START CENTER
STRATEGIC ANALYSIS, RESEARCH & TRAINING CENTER
Department of Global Health | University of Washington

Sexually Transmitted Infections (STIs) as a Cause of Infertility

KEY TAKEAWAYS & RECOMMENDATIONS

Strong Evidence Linking chlamydia to Pelvic Inflammatory Disease (PID) and Infertility: Evidence suggests that chlamydia is a significant cause of both PID and infertility related to tubal inflammation and scarring. *Chlamydia* is the only STI with clinical trial evidence showing that screening and treatment can reduce PID incidence.

Associations between other STIs, PID and Infertility: There is moderate-quality evidence associating *gonorrhea* with PID and infertility. Evidence is mixed or more limited for associations between *T. vaginalis, M. genitalium*, and syphilis with PID and infertility.

Diagnosing STIs and Infertility in Low-Resource Settings: There are difficulties in diagnosing STIs and infertility in low- and middle-income countries (LMICs) related to high testing costs, reliance on symptom-based diagnosis (rather than molecular or antibody tests), and limited access to diagnostic facilities.

Variability in PID and Infertility Definitions: There is extensive variability in the definitions and diagnosis of PID and infertility. Many studies rely on self-reporting or medical records for diagnosis. There is a need for clearly stated and standardized criteria for future studies.

ISSUE STATEMENT

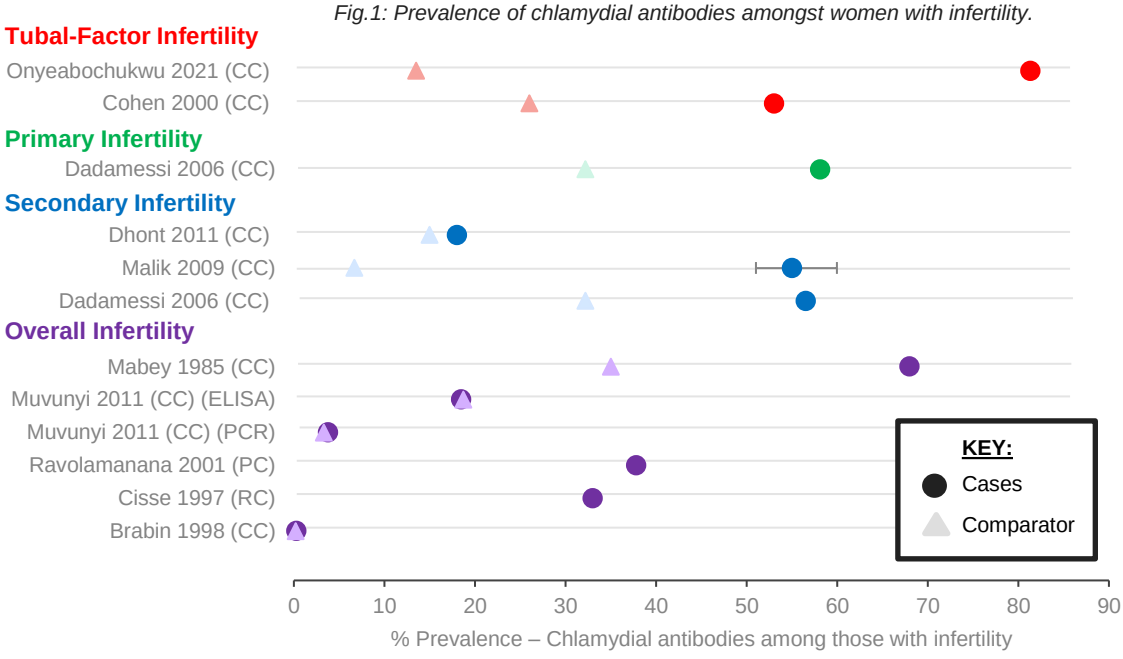
Female infertility is a significant global health concern, leading to substantial financial and healthcare burdens for individuals and health systems. In sub-Saharan Africa (SSA) and Southeast Asia (SEA), limited evidence exists regarding the relationship between STIs and infertility. STIs can lead to both symptomatic and asymptomatic PID, which, if left untreated, may cause infertility, a well-documented sequence supported by causal research. To inform resource allocation and strategic investment, there is a pressing need to better understand the role of STIs in causing infertility in SSA and SEA, with the goal of guiding the design of potential cohort studies or clinical trials. This research aims to address critical questions regarding the prevalence of infertility, and the contribution of specific pathogens including *Chlamydia trachomatis, Neisseria Gonorrhoeae, Mycoplasma genitalium*, *Trichomonas vaginalis*, and *Treponema pallidum* to PID and infertility in SSA and SEA.

EVIDENCE FOR CHLAMYDIA

Among five key STIs studied, chlamydia shows the most substantial associations with both PID and infertility, particularly tubal-factor infertility. This is supported by two randomized trials indicating that screening and treating for chlamydia can reduce the incidence of clinical PID.

Prevalence estimates of chlamydial antibodies among women with infertility and controls are presented in Figure 1.

Fig.1: Prevalence of chlamydial antibodies amongst women with infertility.



ATTRIBUTABLE RISK ESTIMATES

Calculations: Attributable risk percent (AR%) and populational attributable risk percent (PAR%) estimates were calculated using odds ratios from available studies estimating the association between chlamydia and infertility. These calculations assume infertility is a rare outcome among the general population, which may not hold true for key populations. For PAR% estimates, lower and upper lifetime prevalence estimates were calculated using 2- and 4-fold chlamydia prevalence estimates, respectively.

Attributable Risk: Eliminating chlamydia and sequela of chlamydial infection could prevent 25% to over 75% of tubal-factor infertility in women.

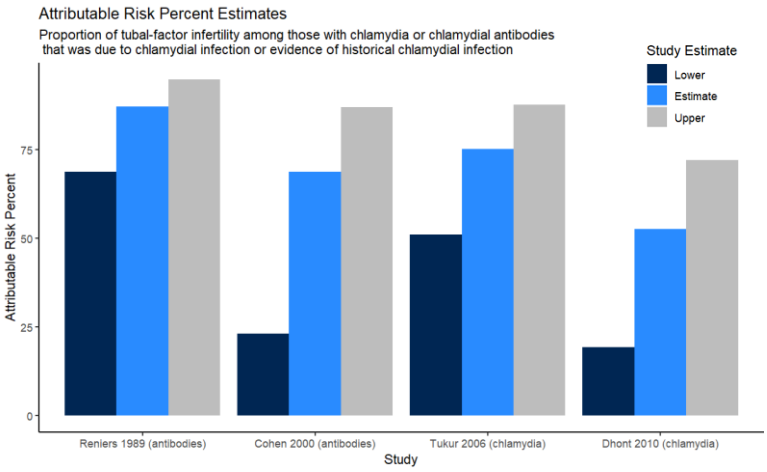


Fig. 2: Attributable risk percent estimates for tubal-factor infertility from chlamydial infection or antibodies.

Attributable Risk Percent: If chlamydia was eradicated, approximately 5-15% of cases of tubal-factor infertility could be avoided in SSA women.

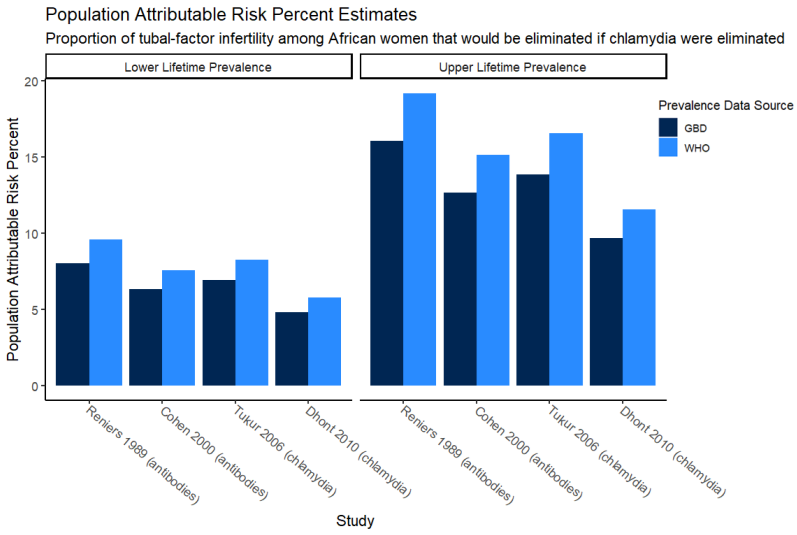


Fig. 3: Population attributable risk estimates for tubal-factor infertility related to chlamydia prevalence in SSA women.

DATA GAPS & INVESTMENT AREAS

STI OF INTEREST	PREVALENCE RANGE (%)	EVIDENCE SUMMARY	DATA GAPS & RECOMMENDATIONS
Chlamydia	AFRO: 4.6- 5.5 SEARO: 1.9- 3.8 Global: 4- 4.56	○ Strong evidence supporting association with PID & infertility ○ Clinical trial evidence for efficacy in screening/treating to prevent PID	○ Additional clinical trials for other outcomes ○ **Conclusion**: Strong evidence supporting focusing investment on chlamydia
Gonorrhea	AFRO: 1.6- 1.85 SEARO: 0.65-0.8 Global: 0.8- 0.95	○ Moderate evidence of association between gonorrhea and PID from observational studies only ○ No clinical trial data to assess reduction strategies	○ Difficulty in assessing historical infection due to lack of antibody testing ○ **Conclusion**: Modest evidence and lower prevalence may position as lower investment priority
M. genitalium	*Prevalence estimates not collected*	○ Moderate evidence for association with infertility, mixed evidence for PID	○ Need clinical trial data to examine effect of screen & treat on PID & fertility outcomes ○ **Conclusion**: *M. genitalium* may be an emerging priority for research
T. vaginalis	AFRO: 12- 12.7 SEARO: 2.7-3.87 Global: 4.9- 5.85	○ Low quality of epidemiological studies in literature review ○ Need to clarify association between PID & *T. vaginalis*	○ **Conclusion:** Additional research needed to examine association but has potential for high impact given high prevalence in areas of interest
Syphilis	AFRO: 1.7- 2.72 SEARO: 0.13- 0.86 Globall: 0.6- 0.86	○ No evidence of association between syphilis and PID ○ Limited evidence of association with infertility; low quality evidence	○ **Conclusion**: Limited evidence of association with PID/infertility, but remains important cause of maternal-child outcomes

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Attributable Risk

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Forest Plot

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