A Systematic Literature Review of Reviews on the Effectiveness of Chlamydia Screening

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Abstract

Chlamydia trachomatis is the most common bacterial sexually transmitted infection, causing significant morbidity and economic burden. Strategies like national screening programs or home-testing kits were introduced in some developed countries, yet their effectiveness remains controversial. This systematic review examined reviews of chlamydia screening interventions to assess their effectiveness and the elements that contribute to their success to guide public policy and future research. The review assessed English material published after year 2000 in PubMed, Cochrane Library, the British Nursing Index, Medical Database, and Sociological Abstract, in addition to World Health Organization Global Health Sector Strategies, the European Center for Disease Prevention and Control guidelines, and PROSPERO. Systematic reviews that focused on chlamydia screening interventions were included. Using the socio-ecological model, we examined the levels of interventions that may affect the uptake of chlamydia screening. 19 systematic reviews were included. Self-collection in home-testing kits significantly increased screening among females 14-50 years of age. At the organizational level, using electronic health records and not creating additional costs facilitated testing. At the community level, outreach interventions in community/parent centers and homeless shelters reached high screening rates. At the policy level, interventions with educational and advisory elements could result in significant improvements in screening rates.

Key words: Sexually transmitted infections; Chlamydia; Screening; Effectiveness; Review

Abbreviation:

PID: pelvic inflammatory disease

Introduction

Chlamydia trachomatis is the most common bacterial sexually transmitted infection and causes significant morbidity and economic burden globally [1]. There are approximately 131 million new cases of chlamydial infection occurring in individuals aged 15-49 years annually, with an incidence rate of 38 per 1000 females and 33 per 1000 males. Among the non-viral sexually transmitted infections, chlamydia is the most costly infection, which costs the US healthcare system approximately US$516 million annually [2]

The majority of chlamydia infections are asymptomatic with only 30% of women and 10% of men develop symptoms [3]. Therefore, infected people often do not seek testing and are unaware of their infection [4]. The symptoms of uncomplicated chlamydia infection in women include abnormal vaginal discharge and post-intercourse bleeding [1]. C*hlamydia trachomatis* is also an important cause of pelvic inflammatory disease (PID) [5]. A community-based study found that the annual incidence of PID among women with untreated chlamydia was about 10% [6]. Other reproductive sequelae of chlamydia include infertility, ectopic pregnancy and chronic pelvic pain [5]. The reported infertility rate after one episode of PID was 8% and it increases to 38% after three PID episodes [7]. Chlamydia infection is also associated with negative psychosocial impact and poor sexual quality of life in young women [8,9].

To reduce the burden of chlamydia control strategies a number of developed countries have implemented national screening programs [10], opportunistic screening for women <25 years [11,12], and targeted screening [13]. England initiated their National Chlamydia screening program where free screening is provided in settings such as genitourinary medicine clinics, general practices,

and community pharmacies. For sustainable benefits to occur, screening and follow-ups should be regular [14]. Such requirements may be difficult as the target population must utilize health service regularly and health providers must offer the tests at appropriate intervals. Administrative systems also need to track individuals who attend various health venues [15]. The introduction of quick and non-invasive testing methods such as nucleic acid amplification tests has allowed testing to be done in more convenient and out-of-clinic settings however chlamydia testing rates remain sub-optimal [16]. Barriers that lead to continued low screening rates include hesitation and embarrassment from patients and limited understanding and training amongst healthcare providers [17,18].

There is an abundance of literature relating to improving the rates of chlamydia screening. Certain interventions target patients while others target the healthcare providers. The heterogeneity of chlamydia screening interventions make clinicians and researchers difficult to determine which are effective. Hence there is a lack of consensus on the most effective way to increase chlamydia screening. To address this issue we carried out a systematic review of systematic review articles, of chlamydia screening, in order to guide our public health policy and research in the area.

Methods

We conducted this systematic review of systematic reviews in accordance with the guideline of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). The systematic review protocol was registered on the PROSPERO database (registration number: CRD42018085514)

Information Sources and Search strategy

Five databases were used to identify review articles that have evaluate chlamydia screening intervention. They are PubMed, Cochrane Library, the British Nursing Index, Medical Database, and Sociological Abstract via ProQuest. Searches in PubMed were conducted with the Medical Subject Headings (MeSH) terms of "Chlamydia" and "mass screening" then filtered for systematic reviews and meta-analysis. In the Cochrane library, the advanced search function was used for the key words "chlamydia" and "screening". In ProQuest, advanced search was carried out for the key words "chlamydia", "mass screening", and "systematic review".

Besides, the reference lists of the World Health Organization Global Health Sector Strategies and the European Center for Disease Prevention and Control guidelines were screened. PROSPERO database was also searched. Experts in our network were approached for suggestions of relevant papers.

Inclusion *Criteria*

We only included systematic reviews and meta-analysis published in English after 2000 because nucleic acid amplification test diagnostic technology was not introduced until then. Interventions must focus on Chlamydia screening (studies regarding sexually transmitted infection screening were accepted as long as chlamydia is included). Interventions must have one or more of these outcome measures: number of chlamydia tests, testing rate, retesting rate, and/or treatment rate of chlamydia.

Screening

One author (Stephanie Lau) screened the titles and abstracts and two authors (Stephanie Lau and Edmond Choi) independently conducted full text screening and data extraction. Discrepancies were resolved through discussion and input from another author (William Wong).

Data Extraction

A raw data extraction sheet was created and included information such as target populations, settings, type of testing, number of people tested, prevalence, number of people treated, effectiveness, and barriers. The data extraction summary sheet is available in the appendix.

Quality Assessment

The quality of the included papers was assessed using the validated scale Assessment of Multiple Systematic Reviews (AMSTAR). It provides a 16-item checklist on the quality of systematic review methodology.

Analysis

The socio-ecological model was used to organize the interventions (Figure 1). The socio-ecological model is a systems model with multiple levels of influence including interpersonal, organizational, community, and policy levels. Interventions based on the individuals' characteristics aim to influence their knowledge, attitude, and beliefs towards a health behavior. Interventions at the interpersonal level influence social norms to overcome individual barriers. Involved parties include friends, family, community health workers, and health service providers. Interventions in the organizational level involve healthcare systems, health

departments, and health clinics. Interventions in the community level try to leverage resources and encourage the participation of community-level institutions. Interventions at the policy level aim to create systemic changes. Health intervention developers often utilize this model to ensure that the intervention accounts for these interwoven bands of influence to result in the greatest impact [19].

Results

200 studies were identified in the initial search of the databases and an additional 5 studies were identified through other sources. During the title screen, 148 studies were excluded because their titles did not mention that it was a systematic review, was not about sexually transmitted infections, or was not in English. During the abstract screen, 33 further studies were excluded because the abstract did not mention anything related to chlamydia screening and testing. 24 reviews were assessed by full text screen in which five was excluded to result in the final inclusion of 19 reviews. The study details are shown in Web Table 1 One study was excluded because it described itself as a review but was ultimately not a systematic review. Two studies were excluded because it was regarding diagnostic tools for detecting chlamydia. Two studies were excluded because it was about rescreening (Figure 2).

Quality Assessment

Papers were marked out of a score of 16 and categorized into groups of low quality (0-5.5 score), medium quality (6-11.5 score), and high quality (≥12 score). Eleven systematic reviews were of low quality, nine of medium quality, and one of high quality. Twelve papers did not define selection criteria of studies. Two papers provided a list of excluded studies with justifications

and one provided the list without justifications. One review reported funding information. Four utilized a satisfactory risk of bias technique for included studies while one obtained a "partial yes" in this criterion.

Individual and Interpersonal Levels

The systematic review by Chacko *et al*. focused on both health provider-based and client-initiated chlamydia screening practices in asymptomatic young women in the United States [20]. The review revealed that the screening of sexually active women under the age of 20 was the top priority. However, the authors of the review pointed out that it was challenging to evaluate the effectiveness of health provider-based screening programs because of the large size of program, variations in prevalence rates in populations targeted and the criteria used to determine effectiveness [20]. Besides, the review found that there was a marked absence of programs and no publication describing intervention to foster client-initiated screening behaviors among asymptomatic young women in the United States, despite of the Centers for Disease Control and Prevention's recommendations [20].

A systematic review by Odesanmi *et al.* compared the screening uptake levels of home-based self-sampling and clinic-based specimen collection for *Chlamydia trachomatis* in females aged 14-50 years old [21]. The review only included randomized control trials. Self-collection is where people bring a kit home and send the sample to a testing facility without needing to attend a health facility [21]. The review supported the use of home sampling to increase screening uptake but cost-effectiveness should be further investigated [21]. Furthermore, the review reported a significant preference for self-collection compared to clinic based testing. Another systematic

review only focused on the home-based screening strategy and divided home-based screening into seven groups according to test kit and specimen delivery methods. The highest median specimen return rate was in outreach programs in which participants were approached at home with immediate collection of specimens (96.5%), programs providing home testing kits only on invitation acceptance (78.9%), home testing kits sent along with an invitation (32.9%), home testing kits requested without an invitation (31.8%), home testing kit offered in person (21.4%), and home testing kits picked up at specific locations (18.6%) [22]. However, the interventions targeted a wide range of target populations hence comparison between each program may not be valid. Nonetheless, this review shows that self-collection programs have been conducted in a variety of countries and with different delivery methods, suggesting that home-based testing is a feasible and acceptable chlamydia screening method. However, further studies regarding its cost-effectiveness are needed [22].

Organizational Level

A systematic review by Taylor *et al.* categorized screening interventions into levels of effectiveness as measured by the absolute difference in percent of target population screened. Effective and low-cost interventions (<USD$1,000) included strategic placement of specimen collection materials, routine consultation collection, and electronic health records use. Effectives and low-moderate costs interventions ($USD<1,001-10,000) utilized patient reminder strategies such as postcards and calls. Effective and high costs (USD10,001-100,000) interventions involved dedicated screening staff. The authors concluded there is a variety of effective and cost-effective screening interventions [23].

Interventions targeting females resulting in significant increases in screening rates include linking screening to pap smears (6.9% vs. 4.5%), computer alerts for doctors (15.5% vs. 12.4%), and free sexual health consultation (16.8% vs. 13.2%) [24-26]. Screening program initiation is associated with chlamydia infection reduction and screening women with a certain range of risk factors reduces PID incidence for 1-year [27,28]. Challenges in implementing healthcare provider screening interventions include lack of protocols of urine sample obtainment, insufficient knowledge about chlamydia and urine-based tests, and reluctance of staff to be engaged in adolescent sexually transmitted infection screening [29]. The effectiveness and feasibility of screening for chlamydia in emergency departments has also been examined [30]. Prevalence of emergency department patients was high (9.1-9.5%) [28,31]. Barriers include finding a location for screening in the emergency department, clinician's willingness and time constraints, and availability of other staff [23,32-36].

The systematic review by Gudka *et al*. examined pharmacy-based screening interventions [37]. Return rates were high in studies with 47% in England, 63.9% in Scotland, 28% in Australia, and 38% in the United States [38-41]. Major barriers of pharmacy-based screening included having to return the specimen to designated sites and lack of privacy [37,41] for patients and increased workload or feeling uncomfortable when offering the test, and lack of in store advertising for pharmacists [42]. The major benefits for patients included convenience, anonymity and no need for appointment, affordability [36], shorter waiting times, and friendly non-judgmental attitude of pharmacists [43]. It was concluded that chlamydia screening in community pharmacies were feasible and could be a convenient option [43].

Community Level

In a review by Bernstein *et al*., screening interventions in non-clinic settings were examined [44]. The review revealed that high number of tests could be carried out in correctional settings and identified a large amount of asymptomatic infections. The total number of people approached was unavailable but high prevalence was found amongst adolescent girls in juvenile detention centers in Southern City (24.7%), Georgia (16.8%), and California (13.0%) [45]. Other community-based screening included homeless shelters, family court, and mobile van but they identified few new infections [46-48]. High chlamydia prevalence was also found when screening in educational settings [49]. The prevalence was 12.4% for males and females in a classroom-based strategy, 18.8% for females in school-based health clinic, 15.6% for male and females in other school locations, and 15.0% in clinical session screening [47,50-52]. Chlamydial screening in educational settings is a feasible approach with a range of delivery methods identifying large numbers of infected adolescents [53].

In the systematic review by Hengel *et al*., outreach interventions targeting young people aged 15-29 years, men who have sex with men, and sex workers were identified [53]. Amongst the outreach settings, the highest participation rate was in community venues such as community centers, parenting centers, and homeless shelters (81.4%) and social venues such as sport venues or bars (80.4%). In interventions targeting adolescents and young adults, Gold *et al*. found a high testing rate (75.2%, tests = 92) in a screening program in a football club changing room in Australia [54]. High testing rates were also found in community venues targeting dropouts, new immigrants, and vocational school students in the Netherlands (79.6%, tests = 74) [52]. Low participation rates were identified in street and public community areas (median=23.9%, n=3) and sex venues

(10.4% and 24.3%, n=2) [55]. The authors concluded that chlamydial outreach programs are able to result in high participation rates but with limited reach. Settings that resulted in higher participation rates seem to be less public [55].

Policy Level

Education and advisory

In the systematic review by Ginige *et. al.,* a cluster randomized control trial assessing the effectiveness of an educational package in general practitioners in Belgium was analyzed [18]. The target population was females aged below 35 years old [56]. The intervention included a stimulated consultation and text messages regarding communication skills. The intervention group performed significantly better by carrying out more screening (median 6 patients per general practitioner vs. 3 patients per general practitioner, p = 0.035) [57]. Another study investigated the effectiveness of having a health advisor in primary healthcare centers to increase awareness of chlamydia and to train the staff in Scotland. Testing rates in the intervention centers was significantly higher than those in the control (120%, vs 11%, p=<0.001). However, the denominator value indicating the number of patients seen was missing in the primary paper [55].

Allison *et al.* carried out a study regarding the effectiveness of an internet-based continuing medical education to increase chlamydia screening by primary care physicians in the US. The continuing medical education course consisted of 4 modules over 3 months. The chlamydia screening rates for before, during and after the intervention were 16.2%, 13.3%, and 15.5% for the intervention group respectively vs. 18.9%, 13.0%, 12.4% for the control (p=0.044 for post-intervention differences) [27].

System-level changes in clinical practice

In the same systematic review by Ginige *et al.* a randomized control trial assessing the effectiveness of a multi-phased intervention aimed to result in system-level changes in clinical practice regarding chlamydia screening was analyzed [43]. The intervention consisted of four stages where the first stage was engagement with the organization's leaders to investigate the discrepancy between current and best practice. The second stage involved the formation of adolescent care teams, a model for practice change, and a staff toolkit. The third stage involved monthly meetings between clinic team members. The final stage developed performance indicators. The intervention clinics saw a significant number of females ages 14-18 screened as compared to the control clinics (478 of 1017 vs 203 of 1194, $p<0.001$) [47]. The authors concluded that there is a variety of ways to increase chlamydia screening but more randomized control trials are needed.

Discussion

Adolescent girls have always been the targets of screening programs but high chlamydial prevalence was also found in adolescent boys [58,59]. Screening all or only high-risk adolescents have strong implications on monetary and human resources. Even if mass screening for adolescents is implemented, it is difficult to ensure the acceptance of the target population. The Centers for Disease Control and Prevention in the United States has recommended annual screening of women under age 26 since 1993 but less than half was screened in 2012 [44,60] . At-risk individuals such as women, adolescents, and those entering juvenile detention centers are often missed due to the lack of awareness in healthcare providers and limited resources [45]. Young women entering correctional services are at higher risk of chlamydia and high prevalence of

chlamydia has been found [20,46,59]. The Centers for Disease Control and Prevention has recommended for the universal screening of females during intake in juvenile correctional services and screening rates increased from 55%-58% from 2005-2008 [21]. Therefore, the questions are how to promote chlamydia infection awareness; how to reach the target population; and what environment changes encourage screening.

While asymptomatic individuals are unlikely to obtain a routine check-up, clinicians also admitted to being hesitant in screening sexually active asymptomatic females [61]. High-risk population should be linked to different health contacts such as pap smears, sexual health consultations or in pharmacy. Self-collection was found to significantly increase uptake of screening and was preferred over clinic-based testing in women aged 14-50 years [62]. Self-collection strategies should be promoted to adolescents via social media because social media is a popular portal for teenagers to exchange and share information [63]. Social media interventions have been shown to be effective in significantly increasing syphilis and human immunodeficiency viruses testing in youth and in promoting human immunodeficiency viruses testing in men who have sex with men [15,55]. However, the effectiveness of social media interventions has not been demonstrated for chlamydia testing. This calls for further research in social media campaigns to increase chlamydia testing amongst adolescents. Another approach is to implement structural changes to alter the attitudes of healthcare providers in that they make testing adolescents a priority. Healthcare providers should also receive proper training so that they are able to approach adolescent patients confidently for chlamydia screening. Structural interventions mentioned previously did not focus on adolescents hence development of adolescent focused programs is needed [64].

In essence, we want to know whether screening interventions are able to reduce chlamydia's disease burden. Some studies revealed that chlamydia screening reduced chlamydia infections and that screening women with a certain range of risk factors reduced PID incidence, other studies claim a lack of evidence in supporting opportunistic screening in the general population below 25 years of age [65,66]. While our review identified a large number of studies of chlamydia screening programs, most studies did not report data on chlamydia associated morbidity. We are not able to determine the impact of chlamydia screening on chlamydia associated morbidity. As we relied on the analysis and data presented by primary authors, this exclusion is sub-optimal. The lack of evidence on the effectiveness of chlamydia screening programs in reducing disease burden has caused several countries to focus on case identification and management [67]. A recent review has suggested a shift from an infection-based focus to increase screening uptake in asymptomatic populations, to a health outcomes-based focus to improve case detection among high-risk populations and case management [66]. Greater emphases need to be on strategies for infected individuals to minimize re-infection such as improving partner notification, treatment of sexual partners or re-testing [67].

Our methodology has a few limitations. Firstly, it depended on the inclusion and analysis of primary studies by the review's authors. Secondly, included reviews differed significantly in terms of intervention design, target populations, settings and study outcomes. Therefore, the heterogeneity of the included systematic reviews has made comparison of effectiveness difficult. Apart from screening coverage and prevalence, other data regarding treatment, partner management, and retesting which is vital in determining its success, was often unavailable. Lastly, the results are presented without focus on the contextual nature of the studies. Factors

such as cultural attitudes, government policies, and differences in healthcare system could have effects on the outcomes.

Conclusion

There is evidence that shows the most important factor that determines the level of chlamydia screening was age. Therefore, national programs should focus on young males and females in the general population rather than individuals with high-risk characteristics. Reminders and outreach in certain community settings increased screening, but further information regarding cost-effectiveness is needed. Four interventions at the policy level were found to be effective; while the interventions differ, they share similar educational, advisory, and supervisory elements. Structural interventions are vital in changing the attitudes and awareness of chlamydia screening to result in systemic change. Therefore, initiatives to train healthcare providers in carrying out appropriate testing for adolescents is needed.

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Figure 1: The socio-ecological model

Figure 2: Preferred Reporting Items of Systematic Reviews and Meta-analyses (PRISMA) flow diagram

Figure 1.

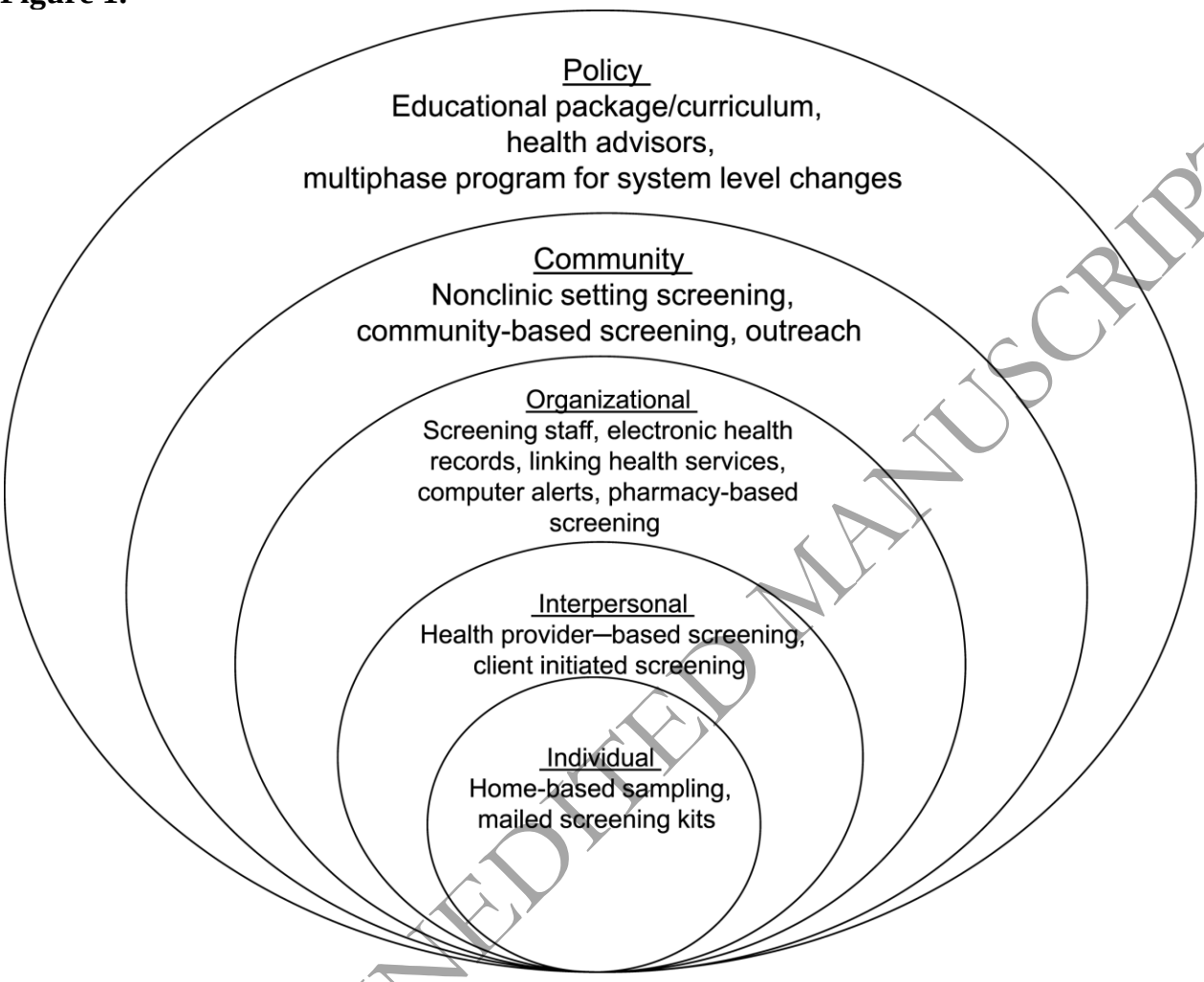

Figure 2.