WHO global research priorities for sexually transmitted infections

World Health Organization

human reproduction programme hrp 50
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Background

Sexually transmitted infections (STIs) are widespread globally and have a profound impact on sexual and reproductive health. The greatest burden of STIs is in low- and middle-income countries (LMICs). STIs disproportionately affect women, adolescents, and marginalized and underserved populations in all settings.

Despite the need, little progress has been made globally in reducing STIs and the associated consequences *(1).* Gaps in evidence and in available tools have hindered STI prevention, control and management, particularly in resource-limited settings. Thus, WHO's global strategy on STIs for 2022–2030 highlighted research and innovation as a fundamental component of the global response *(2).*

In 2022, WHO initiated a research priority setting exercise to identify the most crucial STI research areas to address the global public health need. A detailed description of the methods and results can be found here *(3).* This document summarizes the global STI research priorities to guide researchers, funders, policy-makers, implementing partners, industry and civil society as part of efforts to reduce the global toll of STIs.

Importance of addressing sexually transmitted infections (STIs)

More than one million STIs are acquired every day worldwide.
In 2020, an estimated 374 million new infections occurred with one of four curable STIs: *Treponema pallidum* (syphilis), *Chlamydia trachomatis* (chlamydia), *Neisseria gonorrhoeae* (gonorrhoea), and *Trichomonas vaginalis* (trichomoniasis) *(1).* Additionally, viral STIs can be long-lasting (e.g. human papillomavirus – HPV) or lifelong (e.g. herpes simplex virus – HSV) and affect hundreds of millions of people globally *(4).*

Effectively addressing STIs can lead to the following benefits:

Supporting **sexual health & well-being** for all, including young people

Decreasing the **burden of infertility** due to gonorrhoea & chlamydia

Preventing **adverse pregnancy & neonatal** outcomes due to syphilis

Eliminating cervical cancer caused by HPV infection

Reducing **HIV transmission** associated with HSV-2 and other STIs

Combatting **antimicrobial resistance** to gonorrhoea

STI research prioritization process

The global STI research priority setting process aligned with the WHO global strategy on STIs through 2030 *(2)*, and focused particularly on resource-constrained settings and underserved populations. The scope included all STIs except HIV, hepatitis and HPV-related cervical cancer, which were addressed elsewhere.

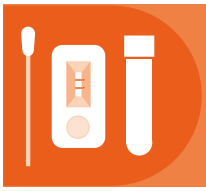
The prioritization process was overseen by an STI research priority working group, comprised of staff from WHO headquarters and regional offices, along with 16 external STI experts with diverse geographical and scientific expertise. The process was based on WHO guidance on setting research priorities, and used an adapted Child Health and Nutrition Research Initiative methodology *(5)*.

The five phases of the STI research prioritization process

September – October 2022	November 2022 – January 2023	April – May 2023	June – July 2023	July – October 2023
Phase 1	Phase 2	Phase 3	Phase 4	Phase 5
Survey 1		Survey 2		
Proposal of STI research areas	**Consolidation of areas**	**Scoring of STI research areas**	**Analysis of scoring**	**Incorporation of final input**
• Open-ended survey sent to STI stakeholders. • 63 stakeholders generated priority STI research areas.	• Duplicates removed. • Related areas combined. • Wording refined.	• Survey sent to >300 stakeholders. • Scoring criteria: – public health relevance – research feasibility – programme feasibility – equity value.	• Mean research priority scores calculated. • Research evaluated within 4 domains: – diagnosis – prevention – management – epidemiology • Scores evaluated by domain.	• Input solicited at international meetings. • Feedback provided by WHO working group.
529 STI research areas proposed	**40** priority STI research areas identified	**289** respondents scored the STI research areas	**4** key domains delineated the priority areas	**WHO global STI research agenda finalized**

WHO global STI research priorities

The global research agenda for STIs prioritizes **40 research areas** to inform STI policies and programmes by 2030 across four key domains: **diagnosis, prevention, management and epidemiology.**



1 Diagnosis

- **Develop low-cost, rapid STI point-of-care tests:**
  - for *N. gonorrhoeae* infection and for *C. trachomatis* infection, or dual tests
  - to distinguish active syphilis from latent or past infection
  - for antimicrobial resistance in *N. gonorrhoeae* and *M. genitalium.*
- **Evaluate implementation of STI testing (e.g. acceptability, feasibility, effectiveness, cost-effectiveness):**
  - screening for *T. pallidum* infection
  - screening for *N. gonorrhoeae, C. trachomatis* and *T. vaginalis* infections
  - assessing STI symptoms with tests as opposed to syndromic management
  - self-sampling or self-testing for STIs.
- **Develop multiplex platforms for diagnosing etiologies of STI syndromes.**
- **Develop other low-cost, rapid STI point-of-care tests for:**
  - HSV infection
  - *T. vaginalis* infection
  - *M. genitalium* infection.
- **Design improved tools for diagnosing pelvic inflammatory disease.**

2 Prevention

- **Design multipurpose prevention technologies to prevent STIs and pregnancy.**
- **Develop STI vaccines for:**
  - *N. gonorrhoeae* infection (including group B meningitis vaccines)
  - HSV infection
  - *T. pallidum* infection
  - *C. trachomatis* infection.
- **Develop communication strategies to increase STI awareness, prevention and service engagement.**
- **Evaluate screening and treatment for STIs to reduce adverse pregnancy outcomes.**
- **Evaluate pre- and post-exposure prophylactic strategies for STIs and their implementation.**

Research to develop better STI diagnostics and to understand how best to implement them is essential. In much of the world, STI care is based on symptoms without testing (syndromic management). A large proportion of infections are asymptomatic, so most STIs are missed *(6)*. New diagnostics are crucial for delivering quality STI services, reducing the spread of STIs and improving data collection.

New STI prevention interventions, such as multipurpose technologies that prevent both STIs and pregnancy, and new STI vaccines, are a priority for long-term, sustainable STI control. Important innovations also include new communication strategies for STIs and novel approaches for preventing STI-related adverse pregnancy outcomes.

WHO global STI research priorities

3 Management

- **Develop new therapeutics for *N. gonorrhoeae* infection at multiple anatomic sites.**
- **Identify oral alternatives to benzathine penicillin for treating syphilis during pregnancy.**
- **Evaluate the implementation of STI partner management, especially in LMICs.**
- **Develop improved STI therapeutic and management options for:**
  - congenital syphilis, neurosyphilis and other syphilis complications
  - HSV infection, ideally curative treatment
  - *T. vaginalis* infection, including drug-resistant infections
  - *M. genitalium* infection, including drug-resistant infections.
- **Design strategies to reduce stigma and adverse psychosocial consequences associated with STI diagnoses.**

4 Epidemiology

- **Estimate the prevalence and incidence of:**
  - *T. pallidum* infection
  - *N. gonorrhoeae* and *C. trachomatis* infections
  - genital HSV infections.
- **Assess patterns of STI healthcare-seeking behaviour in diverse populations.**
- **Evaluate STI antimicrobial resistance and treatment failures at different anatomical sites.**
- **Evaluate the burden of disease outcomes due to:**
  - *T. pallidum* infection
  - *N. gonorrhoeae* and *C. trachomatis* infections
  - genital HSV infections.
- **Evaluate quality of life effects, disability weights, and societal costs associated with STIs.**
- **Gain better understanding of STI transmission in populations using innovative methods.**
- **Investigate whether *M. genitalium* infections lead to important disease outcomes.**
- **Evaluate the interactions between STIs and the vaginal microbiome.**

Current STI treatment challenges threaten to increase STI rates. New therapies for gonorrhoea are needed because of increasing gonococcal antimicrobial resistance *(7)*, and alternatives to benzathine penicillin G for syphilis can address recurrent global shortages *(8)*. Innovative approaches to managing partners of people with STIs can reduce reinfections and ongoing STI transmission.

Improved STI epidemiologic data underpin all the other efforts and are critically needed. This includes STI prevalence and incidence estimates, as well as estimates of disease burden resulting from STIs. Such data can raise awareness about STIs, target prevention and control efforts, monitor impact of existing interventions, and help quantify the full potential value of investing in new STI interventions.

STI research and outbreaks

Planning was underway for the STI research priority setting when a multicountry outbreak of mpox, propagated by sexual transmission of monkeypox virus, was declared a public health emergency of international concern by WHO.

In September 2022, WHO gathered global experts at the International Union Against STIs World Congress in Zimbabwe to discuss important research questions related to sexually acquired mpox. These discussions and mpox-related research areas proposed in the first STI priority survey formed a separate consolidated list. This list was refined with input from WHO mpox experts and the STI research priority scoring survey.

Research priorities related to sexually acquired mpox

1. Evaluate the **efficacy and/or effectiveness of smallpox/mpox vaccines** against sexually acquired mpox and risk of reinfection or recurrence.
2. Evaluate the **efficacy and/or effectiveness of antiviral treatments** for sexually acquired mpox and associated factors (e.g. timing of treatment, drug levels in different body fluids and emerging risk of resistance to treatment).
3. Evaluate the **barriers to prevention and care for mpox**, experiences of stigma and discrimination, and effective risk communication and community engagement strategies in different contexts.
4. Investigate the **spectrum and determinants of mpox clinical presentation**, progression, severity, complications and sequelae, including site and dose of inoculum, type of sexual contact, STI/HIV status, gender and pregnancy status.
5. Evaluate the **duration and dynamics of monkeypox viral persistence** and potential infectiousness in semen and other bodily fluids, shedding from mucosal or skin sites, and immune responses, according to population and immune status.
6. Evaluate the **risk and determinants of acquisition and transmission of monkeypox virus** associated with different types of sexual contact, behaviour and mpox clinical presentations for a variety of populations and settings.

STI research is important in the context of outbreaks and emerging infections. In addition to monkeypox virus, several recent examples, including Ebola virus, have demonstrated that sexual transmissibility can play a key role in outbreaks, even for pathogens with other primary modes of transmission.

Call for action and investment

The WHO global STI research prioritization process identified 40 important STI research needs to address existing gaps in STI prevention, care and control for the greatest public health impact.

For decades, STI control has been based on the same tools, and the world is far from reaching the goals of the WHO global strategy on STIs *(2)*. Innovative new approaches are needed.

Without research and investment, STIs will continue to have a negative impact on the sexual and reproductive health and well-being of people worldwide, especially women and neonates, adolescents and young people, people living in LMICs and marginalized populations in all settings.

These STI research priorities should encourage researchers to focus on these priority areas, and donors to support this large research effort, in order to reach global goals toward ending STIs as a public health problem.

This WHO STI research agenda provides a call to action for focus, investment and innovation to address the global epidemic of STIs and advance sexual and reproductive health and well-being for all.

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