Randomized Controlled Trial on Sexually Transmitted Infections (STIs) and Reproductive Tract Sequelae in Non-Pregnant Women

Grand Challenges

Request for Proposals

Applications due no later than July 7, 2025, 11:30 a.m. U.S. Pacific Time

The information regarding this Grand Challenges Request for Proposals was last updated on June 6, 2025.

Before applying, applicants should familiarize themselves with the supporting documents for this Grand Challenge, including the Rules and Guidelines, Application Instructions, and Frequently Asked Questions.

BACKGROUND

Sexually active young women in low- and middle-income countries (LMICs) experience a high incidence of sexually transmitted infections (STIs), limited access to screening and treatment, and poorly characterized but significant reproductive tract morbidity from untreated infection. Global estimates put the prevalence of gonorrhea and chlamydia among women at 0.8% and 4.0%, respectively, with incidence rates of 1.9 and 3.6 cases per 100 person-years.[1] However, these estimates are limited by sparse data, with few sources providing representative measures of disease frequency, including asymptomatic infections. Studies among young women in LMICs interested in HIV pre-exposure prophylaxis have measured incidence rates per 100 person-years of 12-53 for chlamydia, 6-20 for gonorrhea, and 6-7 for trichomoniasis.[2] Due to the asymptomatic nature of most infections and reliance on syndromic management, most STIs in women go undetected. Untreated STIs have been linked to a range of poor health outcomes, including pelvic inflammatory disease (PID), chronic pelvic pain, infertility, and ectopic pregnancy. However, these estimates of association are imprecise and draw primarily from cross-sectional, case-control, and retrospective cohort studies, mostly conducted in high-income countries. Gaps in available data limit our ability to draw robust inferences on the risk of sequelae following an infection, the timing of pathogenesis, or how factors such as the presence of symptoms or repeat infection may modify these risks.

Better data on the risk of PID and related sequelae are critical to inform prevention and treatment guidelines, motivate funding for product development and provision of services, and shift care-seeking and care-provision behaviors. Research on the prevalence and risk of PID in LMICs has been challenging due to a lack of accurate and scalable diagnostic methods for PID along with funding gaps that limit consistent and comprehensive diagnosis. Although diagnosing subclinical PID remains challenging, targeted research is critical to better understand the risk of developing clinical PID and to evaluate the effectiveness of STI screening and treatment in preventing reproductive tract complications. Strengthening the evidence base in this area will not only advance our understanding of STI-related morbidity but may also stimulate the development and application of improved diagnostic tools to reduce the burden of PID and related outcomes.

THE CHALLENGE

This Grand Challenge on Randomized Controlled Trial on Sexually Transmitted Infections (STIs) and Reproductive Tract Sequelae in Non-Pregnant Women aims to fill critical gaps in understanding of the risk of PID and related sequelae attributable to STIs and to evaluate the impact of etiologic STI screening and treatment on morbidity. With this Grand Challenge we welcome letters of intent (LOIs) from organizations to conduct a randomized controlled trial (RCT) in sub-Saharan Africa comparing STI screening and standard of care syndromic management**.** The primary outcome of this study should be PID, with secondary outcomes possibly including chronic pelvic pain, ectopic pregnancy, and infertility. The study should provide insight into the risk of outcomes following infection with gonorrhea, chlamydia, and/or trichomoniasis and the impact and cost-effectiveness of etiologic screening to prevent morbidity.

Funding Level

We will consider applications requesting awards ranging from $8 million to $10 million USD per project, with a grant duration of up to 48 months. Budgets should align with the scale and complexity of the proposed work. Indirect costs are allowable and should be included within the total requested funding. (subject to the Gates Foundation's indirect cost policy).

Eligibility Criteria

- This initiative is open to nonprofit organizations, for-profit companies, international organizations, government agencies, and academic institutions.
- Study design must be randomized controlled trial or comparable, robust prospective in Sub-Saharan African settings.
- We encourage groups to build upon existing and/or complimentary projects/studies/trials and to collaborate with other institutions.
- We particularly encourage applications involving projects led by African Primary Investigators (PIs), women, early-career researchers, and practitioners seeking to innovate in women's health measurement, or from women-led organizations and applications from institutions based in LMICs.

We are looking for proposals that:

- Are designed to provide insight into the timing of pathogenesis. This insight could come from comparison of outcomes across arms with varying screening intervals and/or from more frequent collection and storage of samples for subsequent batch testing.
- Consider symptom tracking tools (such as symptom diaries) that could be used to track the onset, type, and severity of symptoms. Ideally, based on validated instruments.
- Ideally enable stratification of risk by the presence of symptoms, co-infection, and repeat infection.
- Ideally provide data to estimate STI incidence and the duration of untreated infection.
- Collect detailed sexual behavior data, including the number of current and recent partners, partner type, partnership duration, concurrency, frequency of sex, type of sex, use of condoms, and characteristics and behaviors of partners.
- Captures costs of screening, treatment, and management of sequelae.
- Engage stakeholders and utilize community advisory boards.

We will not fund proposals that:

- Have trial sites that are not based in sub-Saharan Africa.
- Do not include PID as a primary outcome.
- Include women who are pregnant at baseline.
- Include women with a known diagnosis of infertility at baseline as part of the outcome analysis population.
- Restrict the study population based on HIV status without justification.
- Propose purely observational, retrospective, or modeling-only design.
- Do not address the timing of pathogenesis or provide a strategy for identifying or analyzing the onset of sequelae following STI.
- Do not plan for ethical, community, and gender-informed engagement.
- Lack consideration of downstream policy relevance, such as linking findings to potential influence on screening, syndromic management, or STI prevention guidelines.

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[1] World Health Organization. (2025). *Global and regional STI estimates.* The Global Health Observatory. https://www.who.int/data/gho/data/themes/topics/global-and-regional-sti-estimates

[2] Kiweewa, et al. (2019). *JAIDS*, *22*(2), e25257. https://doi.org/10.1002/jia2.25257; Stewart et al. (2020). *AIDS*, 34(5), 651–658. https://doi.org/10.1097/QAD.0000000000002472; Delany-Moretlwe (2023). *Sex Transm Infect*, *99*(7), 433–439. https://doi.org/10.1136/sextrans-2022-055696.