SEXUALLY TRANSMITTED DISEASES IMPORTANT?

Sexually transmitted infections (STIs), which are primarily spread through intercourse, have a long history of impacting health and well-being and are still important for public health. Mentions of STIs date back as far as the Old Testament, where discharge was described as “the running issue” and afflicted men and women were instructed to wash themselves and their clothing and remain apart for 7 days. This suggests that the link between sex and STIs was recognized, but it was not until advances in microbiology and serology following the Industrial Revolution when the causal agents of disease were discovered.1 Although the perception of STIs has changed over time, STIs persist to be a major public health issue, despite increased education, surveillance measures, and even cures.

Gonorrhea and chlamydia are both among the most common STIs. Gonorrhea, colloquially known as “the clap” is caused by the bacterium *Neisseria gonorrhoeae, while* Chlamydia is caused by the bacterium *Chlamydia trachomatis.* Both are mainly contracted through sexual contact with the infected penis, vagina, mouth, or anus of a partner(s), and are often asymptomatic in infected persons. In those who are symptomatic, common symptoms are discharge and pain with urination. Both can be detected via cultures or nucleic acid amplification tests using urine or vaginal swabs, and are easily cured with the right antibiotic therapy.2,3

While easily treatable, gonorrhea and chlamydia can seriously impact health. When left untreated serious complications can occur, such as Pelvic Inflammatory Disease (PID) in women and sterility in men.2,3 Although gonorrhea and chlamydia have a long history and are easily preventable and treatable, both still continue to negatively impact public health.

## EPIDEMIOLOGY OF CHLAMYDIA AND GONORRHEA

In December 2014, the CDC released a surveillance report on STIs in the US. Due to the asymptomatic nature of chlamydia and gonorrhea, it cannot be confirmed whether each case was incident or prevalent.4 Rates within the report were reported as case rates.4 Case rates were calculated as total number of cases over a total population (i.e. U.S. population) and reported per 100,000 people (CDC personnel, personal communication, March 31, 2016).

Nearly 1.5 million (444.6 per 100,000 people) cases of chlamydia, and over 333,000 (106.1 per 100,000 people) cases of gonorrhea were reported to the CDC during 2013. The report found a slight decline between 2012 and 2013. Racial disparities were reported, with non-Hispanic Whites having lower rates of infection compared to most minority groups.4

Chlamydia rates significantly increased from 178 cases to 453.4 cases per 100,000 people between 1993-2011. However, rates prior to 2000 were likely underestimated due to lack of uniform reporting. A slight decrease to 446.1 per 100,000 people was reported in 2012.4 For gonorrhea, the rate in 2009 in the US was as low as 98.1 cases/100,000 people. Similar to chlamydia, although gonorrhea rates have been slowly increasing over time, a minor decrease from 106.7 to 106.1 cases/100,000 people was reported between 2012 and 2013.6 Regional trends for both gonorrhea and chlamydia show the South has the highest rates (128.6 per 100,000 and 485.1 per 100,000 people, respectively) in 2013. 4

 Case rates for chlamydia among females (623.1 per 100,000 women) were more than twice the rate among males (262.6 per 100,000 men).4 Both sexes showed increases in chlamydia case rates between 2009-2013, although the rate among the females decreased between 2012-2013.4 Case rates among males had a slight increase of 0.8% between 2012 and 2013 (up from 260.6 per 100,000 men).4 Men who have sex with women (MSW) had the highest rates among all men.4 For Gonorrhea, rates among both sexes were fairly close (109.5 cases for males and 102.4 cases for females per 100,000 people).4 Between 2012-2013, an increase of 4.3% in gonorrhea prevalence was reported among males, and a reduction of 5.1% was reported among females.4

 In 2013, rates of chlamydia were 6.4 times higher among African Americans compared to Whites, whereas gonorrhea rates in African Americans were 12.4 times higher than Whites (426.6 cases vs. 34.5 cases per 100,000 people, respectively).4 Case rates among American Indians/Alaskan Natives, Hispanics, and Native Hawaiians/Other Pacific Islanders were 2-4 times higher compared to rates in Whites in 2013 for both chlamydia and gonorrhea (FIGURE 1).4 Only the Asian population had a lower rate (111.5 per 100,000 people) than Whites (180.3 per 100,000) for chlamydia, and a rate about half that of Whites for gonorrhea.4 While both gonorrhea and chlamydia overall rates showed a slight decline from 2012 to 2013, they still remain high, especially when race/ethnicity is taken into account. The improvement in testing sensitivity, electronic reporting, and increased screening may contribute to the increase in cases over time. Higher rates among females could be due to more screening. Both infections are often asymptomatic, and frequency of screening varies per person. Not everyone who has the disease is discovered, which could underestimate case rates.

Figure 1. Case rates of chlamydia (top) and gonorrhea (bottom) stratified by race and sex according to the Sexually Transmitted Disease Surveillance report4


## WHY REINFECTION IS A CONCERN?

The immune system fights against foreign invaders such as bacteria. The adaptive immune system can go even further, creating immunological memory of some of the antigens it encounters. If the body’s barriers are broken by an antigen previously encountered and remembered, the immune system is able to fight the infection more quickly and efficiently.5 This is why vaccination is effective. However, immunological memory does not extend to all infections, including gonorrhea and chlamydia.

Reasons why gonorrhea and chlamydia can persist in a body or occur again when re-exposed are not quite known. Several hypotheses have been proposed; for example, it has been hypothesized that gonorrhea can avoid complement-mediated destruction, or resist phagocytic demolition.6 Lack of immunological memory could cause an unaware, or unconcerned, sexually active individual to become reinfected with either (or both) gonorrhea or chlamydia repeatedly throughout their lifetime. People infected with gonorrhea or chlamydia may inadvertently sleep with an infected person. The majority of reinfected people are asymptomatic, allowing them to unknowingly transmit the infection onto others.2,3 Infected couples may reengage in intercourse before one of them is fully disease free, causing them to continue to pass the disease between them.

Each infection increases risk of developing long-term consequences associated with gonorrhea and chlamydia.2,3 In women, gonorrhea and chlamydia can cause Pelvic Inflammatory Disease (PID).2,3 PID occurs when an inflammation spreads from the lower to the upper genital tract, causing damage to the fallopian tubes, uterus, and other surrounding tissues. PID presents subtle signs and symptoms, and many women are unaware of the subclinical development of PID as inflammation spreads. Women with PID can suffer from “reproductive disabilities” including chronic pelvic pain, ectopic pregnancy, and infertility.7 Approximately 5% of sexually active women received treatment for PID in 2010.8 Men and women infected with chlamydia can develop reactive arthritis (joint pain triggered by an infection), or Reiter’s syndrome if the arthritis occurs alongside urethritis and conjunctivitis.3 Gonorrhea can cause disseminated gonococcal infection (DGI), which can lead to arthritis, dermatitis, and tenosynovitis. In rare cases, gonorrhea can lead to infertility in men.2

## WHY FOCUS ON ADOLESCENTS?

The CDC defines adolescents as teenagers between 14-19 years old. According to the CDC, a large number of adolescents suffer from STIs. In 2013, adolescents had the highest number of cases, second only to young adults (ages 20-24). Cases among 14-24 year olds accounted for 68% of all chlamydia infections.9 In 2013, case rate for adolescents were reported as 337.5 per 100,000 people for gonorrhea, and 1852.1 per 100,000 people for chlamydia.4 Both infections declined between 2012 and 2013 (8.7% and 11.6% reductions for chlamydia and gonorrhea, respectively).9 However, the case rate among adolescents is over three times higher for gonorrhea, and over four times higher for chlamydia compared to the overall US rate.4 Cases from reinfection were not reported.

 Adolescents are a vulnerable age group, experiencing hormonal and personal stress, placing them at increased risk for STIs. In the 2006-2010 report from the National Center For Health Statistics, 41.8% of unmarried males and 42.1% of unmarried females (age:15-19) reported having intercourse. Within this group, the proportion was much greater in teenagers aged 18-19 (63.9% and 62.7% in males and females, respectively).10 High rates of sexual activity alongside rates of infection provide a basis to hypothesize on the rate of reinfection likely to be high within this age group.

## Public health significance

Chlamydia and gonorrhea pose a huge problem for public health. They are the top two most commonly reported notifiable diseases in the US. While easily treatable, gonorrhea and chlamydia are accompanied by a number of unwanted long-term conditions, such as arthritis and infertility.4 STIs also negatively impact the health care system financially, costing an estimated $17 billion each year.11 Both infections disproportionally affect the population by sex, race, and by age. Young persons between 14-24 years old are at particularly higher risk.4

Rates of infection are declining overall, but the numbers are still high. The asymptomatic nature of the diseases makes them easy to acquire without notice, and spread without worry. It is vital to understand more about the rates at which reinfection is occurring, and why it is occurring. By initially studying adolescents, results may be used for the development of programs aimed at decreasing rates among adolescents, impacting young and older adults in the process.

## OBJECTIVE

The objective of this targeted literature review was to examine the current data on reinfection rates of gonorrhea and chlamydia among adolescents. In addition, we highlighted potential related risk factors. Literature was appraised on quality and its contribution to STIs research. Recommendations for next steps were made based on the insight provided by the examined literature.

# methods

## LITERATURE SEARCH DATABASES

A literature search was conducted via the PubMed search engine using a combination of search terms between 6 October 2015 to 10 October 2015, and was chosen for its access to University of Pittsburgh students, reliability, and ease of use. A MeSH and preliminary search of key terms was conducted first in order to acquire alternative language that may be used by researchers. Final terms used were: *chlamydia infection*, *chlamydia infections*, *chlamydia trachomatis*, *gonorrhea, neisseria gonorrhoeae*, *reinfection*, *re-infection*, *repeat infection*, and *recurrent infection.* STI-related and reinfection-related terms were combined first using an OR statement separately. They were then combined into a new search using the AND command.

After relevant literature was screened within PubMED, references from those chosen articles were assessed through abstract review. Articles that appeared to contribute to the research topic, and were not discovered in the original PubMED search, were also acquired.

## literature search strategy

Initial search using the previously specified terms yielded 751 relevant papers. Filters were applied to narrow the search to include articles on the adolescent age group of interest (13-18 in PubMed), those on human subjects, and those in English language. This filtering process narrowed search results to 220 papers. In addition to ensuring quality of paper, inclusion/exclusion criteria were developed to narrow down studies which would best contribute to the research problem of interest in this paper, as a means of increasing generalizability (i.e. only studies conducted in the US), or as a quick tool to narrow down papers (i.e. no studies before 1990). Inclusion and exclusion (TABLE 1) criteria were applied to the abstracts of those 220 articles, resulting in 33 abstracts fitting criteria.

Table 1. Inclusion/ Exclusion Criteria for Literature Search\*

\*Table only reflects number of articles excluded during abstract review out of original 220 abstracts acquired

|  |  |
| --- | --- |
| **INCLUSION** | **EXCLUSION** |
| Published in a peer-review journal | No abstract (n=3) |
| Published no earlier than 1990, or later than 2014 (excluded 28) | No/Insufficient mention of adolescent age group in abstract or paper body (n=25) |
| Information gathered in the US (excluded 33) | No/Insufficient mention of reinfection in abstract or paper body (n=11) |
| Focus primarily on gonorrhea and/or chlamydia (excluded 10) | Focus on treatment (i.e. drug trials) (n=20) |
| Able to electronically locate (excluded 3) | Focus on side-effects of diseases (i.e. rates of PID) (n=4) |
|   | Focus on biology/physiology of diseases (n=19) |
|   | Testing efficacy/effectiveness/feasibility of modeling programs, testing procedures, screening procedures, notification systems (n=26) |
|   | Provider protocols (n=4) |
|   | Case studies (n=1) |

Inclusion/exclusion criteria were then applied to the entire body of the remaining papers, yielding 16 articles. Finally, the same criteria were then reapplied to the references in each relevant paper to identify other papers that could have been missed using the main search process (n=5 added). The literature search resulted in 21 total articles that met all inclusion criteria (Figure 2).

Each paper was reviewed based on study objective, methods, results, recommendations, and limitations. Studies with specific rates of reinfection were presented as the percentage of individuals who were positive once during the study, and then who later were diagnosed with a repeat infection, with a few exceptions. For studies where adolescents made up only a proportion of the study population, risk factors were only reported in this paper if the study stratified them by age. Risk factors that were not stratified by reinfection status were reported, but a note was made to clarify this. All risk factors reported were significantly associated with reinfection, with few exceptions as noted in the results section. One study was solely qualitative32, meaning no data that could be analyzed through statistical methods was collected. Reported results were direct responses from participants.

Articles from Pubmed

n = 16

Articles added from PittCAT+ references search = 5

Articles included in final review

n = 21

Articles excluded n = 187

Exclusion criteria:

No abstract = 3

Published before 1990/after 2014 = 28

Conducted outside US = 33

Not focused on gc/ct = 10

No/insufficient mention of adolescents and/or reinfection = 39

Focused on treatment/side effects/biology = 43

Testing program efficacy, etc. = 26

Provider protocols = 4

Case studies = 1

Full text reviewed

n = 33

Articles excluded n = 17

Insufficient mention of adolescents = 10

Insufficient mention of reinfection = 4

Unable to acquire = 3

Titles and abstracts screened

n = 220

Search criteria: reinfection, re-infection, repeat infection, recurrent infection

Filters: human, adolescent, English

n = 220

Gonorrhea and Chlamydia terms

n = 31147

PubMed Database

Figure 2. Search strategy of literature review for gonorrhea and chlamydia reinfection rates and risk factors in adolescents. PubMed search performed October 6-10, 2015

# RESULTS

## Summary of literature review articles

There were a total of 21 articles included in this review. Among them, six were retrospective cohort studies, nine were prospective cohort studies, five were randomized control trials (RCT) or sub-analyses of parent RCTs, and one was a qualitative study conducted through focus groups. With regards to gender, 15 articles reported solely on females, and one reported solely on males. With regards to STIs, 12 articles focused only on chlamydia, while none focused only on gonorrhea. Of the articles that included data on both infections, the majority presented a combined reinfection rate, rather than presenting disease-stratified rates. With regards to minority populations, 3 studies focused on only African-American females, and one focused on Mexican-American and African-American females.

Sample sizes ranged from 10 to 87,338 participants. Michelson et al.14, Burstein et al.17, and Anshuetz et al.28 evaluated over 40,000 participants each. The majority were conducted in urban areas. Sexually transmitted disease (STD) clinics, family planning clinics, and reproductive health clinics were used for recruitment in 12 articles. Whites, African-American, and Mexican-American were the three most common races/ethnicities assessed in these studies.

Excluding the qualitative study32, all researchers made the effort in noting that if those enrolled were diagnosed positive for either gonorrhea or chlamydia, proper treatment had to be prescribed based on CDC treatment guidelines. Still, several studies were missing certain important characteristics including a clear definition of reinfection. Few studies (N = 5) reported on the median time to reinfection, which ranged from 5.2 months to one year. Median time is useful when making recommendations in terms of screening procedures.

APPENDIX A summarizes the studies included in this review. Reinfection rates ranged from 6.5-59.4%, and were reported as incidence or prevalence rates depending on the study. These rates will be expanded on further in the next section. Follow-up length ranged from 4 months through 10 years. Of those studies conducted in specific US cities, only one focused on a rural population. Adolescents made up a subset of the participants in 7 studies. Definition of adolescence varied from study to study, ranging from 10-21 years of age. However, only one study defined adolescence as early as 10 years old15, and one study ended adolescence at 21 years old.16 A wide range of risk factors were reported (Table 2) which will be expanded on in Section 3.3.

## REINfection rates of CHLAMYDIA AND GONORRHEA AMONG ADOLESCENTS

### DEFINITION OF REINFECTION

Definitions for reinfection were not consistent across the 11 studies that included a definition (APPENDIX B). Of those studies, 6 included specific endpoints between initial infection and reinfection to insure success of treatment.12,14,15,17,25,26 Other studies described reinfection as infections seen at more than one visit. All specified that a participant must have at least one previously positive result, either within their history or at baseline enrollment before reinfection can be identified.

### OVERALL INCIDENCE AND PREVALENCE RATES OF REINFECTION

As previously stated, reinfection rates ranged from 6.5-59.4% (excluding 2 studies where the results were only presented stratified, not overall). These rates were largely dependent on size and characteristics of the study population. Some rates were reported as incidence, others as prevalence, depending on the study. Among those reporting prevalence reinfection rates, the average was 20.4%. The highest prevalence rate was reported by Champion et al as 59.4% among those with history of abuse.24 On the other hand, the average incidence rate of reinfection was 23.6%, with Swartzendruber et al. reporting the highest of 40.0%.30 Time frame surrounding incidence depended on the study, ranging from a follow-up period of 4 months18 to up to 6 years.29

The majority of the reviewed studies focused solely on chlamydia infections. Of those that did report chlamydia and gonorrhea, rates specific to each disease were not reported. Figure 3 depicts the reinfection rates for entire study populations for each study, excluding the articles by Craft-Blacksheare et al.32 (qualitative study), Champion et al.24 (only stratified by history of abuse, 59.4% vs. 43.3%), and Orr et al.16 (stratified by sex but did not report overall rate).

Median times until reinfection were presented by five studies. The shortest median time to reinfection was presented by Anshuetz et al.28 as 4.2 months, closely followed by Orr et al.16 as 4.6 months. The longest was reported by Xu et al. as 10.9 months.15 The remaining two studies by Niccolai et al.25 and Burstein et al.17 reported median time to reinfection as 5.2 months and 6 months, respectively.



\*Prevalence rates. Other rates reported as incidence

✝Overall rates for chlamydia and gonorrhea. Other rates for chlamydia only

Figure 3. Overall reinfection rates by study. Presented as the proportion of subjects who experienced reinfection out of subjects with an incident infection.

### GENDER-SPECIFIC PREVALENCE AND INCIDENCE RATES

Limited information was available on gender-specific reinfection rates. Over half of the studies excluded males. Of the five studies that included both sexes, three analyzed rates stratified by sex. Burstein et al. studied adolescents aged 12-19 to determine screening practices within the Kaiser Permanente Mid-Atlantic States (KPMAS) system and the positive chlamydia results from those screenings, reviewing medical histories of adolescents who were screened at least twice. 17 Researchers reported a chlamydia reinfection prevalence rate of 17.1% and 11.1% among females and males, respectively.17 Only 1.5% of the males in the KPMAS system were screened for chlamydia.17 Orr et al. reported a female reinfection prevalence rate of 73% by 7 months and a male reinfection rate of 60% by 7 months among high-risk adolescents aged 14-21 from STD clinics.16 Finally, Michelson et al., who recruited lab confirmed chlamydia from a county health department, reported reinfection incidence rates of 3,982 female cases and 2,223 male cases per 100,000 person years.14 Researchers did not include asymptomatic men in their analysis, limiting the population pool.14 Reitmeijer et al. included both genders but did not stratify reinfection by age.20 Anshuetz et al. evaluated only adolescents, but did not stratify reinfection rate by gender.28

Among studies reporting reinfection rates (n=20), 14 included only females. Reinfection rates reported in these studies were generally high, with only Whittington et al. documenting a low incidence rate of 7.9% up to 5.5 months of follow-up among women who were positive for chlamydia (aged 14-34) from various clinics in 5 cities.18 Women were enrolled only until their next positive test result or until follow-up ended.18

Of the 14 female-specific articles, 6 articles showed incidence rates higher than 20% and 5 articles showed prevalence rates higher than 15%. The highest overall female-specific reinfection prevalence rate of 56.9% was reported by Niccolai et al. among females 14-19 years old recruited from 10 public health clinics. 25 The actual highest rate reported was from Champion et al. who presented rate stratified by history of abuse. Among abused female adolescents, unadjusted cumulative prevalence reinfection rate for years 1 and 2 was 59.4%.24

Only Ellen et al. conducted a male-specific study, and reported a reinfection prevalence rate of 6.5%.22 Acceptance rate into this study was low (44-49% depending on site), the study included only participants from an STD clinic, and follow-up time was only 4 months which may not be long enough to observe reinfection.22 While several studies provide female-specific rates, a limited number provided data on male adolescent populations.

### RACE-SPECIFIC PREVALENCE AND INCIDENCE RATES

Like with gender, limited information was available on race-specific reinfection rates. Only 2 studies out of the 21 reviewed focused on African-American women, and 1 focused on African-American men. 30,31 Magnus et al.23, Batteiger et al.29, Anshuetz et al.28, Whittington et al.18, and Thurman et al.27 all included minorities representing more than 50% of their study populations, but results were not reported by race and/or age.

None of the studies with a mixed population provided results that were stratified by race/ethnicity. Of two studies that included a mixed population of Hispanics and African-Americans, one reported race-specific rates.21,25 Niccolai et al. reported a reinfection prevalence rate of 23% among Hispanics and 17% among African-Americans. 21 Sample size was small (N = 97) and did not have high enough power to detect any significant differences between groups.

Sales et al.31 reported a reinfection prevalence rate of 15% among African-American adolescents. Prevalence of infection at enrollment was not provided, and the reinfection rate presented combined gonorrhea and chlamydia, rather than reporting rates separately by infection.31 Swartzendruber et al.30 found an incidence rate of 40% (time from 24 months) in a similar study, but the sample size was smaller than the Sales et al’ study (N = 123 vs. 556). Ellen at al.22 evaluated only African-American men and reported a reinfection prevalence rate of 6.5%. Lack of available papers and insufficient reporting of results has left limited data on race-specific rate of reinfection.

## RISK FACTORS FOR CHLAMYDIA AND GONORRHEA REINFECTion AMONG ADOLESCENTS

### OVERVIEW OF RISK FACTORS

Including the one qualitative study32, 18 studies reported potential risk factors for reinfection of gonorrhea/chlamydia. Of the 17 quantitative studies, 2 did not find statistically significant risk factors,19, 22 and four did not stratify by age when presenting risk factors.

Remaining studies focused on determining both rates of reinfection as well as potential risk factors, and found several statistically significant risk factors. These risk factors were summarized in Table 2 in 4 different categories: 1) Participant-related risk factors include demographic and physiologic characteristics of the participants; 2) Partner-related risk factors include relationship status of the participants, as well as a few other details pertaining to participants’ partner(s); 3) Behavioral–related risk factors are all factors that the participants are not biologically predisposed to, and are therefore open to future change. Those which did not fit the main 3 categories are placed under other. All factors were found to be significantly related to reinfection rates. Traits involving partner relationships were among the most cited risk factors. Most of the risk factors were determined in female-specific studies.

\*Chlamydia only studies

|  |  |  |  |
| --- | --- | --- | --- |
| Participant | Partner | Behavioral | Other |
| Female17,28 | Multiple partners12,23**\*** | No condom use at last sex13 | History of abuse24 |
| African-American/Non- White 12,23\* | New partner12**\*** | Unprotected sex within 30 days21 | SES-related risk31 |
| Age23,31 | Symptomatic partner12**\*** | Substance abuse24 |  |
| Pregnant12\* | Relationship less than 1 year21 | Unprotected sex with untreated partner27 |  |
| STI at baseline31 | Partner treatment unknown | Greater impulsivity20 |  |
|  | Rapid partner turnover27 |  |  |
|  | Nonmutually monogamous27 |  |  |
|  | Named partners untreated24 |  |  |

Table 2. Statistically significant associated risk factors for gonorrhea and chlamydia reinfection among adolescents

### PARTICIPANT RELATED RISK FACTORS ASSOCIATED WITH REINFECTION

There were 6 participant-related risk factors studied before: being female, being African-American or non-White, being within a specific age, pregnant at baseline, and having an STIs at baseline.

Studies by Mosure et al12 and Magnus et al23 reported race as a potential risk factor for reinfection of chlamydia. Mosure et al. (N=2629) sought to determine rates and potential risk factors of reinfection of adolescent females aged 15-19 who attended family planning clinics.12 Alongside several other risk factors, being Non-White was found to be a risk factor for chlamydia reinfection (OR = 1.3; 95% CI: 1.1-1.4). Magnus et al. (N=496) who evaluated adolescent females aged 14-18 who tested positive for chlamydia at baseline, reported being African-American as a risk factor for chlamydia (OR= 1.27; 95% CI: 1.03-1.56). 23 However, when adjusted for all other potential risk factors (i.e. partner’s age, number of sex partners, condom use at last sex, etc.) race was no longer found to be significant (OR = 1.91; 95% CI: 0.96-3.77).23

Among the 21 studies, only five included both genders within their populations. Within these studies, two had populations of adults and adolescents and did not stratify their results by age.14, 20 Furthermore; one study focused solely on reinfection rates and did not attempt to determine potential risk factors.16 The two remaining studies both reported being female as a risk factor for reinfection for chlamydia and gonorrhea. Burstein et al.17 (N=87338; 50% male) found being male to be more protective against chlamydia reinfection when compared to female participants (OR = 0.2 (95% CI: 0.1-0.2; p < 0.0001)). Anshuetz et al.28 (n=49871; ??% male) analyzed screening data from chlamydia and gonorrhea tests administered to Philadelphia high school students, and found that females with named untreated partners, were more likely to be reinfected than males with named untreated partners (p<0.01).28

Magnus et al. and Sales et al., both of whom included only adolescent participants, reported age as a risk factors for reinfection.23,31 Magnus et al. found that the younger adolescents (14-16 years old) were at greater risk for chlamydia than those over 16 years of age with an unadjusted OR of 1.25 (95% CI: 1.03-1.56).23 The risk associated with younger age became larger after adjusting for other risk factors (OR = 1.94; 95% CI: 1.08-3.46).23 Sales et al. (N=627) examined the risk of socioeconomic strain on risk of STIs infection and reinfection among 14-20 year old African American females. They found that younger age was significantly associated with higher risk of reinfection (p =0.0001). 31 Researchers did not report which ages were associated with increased reinfection risk.

Sales et al. recruited African-American females aged 14-20 who had unprotected vaginal sex within 6 months of enrollment.31 Enrolled participants included adolescents with or without current STIs. Researchers found that in addition to age, having an STI at study baseline was significantly associated with a later reinfection (p = 0.02). Researchers did not go into further detail about risk toward chlamydia or gonorrhea specifically.31

Another risk factor which Mosure at al. found to be significantly associated with reinfection rate was being pregnant. 12 Researchers found that pregnant adolescents had odds of reinfection 1.4 times that of non-pregnant adolescents (95% CI: 1.2-1.7).12 Researchers did not examine behavioral risk factors of participants.12

### PARTNER-RELATED RISK FACTORS ASSOCIATED WITH REINFECTION

Partner-related risk factors were the most commonly reported risk factors. A total of 8 risk factors were reported by 5 studies. Partner-related risk factors included number of partners, longevity of relationships, type of relationship, and treatment status of partner(s).

Some of the risk factors are semantically different, but this creates arbitrary differences. Increased risk from having multiple partners12,23, rapid partner turnover27, and being non-mutually monogamous27 mean that having more than one sexual partner (simultaneously or sequentially) increase risk of reinfection. Non-mutually monogamous, however, may be applied to either participants or their partner(s), which researchers did not specify.27 Thurman et al. found that (over the course of a 12 month RCT promoting behavioral change among Mexican-American and African-American females aged: 14-45 years, n=164) both non-mutually monogamous relationships and rapid partner turnover increased odds of reinfection for gonorrhea or chlamydia.27 Adolescent females with a rapid turnover in their partnerships were found to be twice as likely to have a reinfection (p = 0.05). Those in non-mutually monogamous relationships were 5 times as likely to have a reinfection (95% CI: 1.79-14.73).7 Similarly Mosure et al.12 and Magnus et al23 found that having multiple partners increased risk of reinefection significantly. Magnus et al found an odds ratio of 2.13 (95% CI: 1.05-4.34)23, while Mosure et al. reported an odds ratio of 1.7 (95% CI: 1.3-2.1).12

Length of partnership was documented by two studies.12,21 Along with being Non-White and pregnant, Mosure et al. found that having a new partner within 60 days increased odds of chlamydial reinfection by 1.8 (95% CI: 1.6-2.0).12 In a study to determine if knowledge of partner treatment for a past sexually transmitted infection was related to current infection, Niccolai et al. (N=97) found that being in a relationship for less than one year was associated with reinfection among sexually active 14-19 years old women (p = 0.01).21 Approximately half of the population was pregnant.21

There was a reported significant association between partner infection status and risk of gonorrhea and chlamydia.21,12 Niccolai et al. found that not knowing a partner’s treatment status for an STI to be a statistically significant risk factor for reinfection of chlamydia and gonorrhea (OR = 4.46; 95% CI: 1.41-14.29; p<0.05).21 Mosure et al. found that having intercourse with a symptomatic partner (treatment status and condom use during symptomatic period unknown) to increase odds of chlamydial reinfection by 2.3 times (95% CI: 1.8-3.0).12 As previously stated in section 3.3.2, Anshuetz et al. found untreated named partners to be a risk factor among participating females (p<0.01).28

### BEHAVIORAL RISK FACTORS ASSOCIATED WITH REINFECTION

Behavioral factors are behaviors for which self-efficacy could be increased. Five risk factors were identified among females including no condom use at last sex, substance abuse, and greater impulsivity. As with number of partners, a few of the risk factors may have semantic similarities.

Unprotected sex was a commonly cited risk factor, accounting for three of the five behavioral risk factors. Oh et al. conducted a study to determine both incidence and risk of gonorrhea and chlamydia among sexually active urban adolescent females (N=216) aged 11-19 who originally went to a clinic of the Division of Adolescent Medicine for a pelvic exam. 13 Researchers found that not using condom at last incident of sexual intercourse increased odds of reinfection by approximately 6 times (95% CI: 1.67-21.82; p = 0.0006) for gonorrhea, but was not significant for chlamydia reinfection (p = 0.68). 13 Within the study, 12 participants were reinfected with gonorrhea accounting for 41.2% of total number of incidences of gonorrheal infection. Thirteen participants had recurrent chlamydia but only made up 27.7% of total incidences of chlamydia.13 Niccolai et al. reported unprotected sex within the last 30 days as a strongly significant risk factor for reinfection (OR = 4.98; 95% CI: 1.4-17.77; p<0.0005). 21 This variable was analyzed dichotomously; number of times participants had unprotected sex within the preceding 30-day period was not analyzed.21 Thurman et al. found that having unprotected sex with an untreated partner increased odds of reinfection by 5.58 (95% CI: 2.61-11.95; p<0.01), but the timeframe of the unprotected sex was not defined.27

Associated risk factors were not exclusive to sexual health. Champion et al. (N=241 adolescents) created substance risk categories of low/moderate, high, and ultra-high based on an abuse screen tool utilized by researchers.24 When stratified by abuse (physical or sexual), adolescents at year 2 of the study who were in the high substance risk category had a greater risk of reinfection compared to non-abused adolescents (p<0.05). 24 These differences were not found in year 1 or cumulatively over the study follow-up time. Reinfection risk was greater among non-abused substance abusers, the majority of whom though were adults.24

Swartzendruber et al. (N=701) sought to identify baseline predictors of repeated gonorrhea and/or chlamydia infections among African-American adolescent females aged 14-20 from reproductive health clinics. 30 Like Champion et al24, Swartzendruber et al. did a subanalysis of a parent RCT (HIV prevention).30 Swartzendruber et al. looked at participant impulsivity as a potential risk factor which was measured using a 15 question-item scale designed to determine how much thought goes into actions made. Researchers reported that participants who had greater impulsivity had an odds ratio of 1.55 (95% CI: 1.03-2.34; p = 0.035) compared to those with a lower impulsivity score.30

### OTHER RISK FACTORS ASSOCIATED WITH REINFECTION

Other risk factors found to increase reinfection risk did not fit with previously described categories.24, 31 Champion et al.24 evaluated rates of reinfection by history of abuse, adjusted for the intervention arm of the RCT (evaluating behavioral interventions and STIs counseling) in 14-45 years old women. 24 Researchers found history of abuse (physical and/or sexual) to be associated risk factor for chlamydia and gonorrhea reinfections. 24 Cumulative unadjusted associations between abuse and reinfection was stronger for adolescents (participants under 19 years of age) than adults. Compared to unabused adolescents, those who experienced abuse were significantly more likely to experience reinfection (p = 0.0004).24

Sales et al. specifically sought to determine the effect of SES-related risk (chronic poverty, limited occupation/educational opportunities, frequent housing relocation, unstable employment) on reinfection.31 This factor was found to be significantly associated with both initial acquisition of chlamydia and/or gonorrhea as well as with reinfection (p = 0.015 for reinfection). 31 Researchers attribute this with the “weathering” affect, a cascade of biological responses to stress, over time increasing infection susceptibility. Participants were recruited from urban sexual health clinics, and 44% were living with a single parent.31

### ASSOCIATED RISK FACTORS WITHIN QUALITATIVE STUDY

Only Craft-Blacksheare et al. (N=10) attempted to determine risk factors through qualitative methods, directly asking women with a history of multiple chlamydial infections about their beliefs of reinfection risk.32 Most of the 10 participants reported education or misconceptions as potential risk factors. All girls understood the seriousness of HIV, but felt were not taught this for other STIs. Additionally, some participants were not provided with educational information upon first diagnosis and therefore were not made aware of preventative measures they could take. Several believed that they could tell when a partner is infected. All participants expressed the desire for more sexual education, and felt empowered by their situation to increase condom use adherence. A participant reported that she only uses condoms sporadically with her partner because she trusts him, but is screened every 3 months as a precaution. While none of these factors can be statistically linked to reinfection, they do provide direct insight from those with a history of multiple chlamydia diagnoses.

# discussion

Rates of reinfection as summarized in this literature review were consistently high. While there was a large variability in prevalence and incidence rates depending on study design, size, and population, the vast majority reported a prevalence rate greater than 15% and an incidence rate greater than 20%. There also appears to be a number of risk factors influencing reinfection, such as unprotected sex and being non-monogamous.

The reviewed studies, even among similar populations, exhibited a high level of variability. Excluding the study conducted by Champion et al.24 which was specifically among a high risk population, reinfection prevalence and incidence rates could vary by 50% throughout the evaluated studies. It is difficult to determine the true reinfection rate among adolescents due to lack of consistency in the results. It is important to know overall what the incidence of gonorrhea and chlamydia are within a population, but there also needs to know of how much of that incidence attributed to reinfection, and which populations appear to be the most vulnerable to those reinfections. A substantial part of understanding reinfection is having a proper case definition, for which there was not much consensus across the studies (APPENDIX B). Additionally, median time to reinfection was not reported by the majority of the reviewed studies. This number is helpful in making screening and rescreening recommendations, as well as to estimate a potential time frame of risk. Populations with shorter median time to reinfection could be experiencing a great number of associated risk factors than counterparts with longer median time. Based on the current literature review, a large proportion of reinfection occurred within 6 months of the initial infection.

The large focus on female populations was probably influenced by the high prevalence rate of reinfection in that group. This is a valid concern as approximately one quarter on average of female participants went on to incur a repeat infection within study periods. Prevalence and incidence rates were often higher among minority women. Swartzendruber et al.30 reported an incidence rate to be around 40%. Champion et al.13 showed that prevalence rate could climb even higher if history of abuse was taken into account. 13 However, it cannot be assumed that female adolescent incidence or prevalence rates of reinfection specifically are higher than those of males without sufficient data on male for comparison. Only one small study focused on male adolescents, and showed a prevalence rate of reinfection of 6.5%.22 This study, though, included a small sample size, had a low acceptance rate, and a follow-up period of only 4 months, all of which could contribute to an underestimation of reinfection. The other studies that included males often did not stratify results by gender and therefore a relationship between male gender and reinfection could not be assessed.

Potential risk factors have been poorly examined. Some studies did not stratify results by age and therefore conclusions specific to adolescents could not be drawn. Some did not find any associations, possibly due to small sample sizes and the bias that comes with self-reporting behaviors. Others did not assess any risk factors. Of those that did report significant risk factors, only Anshuetz et al. included males in their study population. Researchers did not find associations for males due to high attrition rates (>50%) among male students.28 Age was evaluated as a potential risk factor by two studies, but both did little to explain why specific ages in an already narrow age range would influence reinfection significantly.23,31 Magnus et al. attempted to explain this result by stating that 14-16 year olds are more prone to actions like increased partner turnover and lower rates of condom use.23 Sales et al. did not even report which ages showed higher risk.31 Abuse of any sort is known to have adverse health effects.33 Partners perpetrating intimate partner violence (IPV) of young adult and adolescent females are less likely to seek treatment or screening, and victims of IPV are more often afraid of partner notification.34 IPV could increase risk of reinfection. Only one study addressed abuse as a potential risk factor.13

Despite the small number of studies that assessed potential risk factors of chlamydia and gonorrhea reinfection, 20 associated risk factors were identified spanning across 4 categories (Table 2). The majority of the evaluated risk factors was related to sexual health (partner-related and behavioral). However, being female17 and having a history of abuse (among minority women)24 were highly related to reinfection risk. Additionally, SES-related risk and greater impulsivity were shown to affect rates.

Impulsivity may have been the most unique risk factor. Impulsivity is not a characteristic that is generally recorded. Sexual behaviors could be determined during screening or within a patient’s medical history. Impulsivity, however, is typically measured separately and is common among adolescents. Teenagers tend to engage in risky behaviors, and yet only one study attempted to measure this factor on the real-life consequence of repeat STIs infection.30 A study by Monahan et al. found that psychosocial maturity continues to develop through an individuals mid-20s, and may be stunted by antisocial behavior and influence risk taking.35 Craft-Blacksheare et al. also demonstrated the need to ask those who are reinfected directly what barriers and reasons they believe are causing their history of multiple STIs.32 Participants’ responses cannot be backed up with quantitative data, but do provide insight on issues that are not determined by the other studies.32

A key conclusion that could be drawn from this review is the urgent need to close the gaps in the literature regarding reinfection among adolescents, especially as related to study population demographics. A large proportion of the reviewed studies focused on females, but there was an insufficient focus on males even among studies included both genders. This is in part due to males consistently having higher attrition rates than their female counterparts.16,20,22 In the case of Burstein et al., only 1.5% of eligible males were tested at all.17 Additionally, of the studies that included male adolescents, none reported any information on sexual orientation. Few studies focused specifically on minority populations, most of them included females’ subjects only. There needs to be a greater body of research done on males, minorities, minority males, and sexual minority adolescents. Adolescents made up only a subset of study populations in one third of the reviewed papers. Many studies were excluded from this review because adolescents were hardly mentioned. Adolescents have the second highest prevalence of gonorrhea and chlamydia in the US, more research needs to be conducted within adolescent populations to shed light on this phenomenon, providing potential explanation for these high rates.4

This targeted literature review also highlighted additional gaps that pose great public health impact. Most of the studies focused on chlamydial infections while none focused on gonorrhea. Although chlamydia rates overall are much higher than gonorrhea,4 gonorrhea is a notifiable disease with harmful consequences if left untreated and is the second most reported STIs in the country.4 Understanding its reinfection rate is therefore critical. Researchers need to better report median time to reinfection so that proper screening recommendations can be made. This may mean conducting more studies with long follow-up times, either prospectively or retrospectively (i.e. surveillance data or medical history databases). The short follow-up times found in two studies could have led to inaccurate representations of reinfection rates.18,22 A reoccurring limitation cited within studies was that investigators were not certain on whether participants’ medical histories were complete. Participants could conceivably be screened and treated at clinics not affiliated with the studies. If patients were tested elsewhere, researchers would be unaware of the results due to lack of record sharing. Unexpectedly, only about half of the reviewed studies included a case definition of reinfection. Lack of universal definition negatively impacted interpretation of prevalence rate and comparison of results between studies. Additionally, improper definitions could lead to misclassification bias.

There were a number of limitations to this review. It was difficult to interpret results due to methodological concerns, namely attrition rates, homogenous populations, incomplete sexual/medical histories, and inadequate follow-up times and intervals, which also influenced validity and generalizability of results. Despite the University of Pittsburgh’s comprehensive access to a number of databases and journals, not all eligible papers could be accessed. Finally, as a novice reviewer, lack of experience and limited outside help may have led to some pertinent studies being missed. There are often inherent biases associated with conducting a literature review, particularly when excluding studies based on reading abstracts and whole articles. There was a chance that despite attempting to do so, this literature review was not conducted in a wholly objective manner.

Screening is an important tool that must be utilized, especially with male adolescents, who were underrepresented based on this literature review. The array of risk factors presented in this literature review suggested that populations at-risk may not be immediately determined from medical background, and therefore screening should be targeted broadly to the adolescent population. It is currently recommended that sexually active persons 26 years old and under be screened annually6, but these studies show that reinfection rates can occur within less than a year of infection among adolescent populations. However, the CDC reported that while screening practices are expanding, not everyone who should be screened is.9 Additionally, there needs to be a universal sharing of medical history data between providers to gain an accurate representation of infection/reinfection rates and reduce underreporting of reinfection rates. An accurate depiction of the problem could help to better inform potential solutions. Finally, barriers to sexual health education need to be addressed. The misconception that HIV is the only sexually transmitted disease worth worrying about shows a lack of understanding of the diseases that adolescents are most at risk for (gonorrhea and chlamydia). This incomplete understanding leaves adolescents unaware of the negative impact those diseases have on their health (PID and infertility).

In conclusion, variability in reinfection prevalence and/or incidence rates and associated risk factors demonstrate the need for more research among the adolescent population. The high rates that were shown in the reviewed studies emphasize a related public health issue. In order to gauge more accurate rates, screening must be done more thoroughly, engage more than just the female population, and be shared across providers. Once more consistent information is determined, better designed prevention tactics can be developed and aimed at the adolescent populations who are at greater risk. Targeting this younger population could have positive effects on the even higher rates of gonorrhea and chlamydia that are seen in the young adult population. This literature review highlighted a gap in knowledge surrounding adolescent research in gonorrhea and chlamydia reinfection rates, especially around gender and race. In order to improve public health within this demographic, these gaps must be addressed in future research.

**APPENDIX A: SUPPLEMENTAL TABLE ON THE LITERATURE**

Table 3. Comprehensive Summary Table on Review Literature

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Objective** | **Population** | **Study Design** | **Disease** **Incidence or Prevalence** | **Reinfection Results** | **Limitations** |
| Mosure et al. [12] | Determine rates and predictors of chlamydia reinfection | 15-19 year old females; Family planning clinics in 4-state region | Retrospective cohort. Medical database review. | Prevalence = 22% | 18.0% | Majority did not make second visit; history of STI not in analysis; could have been tested at non-family planning clinics |
| Oh et al. [13] | Determine incidence and risk of gonorrhea/chlamydia reinfection among adolescent females | Sexually active females 11-19 years old; Adolescent clinics of Dvision of Adolescent Medicine Southeastern U.S. | Prospective cohort. Analysis on subjects with at least 2 visits | Overall incidence = 15% Gonorrhea = 11.6% Chlamydia = 23.2% | 25.3% Overall; 40% Gonorrha; 18% Chlamydia | Intervals between rescreening not uniform; high attrition rates; small sample size; not generalizable; does not include history of STDs in analysis |
| Michelson et al. [14] | Describe demographics, risk, and geographical distribution of chlamydia infections | Lab confirmed chlamydia tests sent to STEP County Health Department  | Retrosective cohort. Review of test results. | Incidence = 563 infections per 100,000 person-years  | 13.0% | Cases reported dependent on site of diagnosis; excluded asymptomatic males; excluded those who did not seek treatment |
| Xu et al. [15] | Use population-based registry to analyze frequency and predictors of repeat chlamydial infection in women | Women 10-44 years old; Initial positive test during study period | Retrospective cohort. Medical database review. | N/A | 20.2% | Women may have moved out of state; non-universal screening; non-universal reporting  |

**Table 3 Continued**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Objective** | **Population** | **Study Design** | **Disease Incidence or Prevalence** | **Reinfection Results** | **Limitations** |
| Orr et al. [16] | Compare rates of subsequent and reinfection of chlamydia and gonorrhea in high-risk adolescnts | Ages 14-21; STD clinic and 3 urban adolescent community clinics; Positive for gc/ct | Prospective cohort. STI screening. | N/A | 60% men 73% women | Testing variability; high attrition rates especially among men |
| Burstein et al. [17] | Determine screening practices and resulting positive test results | Adolescents 12-19; Enrolled in KMPAS health plan; At least 1 positive ct test | Retrospective cohort. Medical chart review. | Incidence = 14.6% | 16.4% | Only 1.5% males in system tested; no race, SES, behavior, sexual activity available; variability in testing among sites; screening outside KMPAS system |
| Whittington et al [18] | Identify factors associated with persistent and recurrent chlamydial infection in young women | Females 14-34; Reproductive health/STD/adolescent medicine clinics in 5 cities; Positive ct result | Prospective cohort. Interviews and ct screening | N/A | 7.9% | High attrition; short follow-up period; variability of follow-up intervals; variability in testing; recall bias; confounding from couseling; insufficient power; not generalizable |
| Kissinger et al. [19] | Determine if age of partner influences chlamydia reinfection  | Women 14-30 years old; Initial ct positive at public family planning/STD clinic in 5 cities | Prospective cohort. Ct screening interim behavior history.  | N/A | 13.8% | Insufficient power; not generalizable; high attrition; recall bias |
| Rietmeijer et al. [20] | Study incidence and repeat infection among clients of STD clinic | Client of an STD clinic; Screened for ct more than once 30 days apart | Retrospective cohort. Medical database review. | Incidence = 26.1% | 22.8% | Not generalizable; influence of asymptomatic chlamydia; history of STI not included; high attrition; screening from outside provider |

**Table 3 Continued**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Objective** | **Population** | **Study Design** | **Disease Incidence or Prevalence** | **Reinfection Results** | **Limitations** |
| Niccolai et. al [21] | Determine relationship between knowing your partner has been treated for past STI and current infection | Sexually active women; 14-19 years old; 50% pregnant; history of STI | Prospective cohort. Interviews and ct/gc screening. | Not provided | 17.5% | Unsure of infection origins; recall bias; small sample size. |
| Ellen et al. [22] | Examine risk for repeat infections with reducing number of sexual partners among men 13-25 | Men 13-25 from screening project; Asymptomatic; 2 U.S cities | Prospective cohort. Interviews and ct/gc screening | N/A | 6.5% | Small sample size; limited power; low acceptance rate; short follow-up |
| Magnus et al. [23] | Determine if older sexual partners associated with recurrent chlamydia among adolescent women | Females 14-18; Infected with ct | Subanalysis of parent RCT | N/A | 16.1% | Selection bias; short follow-up; recall bias; not generalizable; unable to link 19.9% of partners |
| Champion et al [24] | Evaluate rate of reinfection stratified by history of abuse | 14-45 year old English-speaking women | Subanalysis of parent RCT | Not provided | 59.4% abused 43.3% unabused | Recall bias; limited power in some risk categories |
| Niccolai et. al [25] | Determine frequency and patterns of chlamydia among adolescent women | 14-19 year old females; 10 public health clinics | Prospective cohort. Interviews, medical record review, ct screening, review of health department reports. | Prevalence = 52.6% | 56.9% | Did not confirm STI history; did not confirm treatment; do not know if screened between follow-ups |

**Table 3 Continued**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Objective** | **Population** | **Study Design** | **Disease Incidence or Prevalence** | **Reinfection Results** | **Limitations** |
| Gaydos et al [26] | Determine reinfection rates of chlamydia for females attending school-based health centers | Adolescent females; School-based health centers in Baltimore City (8 high schools, 3 middle schools | Retrospective cohort. Medical database review. | Incidence = 18.1% | 26.3% | Majority not rescreened; may miss asymptomatic individuals; outside network screening |
| Thurman et al. [27] | Compare efficacy of SAFE behavioral intervention on teenage females compared to adults with rates of reinfection with chlamydia/gonorrhea, and identify associated behaviors | Mexican-American and African-American females; 14-45 years old; Enrolled in SAFE; Positive for non-viral STI | RCT. Intervention arm: 3, weekly multicomponent behavioral group sessions. Control arm: 15 min STD risk reduction phone call sessions | N/A | 33.1% overall 24.2% study group 40.2% control group | Teens' parents/partners not involved; recall bias |
| Anshuetz et al. [28] | Analyze screening data for gonorrhea and chlamydia | 15-19 high school students; Philadelphia | Prospective cohort. Confidential screening during school year | Prevalence = 4.5% | 13.6% within same school year | Self-selected screening; high absence rates; no rescreening after March 1; could not located >50% of students eligible for retesting |
| Batteiger et al. [29] | Determine reinfection rates among adolescent women | Convenience sample from 3 primary care clinics; Women 14-17 years old | Prospective cohort. Interviews and ct screening every 3 months, plus daily diaries and self-swabs | Prevalence = 54.4% | 31.3% | Convenience sampling; not generalizable; did not include history of STI; incomplete data on partner infection status |

**Table 3 Continued**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Objective** | **Population** | **Study Design** | **Disease Incidence or Prevalence** | **Reinfection Results** | **Limitations** |
| Swartzendruber et al. [30] | Identify baseline predictors of repeat infection of gonorrhea and/or chlamydia among African-American adolescent females | Female 14-20 years old; African-American; 3 Atlanta reproductive health clinics; Completed more than one follow-up | Subanalysis of parent RCT | Incidence chlamydia = 16.5% Gonorrhea = 6.5% | 40.0% | Factors subject to change over time; influence of parent intervention; attrition rate different between groups; excluded different from included |
| Sales et al. [31] | Examine SES strain on STI risk, acquisition and reinfection | Females 14-20 years old; African-American; 3 clinics in Altanta, GA | Subanalysis of parent RCT | Not provided | 15.0% | SES status change over lifetime; not generalizable; recall bias; sexual risk and intervention condition included as potential confounders in analysis |
| Craft-Blacksheare et al. [32] | Explore reasons for high recurrance rate among African-American urban women | African-American women ages 15-19; 3 urban health clinics in Michigan | Qualitative. Audiotaped interviews. Health Belief Model | N/A | N/A - Self-reported  | Small sample size; homogeneous sample; did not address self-esteem, relationship quality, or partner involvement; not reproducible |

**APPENDIX B: SUPPLEMENTAL TABLE OF DEFINITIONS**

Table 4. Definitions of Gonorrhea and Chlamydia Reinfection

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| Reference | Definition of Reinfection |
| Mosure et al. [12] | Infection at least 1 month after previous test |
| Oh et al. [13] | At least 2 episodes of cervicitis owing to ct/gc |
| Michelson et al. [14] | Infection at least 15 days after, and within 6 months of a previously reported infection |
| Xu et al. [15] | Infection detected at least 30 days after treament of preceding infection |
| Burstein et al. [17] | Infections more than 30 days apart |
| Rietmeijer et al. [20] | Incident infections among persons whose baseline results were positive |
| Niccolai et. al [25] | Diagnoses by any source that occurred more than 30 days after previous diagnosis |
| Gaydos et al [26] | Positive ct result occurring between 30 and 365 days after initial positive result |
| Batteiger et al. [29] | Episode pairs with different genotypes, or same genotype but with interim unprotected coitus |
| Swartzendruber et al. [30] | Positive ct/gc test following a negative result or documented treatment, among participants positive at baseline |

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