Title: Protocol for a Scoping Review of Evidence Pertaining to Public Willingness to Receive Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis Vaccines

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Abstract

Objective: The objective of this scoping review is to map the existing literature pertaining to individuals' willingness to receive Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis vaccines, understand the methods researchers are using to assess these attitudes, and provide a foundational summary to inform future vaccine rollout.

Background: STIs like Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis, are a persistent problem despite current intervention strategies. While there are vaccines in development for these diseases, without effective implementation, their utility may fall short. This scoping review will map the existing information about individuals' willingness to receive Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis vaccines and identify gaps or disparities in the existing literature.

Inclusion Criteria: We will examine texts that assess individuals' attitudes and/or hesitancy towards Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis vaccines intended for humans in any geographic context. Studies of all designs will be included.

Methods: For this synthesis, we will test our search terms in PubMed and Scopus, conduct searchers in a series of databases, perform title and abstract reviews on all returned texts, and then perform full-text reviews to confirm inclusion. We will review references of selected texts. The reviewers will conduct data abstraction on selected texts to map the synthesized evidence, and conduct basic thematic analysis on the survey instruments utilized in the selected texts.

Discussion: For vaccines to reduce the impact of disease, they must reach their intended audiences while remaining accessible and unstigmatized. With this scoping review, we will provide insight into individuals' attitudes towards curable STI vaccines, while also highlighting gaps in knowledge, so that future implementation programs have the background knowledge necessary to ensure vaccine rollouts are successful.

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Background

Sexually Transmitted Infections (STIs) are a persistent threat to the health and wellbeing of the global population. According to Rowley et al, there was a daily average of over 1 million new infections of Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis in 2016, with an annual global prevalence of 2.7% for Chlamydia, 0.6% for Trichomoniasis, 0.7% for Gonorrhea, and 0.5% for Syphilis [1]. In the United States alone, Chlamydia, Trichomoniasis, Gonorrhea, and Syphilis had an estimated 2,353,000, 2,576,000, 209,000, and 156,000 prevalent cases in 2018, respectively [2], resulting in nearly \$1.3 billion in direct medical costs [3].

Despite the treatability of Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis, these curable STIs have remained a persistent burden to both physical health and socioeconomic wellbeing. Social stigma and behavioral barriers surrounding sexual practices and STIs, lack of access to testing and treatment, low levels of screening, high prevalence of asymptomatic or mildly symptomatic cases, length of infection, the rising threat of antibiotic resistance, and the prevalence of repeat infections all contribute to an attenuation of the efficacy of bacterial STI interventions [4].

One intervention that has the capacity to combat these barriers is vaccination. Alongside the existing success of the HPV and Hep B vaccines, researchers are making promising progress towards vaccines [5] that may help curb the spread of curable STIs and thus reduce their public health burden. Champredon et al's mathematical model demonstrated that an effective Syphilis vaccine has the capacity to be notably more effective at reducing Syphilis prevalence than non-vaccination interventions [6]. Similarly, Craig et al's model demonstrates that a moderately effective Gonorrhea vaccine could have a sizable impact on Gonorrhea prevalence, given high coverage [7], and Brunham et al's model suggests that given sufficient coverage, an effective Chlamydia vaccine could drive the disease to elimination [8].

However, reaping the full benefits of new STI vaccines requires careful planning and effective vaccine rollout programs. To achieve this goal, it is crucial to understand how members of the public—both higher-risk groups and the general populace—feel about curable STI vaccines and what degree of willingness or hesitancy they feel towards potential vaccinations.

The purpose of this scoping review is to map the existing information about individuals' attitudes towards Syphilis, Trichomoniasis, Gonorrhea, and Chlamydia vaccines, while also examining how researchers have investigated the question with participants, what groups vaccine willingness has been examined in, and what gaps or disparities might exist in the literature. In this way, we hope to establish a sturdy foundation for future vaccine rollouts to build upon and provide a framework on how to most effectively discuss this topic with the public. As of August 3, 2022, the reviewers could not readily find a comparable evidence synthesis.

Review Ouestion

In order to maintain breadth in our review while also exploring more tailored topics, our primary question is "What evidence is there about public willingness to receive Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis vaccines" with the following sub-questions:

- 1) What methods and survey tools are used to assess willingness?
- 2) In what populations and geographic regions has public willingness to receive curable STI vaccines been studied?
- 3) Are there any documented disparities by demographic group in willingness to receive bacterial STI vaccines?

Eligibility Criteria

<u>Participants</u>- Studies conducted on any human population about willingness to receive vaccines in human populations is eligible for this analysis. Texts concerned with feelings towards Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis vaccine usage in non-human populations are ineligible for inclusion.

<u>Concept</u>- Selected texts must discuss individuals' willingness to receive a Chlamydia, Trichomoniasis, Gonorrhea, or Syphilis vaccine, or the willingness of a parent/guardian to have a dependent vaccinated in the case of children. Texts must assess the attitudes, willingness, or hesitancy that participants have towards receiving the vaccine of focus; studies examining attitudes towards the disease itself or non-vaccination interventions are ineligible. Studies that discuss the development of the vaccines of interest but not willingness to receive them are ineligible. Any text that does not examine willingness to receive vaccines for Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis specifically are ineligible.

<u>Context</u>- Studies examining human populations in any context are eligible for inclusion. Opinions towards vaccines for curable STIs in any geographic regions, cultures, communities, and focus groups are of interest.

Types of Study

This review will consider studies of any research design for inclusion, including both qualitative and quantitative studies; this will allow us a fittingly broad scope to examine how researchers have approached examining attitudes towards Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis vaccines. Applicable evidence syntheses, like systematic reviews and scoping reviews, will also be considered if they meet inclusion criteria. Text and opinion papers, as well as non-peer-reviewed publications like conference abstracts, will also be considered for inclusion.

Methodology

Our goal for this review is to identify research that has been conducted on public willingness to receive vaccines for curable STIs, examine how we discuss STI vaccines, and identify what populations, if any in particular, have been the focus of this research. We selected a scoping review to allow for mapping and synthesis of existing evidence on attitudes towards curable STI vaccines, while also identifying gaps in evidence and consideration. To plan the protocol for this scoping review, we used Arksey and O'Malley's framework [9], guided also by Levac et al's recommended enhancements [10]. As such, our scoping review will follow the five

following stages: 1) identifying the research question; 2) identifying relevant studies; 3) study selection; 4) charting the data; and 5) collating, summarizing, and reporting the results [9] [10].

Identifying Relevant Studies

In order to identify a comprehensive collection of information and ensure our search terms cover an appropriate breadth, we will use the three-step search strategy recommended by the Joanna Briggs Institute (JBI) [11] and test our proposed search terms (Supplemental table 1) in PubMed® and Scopus® to identify any keywords and index terms used by included studies that could refine our search strategy. After identifying these supplementary search terms and finalizing our search strategy, we will search for both published and grey literature by searching the following databases and sites: PubMed®, Embase®, Scopus®, Cochrane Library®, PsychInfo®, Global Index Medicus, and Google Scholar®. We will also review the references of included studies to help identify additional sources not captured by the initial searches.

Only publications in English will be included. Searches will not be restricted by publication date.

Study Selection

We will utilize the eligibility criteria detailed above to determine if texts qualify for inclusion in the review. As recommended by JBI, we will pilot the study selection criteria by selecting twenty-five articles at random and reviewing their titles and abstracts to determine if they would be appropriate for a full text review [11]. The two reviewers will discuss any discrepancies in decision-making and gaps in the selection criteria, and will proceed when 75% agreement is achieved [11].

After that point, the two reviewers will proceed with a title and abstract review of the searched texts. This review will be blinded, and both reviewers will make their decisions independently. As recommended by Levac et al, the reviewers will check in throughout the abstract review period to clarify any questions concerning inclusion and exclusion criteria, and alter the selection protocol if necessary [10]. After the abstracts have all been reviewed, the reviewers will meet to discuss their decisions, settle any disagreements about inclusion by consensus or the input of a third reviewer if consensus cannot be reached, and proceed with the full-text review of selected texts. As with the abstract and title review, any disagreements between the reviewers will be settled with consensus, or, if consensus is not achieved, the decision of a third reviewer. The references in selected texts will also be examined for any relevant texts not captured by the initial searches. All articles will be managed in Rayyan (Rayyan Systems Inc., Cambridge, MA).

Charting the Data

Our team will use a data extraction instrument that will collect authors, publication year, study design, study setting, target population, disease(s) of interest, sampling method, survey instruments/questions, analysis techniques, relevant finding, and other aspects the team deems

necessary after development and review. We will pilot the abstraction form on five randomly selected publications to test its utility and add or revise sections as necessary. After the data extraction is complete, the reviewers will compare their abstractions to ensure consistency; any disagreements will be reconciled through consensus or the input of a third reviewer.

Collating, Summarizing and Reporting the Results

We will produce a narrative report of the characteristics of the studies—study design, study setting, target population, disease of interest, and sampling method—as well as map the relevant findings about willingness to receive a vaccine. We will also conduct a basic thematic analysis of the survey instruments and questionnaires to provide insight into how investigators inquire about willingness to receive Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis vaccines. Through these two approaches, we will map the existing evidence on curable STI vaccine willingness while also examining gaps that exist in the literature, particularly in regards to demographic groups studied or disparities between diseases of interest.

Discussion

This review will help map existing information about attitudes towards Chlamydia, Gonorrhea, Syphilis, and Trichomoniasis vaccines while also identifying gaps that exist in the literature. In this way, our scoping review will provide a foundation for future researchers to build off of and for public health officials to utilize while making decisions about potential interventions. As the technology for STI vaccines continues to improve and advance, this work will be crucial to ensuring that the implementation of these vaccines is done in a way that is accessible and attractive to the public, with tools that are effective without being stigmatizing.

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Sources

- [1] Rowley J, Vander Hoorn S, Korenromp E, Low N, Unemo M, Abu-Raddad LJ, Chico RM, Smolak A, Newman L, Gottlieb S, Thwin SS, Broutet N, Taylor MM. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. Bull World Health Organ. 2019;97(8):548-562P. doi: 10.2471/BLT.18.228486.
- [2] Kreisel KM; Spicknall IH, Gargano JW, Lewis, Felicia MT, Lewis RM, Markowitz LE, Roberts H, Johnson AS, Song R; St. Cyr SB; WestonEJ; Torrone EA, Weinstock HS; Sexually. Transmitted Infections Among US Women and Men: Prevalence and Incidence Estimates, 2018. *Sexually Transmitted Diseases*. 2021;48(4), 208-214. doi: 10.1097/OLQ.000000000001355
- [3] Sexually Transmitted Infections Prevalence, Incidence, and Cost Estimates in the United States, cdc.gov. Updated January 25, 2021. Accessed July 1, 2022. https://www.cdc.gov/std/statistics/prevalence-2020-at-a-glance.htm
- [4] Gottlieb SL, Low N, Newman LM, Bolan G, Kamb M, Broutet N. Toward global prevention of sexually transmitted infections (STIs): The need for STI vaccines. *Vaccine*. 2014; 32(14),1527-1535. doi:10.1016/j.vaccine.2013.07.087.
- [5] McIntosh EDG. Development of vaccines against the sexually transmitted infections gonorrhoea, syphilis, Chlamydia, herpes simplex virus, human immunodeficiency virus and Zika virus. *Therapeutic Advances in Vaccines and Immunotherapy.* 2020;8. doi:10.1177/2515135520923887
- [6]Champredon D, Cameron CE, Smieja M, Dushoff J. Epidemiological impact of a syphilis vaccine: a simulation study. *Epidemiology and Infection*. 2016;144(15):3244-3252. doi:10.1017/S0950268816001643
- [7] Craig AP, Gray RT, Edwards JL, Apicella MA, Jennings MP, Wilson DP, Seib KL. The potential impact of vaccination on the prevalence of gonorrhea. Vaccine. 2015;33(36),4520-4525. doi:10.1016/j.vaccine.2015.07.015
- [8] Rönn MM, Wolf EE, Chesson H, Menzies NA, Galer K, Gorwitz R, Gift T, Hsu K, Salomon JA. The use of mathematical models of Chlamydia transmission to address public health policy questions: a systematic review. *Sex Transm Dis.* 2017 May;44(5):278-283. doi: 10.1097/OLQ.000000000000598.

- [9] Arksey H, O'Malley L. Scoping Studies: Towards a methodological framework. *International Journal of Social Research Methodology: Theory & Practice*. 2005;8(1),19-32. doi:10.1080/1364557032000119616
- [10] Levac D, Colquhoun H, O'Brien K. Scoping studies: advancing the methodology. *Implementation Science*. 2010;5(69). doi:10.1186/1748-5908-5-69
- [11] Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil, H. Chapter 11: Scoping Reviews (2020 version). In: Aromataris E, Munn Z (Editors). *JBI Manual for Evidence Synthesis*, JBI, 2020. Accessed June 20, 2022. do:10.46658/JBIMES-20-12

Supplemental Tables:

Table 1: Example of preliminary search terms for Scopus, subject to change during testing.

Preliminary Scopus Search Terms	(Syphilis OR "Treponema pallidum" OR
Tremmary Scopus Scaren Terms	"Treponemal Infection" OR Gonorrhea OR
	"Neisseria gonorrhoeae" OR "Neisseriaceae
	Infection" OR Chlamydia OR "Chlamydia
	trachomatis" OR Trichomoniasis OR "Trichomonas vaginalis" OR "Trichomonas
	Infection")
	OR ("Bacteria* STI" OR "Bacteria* Sexually
	Transmitted Infection" OR "Curable STI" OR "Curable Sexually Transmitted Infection" OR
	"Curable STD" OR "Curable Sexually
	Transmitted Disease" OR "Bacterial STD"
	OR "Bacterial Sexually Transmitted Disease")
	AND(((vaccin* OR Immuniz* OR Inoculat*)
	AND (attitude* OR Knowledge OR Opinion*
	OR Willing* OR Recept* or Hesitan* OR
	Thoughts OR Sentiment* OR Stigma))
	OR("vaccination hesitancy" OR "vaccination
	refusal"))