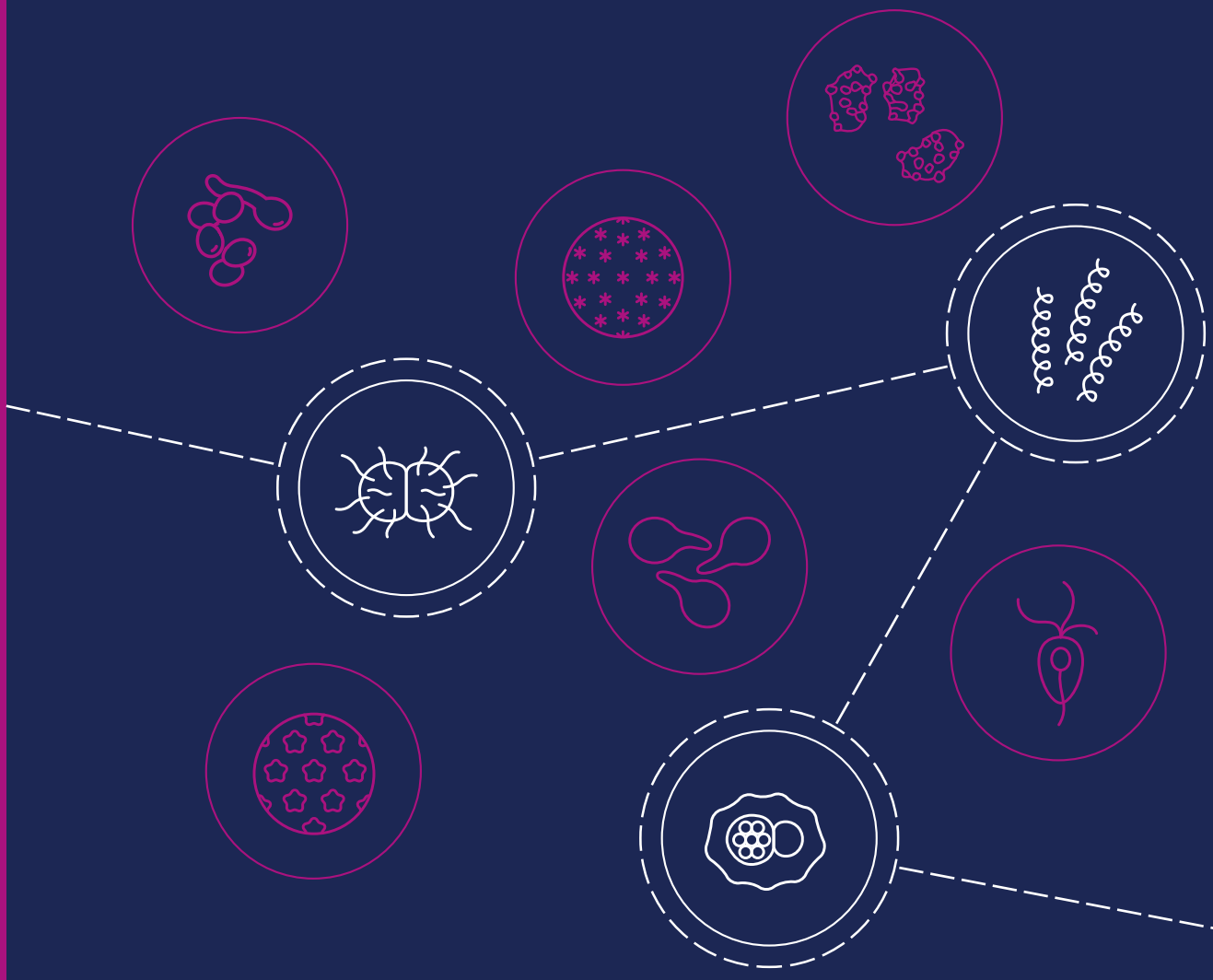
Updated recommendations for the treatment of *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Treponema pallidum* (syphilis), and new recommendations on syphilis testing and partner services



World Health Organization

Updated recommendations for the treatment of *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Treponema pallidum* (syphilis), and new recommendations on syphilis testing and partner services

World Health Organization

Updated recommendations for the treatment of *Neisseria gonorrhoeae, Chlamydia trachomatis* and *Treponema pallidum* (syphilis), and new recommendations on syphilis testing and partner services

ISBN 978-92-4-009076-7 (electronic version)
ISBN 978-92-4-009077-4 (print version)

Suggested citation. Updated recommendations for the treatment of *Neisseria gonorrhoeae, Chlamydia trachomatis* and *Treponema pallidum* (syphilis), and new recommendations on syphilis testing and partner services. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at https://iris.who.int/.

Design and layout: Green Ink Publishing Services Ltd.

Contents

Acknowledgements

The World Health Organization (WHO) Department of Global HIV, Hepatitis and Sexually Transmitted Infections Programmes (HHS) is grateful to and thanks all the individuals and organizations that contributed to developing these guidelines. Further details for all contributors are provided in Annex 1.

The guideline methodologist for Grading of Recommendations Assessment, Development and Evaluation (GRADE) was Maria Ximena Rojas Reyes of the Institut d'Recerca Hospital de la Santa Creu i Sant Pau, Spain. The systematic reviewers for the treatment recommendations were Angela Barbara, Meha Bhatt and Nancy Santesso of the Michael G. DeGroote Cochrane Canada Centre, McMaster University, Canada. For syphilis testing, the systematic reviewers were Eric Chow, Christopher Fairley, Su Mei Goh, Jason Ong, Warittha Tieosapjareon, Janet Towns and Ying Zhang of Monash University and Melbourne Sexual Health Centre, Australia. The systematic reviewers for partner services were Nicholas Henschke (Cochrane Response, Germany), Michael Marks (London School of Hygiene & Tropical Medicine, United Kingdom of Great Britain and Northern Ireland), Oriol Mitjà (Fight AIDS and Infectious Disease Foundation, Spain), Minh Duc Pham (Burnet Institute, Australia) and Gemma Villanueva (Cochrane Response, United Kingdom).

The members of the STI Guideline Development Group (GDG) provided invaluable guidance and comments during the development of these guidelines through virtual meetings and comments by correspondence. Their meticulous attention to detail, expert comments and feedback ensured the consistency and relevance of these guidelines. These external experts included: Laith Abu Raddad (Weill Cornell Medical College, Qatar), Yaw Adu-Sarkodie (Kwame Nkrumah University of Science and Technology, Ghana), Mircea Betiu (Nicolae Testimitanu State University of Medicine and Pharmacy, Republic of Moldova), Catriona Bradshaw (Monash University and Alfred Hospital, Australia), Xiang-Sheng Chen (National Center for AIDS/STD Control and Prevention, China), Chido Dziva Chikwari (Biomedical Research and Training Institute, Zimbabwe), Amina El Kettani (Ministry of Health, Morocco), Patricia Garcia (Universidad Peruana Cayetano Heredia, Peru), William M. Geisler (University of Alabama at Birmingham, United States of America [USA]), Kimberly Green (PATH, Viet Nam), Somesh Gupta (All India Institute of Medical Sciences, India), Edward W. Hook III (University of Alabama at Birmingham, USA), Rena Janamnuaysook (Institute of HIV Research and Innovation, Thailand), Nathalie Kapp (International Planned Parenthood Federation, United Kingdom), Hamida Khattabi (independent consultant, Morocco), Rossaphorn Kittyaowamarn (Ministry of Public Health, Thailand), Jeffrey D. Klausner (University of California, Los Angeles, USA), Ranmini Kularatne (Labtests, New Zealand), Peter Kyambadde (Ministry of Health, Uganda), David Lewis (Western Sydney Sexual Health Centre, Australia), Philippe Mayaud (London School of Hygiene & Tropical Medicine, United Kingdom), Saiqa Mullick (Wits Reproductive Health and HIV Institute, South Africa), Francis Ndowa (Skin and Genito-Urinary Medicine Clinic, Zimbabwe), Lilani Rajapaksa (Ministry of Health, Sri Lanka), Kees Rietmeijer (Denver Public Health Department, USA), Danvic Rosadiño (LoveYourself Inc., Philippines), Jonathan Ross (University Hospitals Birmingham NHS Foundation Trust, United Kingdom), Anna Shapiro (Global Network of Sex Work Projects, United Kingdom), Daniel Simões (Coalition Plus, Portugal), Jane Thiomi (LVCT Health, Kenya), Jane Tomnay (University of Melbourne, Australia), Magnus Unemo (Örebro University Hospital, Sweden), Bea Vuylsteke (Institute of Tropical Medicine, Belgium) and Judith Wasserheit (University of Washington, USA).

The following observers, representing a range of international organizations, also attended the GDG meetings without taking any role in the formulation of the WHO recommendations: Laura Bachman (Centers for Disease Control and Prevention [CDC], USA), Azadeh Baghaki (Unitaid, Switzerland), Lindley Barbee (CDC, USA), Francis Kakooza (Makerere University, Uganda), Fernando Pascal Martinez (Global Antibiotic Research & Development Partnership, Spain) and Tim Sladden (United Nations Population Fund, USA).

The External Review Group, who peer-reviewed drafts of the recommendations and guidelines, included: Henry J.C. de Vries (Amsterdam Sexual Health Clinic, Kingdom of the Netherlands), Kristina Grabbe (Jhipiego, USA), Hans Benjamin Hampel (University of Zurich, Switzerland), Kausar Jabeen (The Aga Khan University, Pakistan), Monica Lahra (Prince of Wales Hospital, Australia), Pham Thi Lan (Hanoi Medical University, Viet Nam), Ahmed Latif (public health consultant, Australia), Ioannis Mameletzis (consultant, Ukraine), Angelica Espinosa Miranda (Ministry of Health, Brazil), Koleka Mlisana (National Health Laboratory Service, South Africa), Lori Newman (National Institutes of Health, USA), Catherine Ngugui (Ministry of Health, Kenya), Remco Peters (University of Pretoria, South Africa), Reshmie Ramautarsing (Institute of HIV Research and Innovation, Thailand), Pachara Sirivongrangson (Ministry of Public Health, Thailand), Melanie Taylor (CDC, USA), Janet Wilson (Leeds Teaching Hospitals NHS Trust, United Kingdom) and Valerie Wilson (Caribbean Med Labs Foundation, Trinidad and Tobago).

At WHO headquarters in Geneva, overall coordination for the development of these guidelines was provided by Teodora Wi with support from Rachel Baggaley, Magdalena Barr-DiChiara, Maeve Brito de Mello, Cheryl Johnson, Ismail Maatouk, Daniel McCartney and Yamuna Mundade (all at the HHS Department), under the leadership of Meg Doherty (Director of the HHS Department).

The WHO Steering Committee for these guidelines was composed of WHO staff from the HHS Department, other WHO departments and from WHO regional offices around the globe. From the HHS Department in Geneva, WHO extends thanks to Rachel Baggaley, Magdalena Barr-DiChiara, Maeve Brito de Mello, Peter Cherutich, Cheryl Johnson, Celine Lastrucci, Niklas Luhmann, Ismail Maatouk, Antons Mozalevskis, Yamuna Mundade, Morkor Newman Owiredu, Jane Rowley, Annette Verster, Marco Vitoria, Lara Vojnov and Teodora Wi. From other departments at WHO headquarters, sincere thanks are due to Avni Amin, Sami Gottlieb, James Kiarie, Gitau Mburu, Igor Toskin (Department of Sexual and Reproductive Health and Research), Kingsley Asiedu (Department of Neglected Tropical Diseases), Carmen Pessoa da Silva (Department of Surveillance, Prevention and Control), Benedikt Huttner (Department of Access to Medicines and Health Products), Mark Lanigan and Anne-Laure Page (Regulation and Prequalification) and Özge Tunçalp (Department of Maternal, Newborn, Child and Adolescent Health and Ageing). WHO is also grateful for the input of representatives from the regional offices (in alphabetical order by region): Frank Lule (Regional Office for Africa, Republic of Congo), Ruben Mayorga Sagastume (Regional Office for the Americas, USA), Joumana Hermez (Regional Office for the Eastern Mediterranean, Egypt), Stela Bivol (Regional Office for Europe, Denmark), Bharat Rewari (Regional Office for South-East Asia, India), Kiyohika Izumi (Regional Office for the Western Pacific, Philippines) and Van Nguyen (Country Office, Viet Nam).

The HHS Department appreciates the support of the Secretariat of the WHO Guidelines Review Committee during the guideline development process.

The HHS Department provided funding for these guidelines. Additional funding was provided by the United States Agency for International Development (USAID), the Bill & Melinda Gates Foundation and Unitaid to develop components of these guidelines, including systematic reviews of evidence, evidence compilation and document development, editing and publication. These funders had no role in the GDG's formulation of the recommendations or writing of the guidance document.

Abbreviations

AMR	antimicrobial resistance
AWaRe	WHO Access, Watch and Reserve
CI	confidence interval
COVID-19	coronavirus disease 2019
EPT	expedited partner therapy
ERG	External Review Group
GARDP	Global Antibiotic Research and Development Partnership
GDG	Guideline Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HCV	hepatitis C virus
HHS	World Health Organization Department of Global HIV, Hepatitis and Sexually Transmitted Infections Programmes
HPV	human papillomavirus
PICO	population, intervention, comparison, outcome
PrEP	pre-exposure prophylaxis
RCT	randomized controlled trial
RDT	rapid diagnostic test
RPR	rapid plasma reagin
SARS-CoV-2	severe-acute-respiratory-syndrome-related coronavirus 2
STI	sexually transmitted infection
TB	tuberculosis
TPHA	*Treponema pallidum* haemagglutination assay
TPPA	*Treponema pallidum* passive particle agglutination assay
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNFPA	United Nations Population Fund
UNHCR	United Nations High Commissioner for Refugees
UNICEF	United Nations Children's Fund
VDRL	Venereal Disease Research Laboratory
WHO	World Health Organization

Glossary

Accuracy: This is defined as the close agreement between the mean value obtained from a large series of test results and an accepted reference value.

Adolescence: The phase of life between childhood and adulthood, from ages 10 to 19 years (see also definition of **young people**).

Delayed provider referral (also known as contract referral, provider-assisted delayed referral or delayed assisted partner services): A patient with possible or confirmed STIs enters into an agreement with a trained health worker to disclose their diagnosis or the potential exposure to their sexual partner(s) by themselves and to suggest that the partner(s) seek STI testing within an agreed period. If a partner does not access STI testing services or contact the health worker within that period, the health worker will contact the partner directly and offer STI testing.

Enhanced patient referral (also known as enhanced partner referral): A trained provider uses various support tools to facilitate disclosure and the offer of testing by patients with possible or confirmed STIs to their sexual partners. These tools may include providing written information, leaflets and a referral slip or card for a partner, use of web-based messaging platforms to inform a partner anonymously. STI self-collection kits could also be provided to patients to give to partners to collect a sample for testing.

Expedited partner therapy (EPT): The clinical practice of treating the sex partners of patients diagnosed with one or more STIs by providing prescriptions or medication to these patients to give to their partners without the health worker first examining the partners.

Intimate partner violence: Behaviour by one person in an intimate relationship that causes physical, psychological or sexual harm to another person in the relationship, including acts of physical violence, sexual violence, emotional or psychological abuse and controlling behaviours.

Key populations: Defined groups that, due to specific higher risk behaviours, are at increased risk of HIV irrespective of the epidemic type or local context. This includes: men who have sex with men, people who inject drugs, people in prisons and other closed settings, sex workers and transgender people.

Non-treponemal tests: Serological tests that measure indirect markers of *Treponema pallidum* infection, such as antibodies to lipoidal antigens. Non-treponemal (lipoid antigen) serologic tests can provide quantitative results through serial twofold dilutions and can also be used to assess patients for reinfection and monitor treatment outcome.

Partner services: A range of voluntary services whereby a trained health worker asks for information about sexual partners and offers individuals with an STI effective options for notifying their sexual partners about a possible exposure and the benefits of seeking STI services, and ensures that sexual partners are appropriately managed or linked to care and other preventive services.

Patient referral (also known as simple patient referral, passive referral or partner referral): A trained health worker encourages a patient with possible or confirmed STIs to disclose their diagnosis or the potential exposure to their sexual partner(s) by themselves and to suggest that the partner(s) seek testing. Patient referral involves advice from the trained health worker regarding the need for partner(s) to get tested, strategies for safely disclosing one's diagnosis and information about where and how the partner(s) can access STI testing services.

Provider-assisted referral (also known as assisted partner notification or provider-assisted partner services): A trained provider (health worker) asks people with possible or confirmed STIs about their sexual partners and then, with the consent of the patient, informs the partners of their potential STI exposure. The provider then offers STI testing to partners.

Provider–patient referral: A process whereby a trained health worker accompanies and provides support to a patient with possible or confirmed STIs when they disclose their diagnosis and the potential exposure to an STI to the patient's partner(s). The health worker then offers STI testing to the partner(s). This can be useful when the patient prefers to disclose their diagnosis or potential exposure to a partner but needs support from a provider.

Quality assurance: The arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use. Quality assurance therefore incorporates good manufacturing practice and other factors, such as product design and development.

Quality control: All measures taken, including the setting of specifications, sampling, testing and analytical clearance, to ensure that raw materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics.

Quality management system: An appropriate infrastructure, encompassing the organizational structure, procedures, processes and resources, and systematic actions necessary to ensure adequate confidence that a product or service will satisfy given requirements for quality.

Rapid diagnostic test (RDT): An in vitro diagnostic medical device of immunochromatographic or immunofiltration format for the rapid detection of antibodies and/or antigens.

Reactive test result: A test result that shows a reaction indicating the presence of analyte. In the context of syphilis, the analyte would be *T. pallidum*-specific antigens or indirect antigens.

Sensitivity: The probability that an assay or algorithm will correctly identify all specimens that contain antibodies and/or antigens for the target infection.

Social harm: Any intended or unintended physical, economic, emotional or psychosocial injury or hurt caused by one person to another, a person to themselves or an institution to a person, occurring before, during or after having been diagnosed with an STI.

Social network approaches (also known as social network testing services): A trained health worker asks people who are identified as having a high ongoing risk of acquiring STIs (including HIV), independently of STI diagnosis, to encourage and invite individuals in their sexual or social networks to seek STI testing services.

Specificity: The probability that the assay or algorithm will correctly identify all specimens that do not contain antibodies and/or antigens for the target infection.

Syphilis self-testing: A process in which a person collects their own specimen, performs a test and interprets the result, often in a private setting, either alone or with someone they trust.

Testing algorithm: When specific products are populated into a **testing strategy** (see below). A specific product is defined with a product name, product code(s), a manufacturing site and regulatory version. The testing algorithm is likely to change depending on which specific products are verified for use together and are procured for this purpose.

Testing strategy: A sequence of tests conducted on assays to achieve a specific objective, such as screening for infection or diagnosing infection.

Treponemal tests: Serological tests that measure antibodies to *T. pallidum*-specific antigens.

Young people: WHO defines young people as individuals aged 10–24 years (see also definition of **adolescence**).

Executive summary

The global burden of sexually transmitted infections (STIs) is high. Recent World Health Organization (WHO) estimates for 2020 suggest that there were 374 million new cases of four curable STIs (gonorrhoea, chlamydia, syphilis and trichomoniasis) among people aged 15–49 years, including 156.3 million new cases of trichomoniasis, 128.5 million new cases of chlamydia, 82.4 million new cases of gonorrhoea and 7.1 million new cases of syphilis, or approximately 1 million new curable STIs every day.[1]

Chlamydia, caused by *Chlamydia trachomatis*, and gonorrhoea, caused by *Neisseria gonorrhoeae*, are the most common bacterial STIs worldwide and result in substantial morbidity and economic costs. Syphilis is a bacterial STI caused by *Treponema pallidum* that results in substantial morbidity and mortality. Additionally, congenital syphilis can be devastating to a fetus if infection during pregnancy is not detected and treated sufficiently early in pregnancy.

WHO has set ambitious targets for STI reductions in the recent global health sector strategy for HIV, viral hepatitis and STIs. The aim is to achieve a 90% reduction in both gonorrhoea and syphilis infections by 2030, and to eliminate congenital syphilis as a public health problem. To achieve these targets, the strategy highlights the importance of making it easier for people with STIs to access prevention, diagnostic and treatment services.

The treatment of STIs is complicated by the rapidly changing antimicrobial susceptibility patterns of various sexually transmitted pathogens to available antibiotics. For *N. gonorrhoeae*, there are concerns about the eventual development of untreatable gonococcal infections with serious sexual and reproductive health consequences. Antimicrobial resistance (AMR) in *N. gonorrhoeae* has emerged for every drug available for empirical first-line treatment, with the extended-spectrum cephalosporin, ceftriaxone, being the last option in most countries. Certain antibiotics, including azithromycin, have been classified as highly susceptible to bacterial resistance, such that their use needs to be reserved for certain pathogens. Additionally, potential adverse allergic reactions in users associated with medicines such as penicillin need to be considered.

These guidelines include updated treatment recommendations for *N. gonorrhoeae, C. trachomatis* and *T. pallidum* (syphilis) based on new evidence, and new recommendations on partner services for curable STIs and syphilis testing approaches, particularly the use of dual treponemal/non-treponemal rapid diagnostic tests (RDTs) and syphilis self-testing.

In 2016–2017, WHO published a series of four guideline documents for the treatment of *N. gonorrhoeae*, *C. trachomatis* and *T. pallidum*, and for screening and treatment for *T. pallidum* (syphilis) during pregnancy, taking into consideration the latest evidence available. The recommendation for treatment of *N. gonorrhoeae* is being updated, primarily by increasing recommended treatment dosages. These dosage increases are intended to delay the development of resistance to last-line treatment options and provide additional treatment options for specific settings. For *C. trachomatis*, the updates to the treatment recommendation highlight the efficacy of doxycycline as a treatment, while reserving azithromycin for emerging infections, such as *Mycoplasma genitalium*. The previous syphilis treatment recommendation is updated here to emphasize that benzathine penicillin remains effective for the treatment of syphilis compared with alternative treatment regimens, especially to prevent vertical transmission during pregnancy. These recommendations

1 The most up-to-date STI estimates are always made available at this page of the WHO Global Sexually Transmitted Infections Programme's website: https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/stis/strategic-information.

are aligned with the WHO Access, Watch and Reserve (AWaRe) antibiotic categorization of WHO's Model List of Essential Medicines, ensuring accessibility and promoting antibiotic stewardship (see Box 1).

Given the rapid increase in syphilis cases, new recommendations are being proposed to increase testing coverage through offering rapid diagnostic tests (RDTs) for both treponemal and non-treponemal components, and by offering syphilis self-testing as an option. Additionally, there is a focus on evidence-based recommendations to improve STI partner services for people with STIs, with the aim of reducing reinfection and onward transmission.

In addition to being presented in this current publication, these new and updated recommendations will be included within the forthcoming edition of WHO's consolidated guidelines for the prevention, diagnosis, treatment and care of STIs.

The objectives of these present guidelines are:

- to provide updated evidence-informed guidance on treating infections caused by *N. gonorrhoeae* and *C. trachomatis* and treating syphilis infection during pregnancy;
- to provide recommendations on syphilis testing, specifically on the use of dual treponemal/non-treponemal RDTs and syphilis self-testing as additional options for STI services;
- to provide recommendations on STI partner services; and
- to support countries and national programmes in updating their national guidelines with a view to reaching the 2030 global health sector strategy targets on STIs.

These guidelines are intended for policy-makers, programme managers, health workers and any other public health professionals responsible for planning or implementing STI services (stand-alone or integrated with other health services). These guidelines will also be a resource for donor and development agencies as well as international, nongovernmental, civil society and community-based organizations, and those working with or led by key populations and the communities affected the most by STIs, including HIV.

These guidelines were developed following the methods outlined in the 2014 *WHO handbook for guideline development*. Multiple systematic reviews were conducted to address the guideline objectives. The members of the STI Guideline Development Group reviewed the evidence and made recommendations. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to assess the evidence and formulate the recommendations. The External Review Group reviewed the guidelines prior to submission to the WHO Guidelines Review Committee.

Updated treatment recommendations

These guidelines provide updated treatment recommendations for specific conditions caused by *N. gonorrhoeae*, *C. trachomatis* and *T. pallidum*. The recommendations for treating gonococcal and chlamydial infections (Tables 1 and 2) apply to all adults and adolescents, including during pregnancy, and including people living with HIV and key populations (men who have sex with men, people who inject drugs, people in prisons and other closed settings, sex workers and transgender people). A separate recommendation on treating uncomplicated chlamydial infections applies specifically to pregnant and breastfeeding women. The updated treatment recommendations for syphilis infections apply to pregnant women, and vary depending on the duration of infection (Table 3).

Table 1. Summary of the updated recommendations and good practice statements on treatment of gonococcal infections (see further detail in section 3.1)

Recommendations	Strength of recommendation and certainty of evidence
Genital, anorectal and oropharyngeal gonococcal infections	
WHO recommends that national or local antimicrobial resistance data should determine the choice of therapy when available.	**Good practice statement** *(updated 2023)*
For adults and adolescents (including pregnant women) with genital, anorectal and/or oropharyngeal gonococcal infections, **WHO suggests**: • ceftriaxone 1 g intramuscularly as a single dose. If ceftriaxone is not available or refused, **WHO suggests**: • cefixime 800 mg orally and performing test of cure. If test of cure is not possible or when oropharyngeal infection is diagnosed or is a potential concern, **WHO suggests**: • cefixime 800 mg orally plus azithromycin 2 g orally. When resistance, allergy or availability of cephalosporins is a concern, **WHO suggests** one of the following options: • spectinomycin 2 g intramuscularly as a single dose plus azithromycin 2 g orally; or • gentamicin 240 mg intramuscularly as a single dose plus azithromycin 2 g orally. *Remarks:* • Ceftriaxone 1 g intramuscularly may be painful; discuss with the individual the option of using lidocaine as diluent with the injection. • Azithromycin 2 g may cause gastrointestinal side-effects, especially on an empty stomach. To reduce side-effects, consider azithromycin 1 g taken at 6- to 12-hour intervals. • Sexual abstinence, condom use and partner treatment should be discussed. • WHO guidance on surveillance of antimicrobial resistance in *N. gonorrhoeae* and test of cure is available.[a] • Pregnant women should be closely monitored for adverse reactions (e.g. allergic reactions including anaphylactic shock, premature delivery and premature rupture of membranes).	**Conditional recommendation**, low certainty in evidence of effects *(updated 2023)*

[a] Enhanced gonococcal antimicrobial surveillance programme (EGASP): general protocol. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/341333). Licence: CC BY-NC-SA 3.0 IGO.

Recommendations	Strength of recommendation and certainty of evidence
Retreating gonococcal infections after treatment failure	
For adults and adolescents (including pregnant women) with gonococcal infections for whom treatment has failed as evidenced by persistent symptoms or a positive test of gonococcal infection, **WHO recommends** that the possibility of reinfection or antimicrobial resistance be considered to determine the choice of therapy.	**Good practice statement** *(new 2023)*
If treatment failure occurred after a non-WHO-recommended treatment, **WHO suggests** retreating with a WHO-recommended therapy. If reinfection is suspected, **WHO suggests** retreating with a WHO-recommended therapy, reinforcing the need for sexual abstinence, condom use and partner treatment. If treatment failure occurred and antimicrobial susceptibility testing data are available, **WHO suggests** retreating according to susceptibility profile. If treatment failure occurred after a WHO-recommended therapy and reinfection is assessed to be unlikely, **WHO suggests** retreating with a regimen not used previously from one of the following options and performing test of cure: • ceftriaxone 1 g intramuscularly as a single dose plus azithromycin 2 g orally, only if ceftriaxone was not used previously; • spectinomycin 2 g intramuscularly as a single dose plus azithromycin 2 g orally; or • gentamicin 240 mg intramuscularly as a single dose plus azithromycin 2 g orally. *Remark:* • Retreatment should not be delayed. If an individual does not respond to these treatment failure recommendations, refer the individual to a specialist for further assessment and management.	**Conditional recommendation**, very low certainty in evidence of effects *(updated 2023)*

Table 2. Summary of the updated and edited recommendations on treatment of chlamydial infections (see further detail in section 3.2)

Recommendations	Strength of recommendation and certainty of evidence
Uncomplicated chlamydial infections (genital, anorectal and oropharyngeal)	
For adults and adolescents with uncomplicated chlamydial infections (genital, anorectal and/or oropharyngeal), **WHO suggests**: • doxycycline 100 mg orally twice a day for 7 days. If doxycycline is not available or adherence to multiple doses is a serious concern, **WHO suggests**: • azithromycin 1 g orally as a single dose. If doxycycline and azithromycin are not available, **WHO suggests** one of the following options: • erythromycin 500 mg orally four times a day for 7 days; • ofloxacin 200–400 mg orally twice a day for 7 days; or • tetracycline 500 mg orally four times a day for 7 days. *Remarks:* • Doxycycline extended release (ER) may be an alternative to twice daily dosing of doxycycline, but the high cost may prohibit its use. • If using an alternative treatment for gonococcal infection (cefixime 800 mg plus azithromycin 2 g), maintain the 2 g dosage of azithromycin to cover chlamydial infection. • Note that doxycycline, tetracycline and ofloxacin are contraindicated in pregnant and breastfeeding women (see separate recommendations for pregnant and breastfeeding women).	**Conditional recommendation**, moderate certainty in evidence of effects *(updated 2023)*
Uncomplicated chlamydial infection in pregnant and breastfeeding women	
For pregnant and breastfeeding women with uncomplicated chlamydial infection, **WHO recommends**: • azithromycin 1 g orally as a single dose.	**Strong recommendation**, moderate certainty in evidence of effects *(edited 2023)*
When azithromycin is not available, **WHO suggests** one of the following options: • amoxicillin 500 mg orally three times a day for 7 days; or • erythromycin 500 mg orally four times a day for 7 days. *Remark:* • If using an alternative treatment for gonococcal infection (cefixime 800 mg plus azithromycin 2 g), maintain the 2 g dosage of azithromycin to cover chlamydial infection.	**Conditional recommendation**, low certainty in evidence of effects *(edited 2023)*

Table 3. Summary of the updated recommendations on treatment of *Treponema pallidum* (syphilis) during pregnancy (see further detail in section 3.3)

Recommendations	Strength of recommendation and certainty of evidence
Early syphilis (primary, secondary and early latent syphilis of not more than two years' duration) in pregnant women	
In pregnant women with early syphilis, **WHO recommends**: • benzathine penicillin G 2.4 million units once intramuscularly.	**Strong recommendation**, very low certainty in evidence of effects *(updated 2023)*
If benzathine penicillin is not available, **WHO suggests**: • procaine penicillin 1.2 million units intramuscularly once daily for 10 days. In **rare situations** when benzathine or procaine penicillin cannot be used (e.g. due to confirmed penicillin allergy, which occurs in less than 3% of the population, and where penicillin desensitization is not possible) or are not available (e.g. due to stock-outs), **WHO suggests** one of the following options with caution and enhanced follow-up: • ceftriaxone 1 g intramuscularly once daily for 10–14 days; or • erythromycin 500 mg orally four times daily for 14 days. *Remarks:* • If the stage of syphilis is unknown, follow recommendations for pregnant women with late syphilis. • Although erythromycin treats the pregnant woman, it does not cross the placental barrier completely and as a result the fetus is not treated. It is therefore necessary to treat the newborn infant soon after delivery (see recommendations in the WHO guidelines referring to congenital syphilis).[a] • Doxycycline is contraindicated during pregnancy.	**Conditional recommendation**, very low certainty in evidence of effects *(updated 2023)*

Recommendations	Strength of recommendation and certainty of evidence
Late syphilis (late latent and tertiary syphilis of more than two years' duration without evidence of treponemal infection) or unknown duration in pregnant women	
In pregnant women with late syphilis or an unknown duration of infection, **WHO recommends**: • benzathine penicillin G 2.4 million units intramuscularly once weekly for three consecutive weeks. *Remark:* • The interval between consecutive doses of benzathine penicillin G should not exceed 14 days.	**Strong recommendation**, very low certainty in evidence of effects *(updated 2023)*
If benzathine penicillin is not available, **WHO suggests**: • procaine penicillin 1.2 million units intramuscularly once daily for 20 days. In **rare situations** when benzathine or procaine penicillin cannot be used (e.g. due to confirmed penicillin allergy, which occurs in less than 3% of the population, and where penicillin desensitization is not possible) or are not available (e.g. due to stock-outs), **WHO suggests** using, with caution and enhanced follow-up: • erythromycin 500 mg orally four times daily for 30 days. *Remarks:* • Although erythromycin treats the pregnant woman, it does not cross the placental barrier completely and as a result the fetus is not treated. It is therefore necessary to treat the newborn infant soon after delivery (see the recommendations in the WHO guidelines referring to congenital syphilis).[a] • Doxycycline is contraindicated during pregnancy.	**Conditional recommendation**, very low certainty in evidence of effects *(updated 2023)*

[a] WHO guidelines for the treatment of *Treponema pallidum* (syphilis). Geneva: World Health Organization; 2016 (https://apps.who.int/iris/handle/10665/249572) and WHO guideline on syphilis screening and treatment for pregnant women. Geneva: World Health Organization; 2017 (https://apps.who.int/iris/handle/10665/259003).

Box 1. The WHO Access, Watch, Reserve (AWaRe) categorization of the antibiotics recommended in these guidelines

Access group	Watch group	Reserve group
Amoxicillin	Azithromycin	–
Benzathine penicillin G (benzathine benzylpenicillin)	Ceftriaxone	
Doxycycline	Cefixime	
Gentamicin	Erythromycin	
Procaine penicillin (procaine benzylpenicillin)	Ofloxacin	
Spectinomycin		
Tetracycline		

Source: The WHO AWaRe (access, watch, reserve) antibiotic book. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/365237).

New STI service-delivery recommendations

These guidelines provide recommendations for syphilis testing including the use of dual treponemal/non-treponemal RDTs within existing syphilis testing strategies, syphilis self-testing as an additional testing approach (Table 4), and STI partner services (Table 5).

Table 4. Summary of the new recommendations on syphilis testing services (see further detail in Chapter 4)

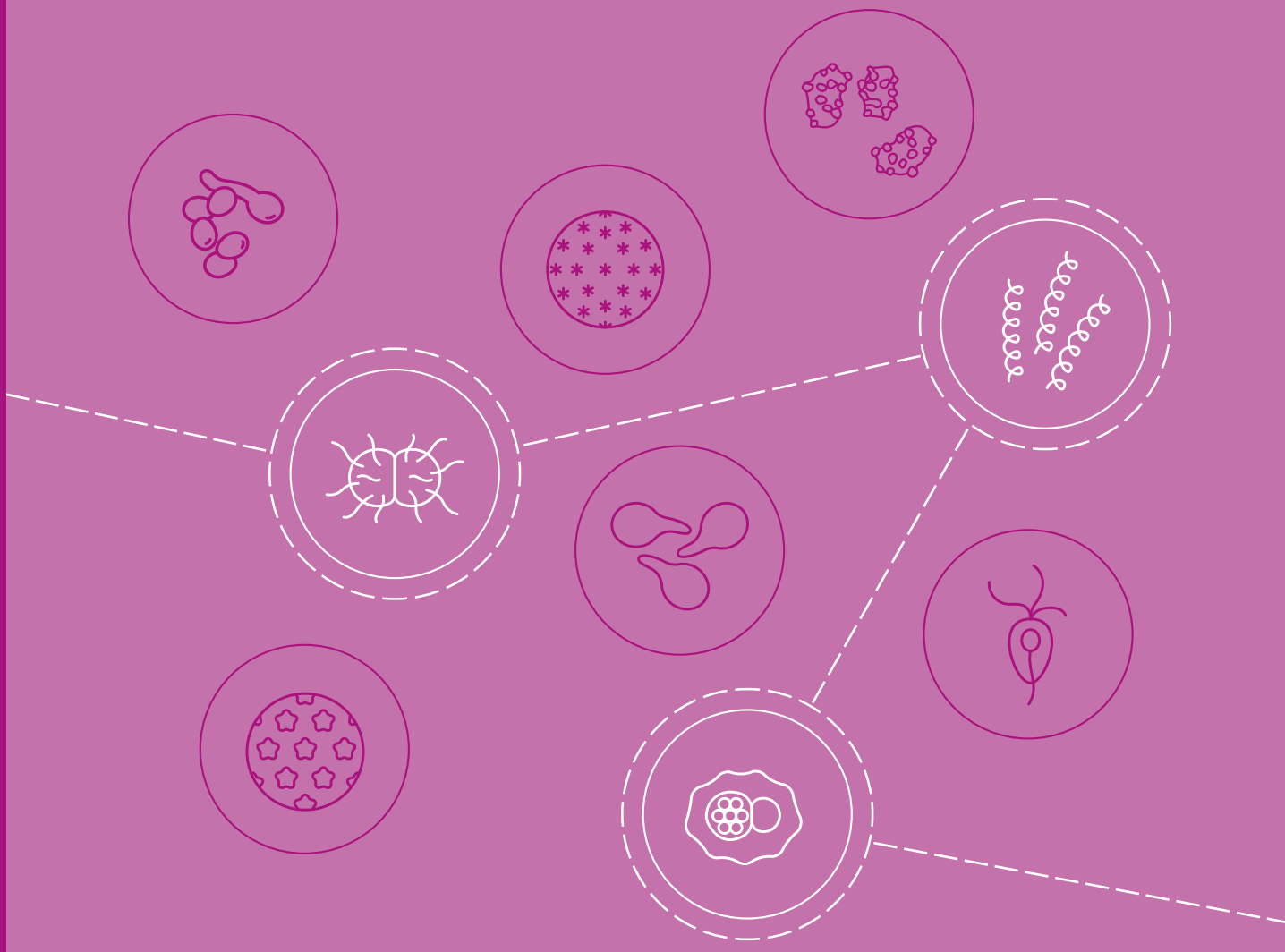
Recommendations	Strength of recommendation and certainty of evidence
Dual treponemal/non-treponemal rapid diagnostics tests (RDTs)	
WHO recommends offering dual treponemal/non-treponemal rapid diagnostic tests as an additional approach within syphilis testing strategies. *Remarks:* • **Epidemiology and context**: Dual treponemal/non-treponemal rapid diagnostic tests (RDTs) can be incorporated into syphilis testing strategies and algorithms based on the needs of different populations, epidemiology and settings. Policy-makers and implementers need to have a clear understanding of how to use and interpret reactive results based on their context, particularly when determining how to deliver the test to specific populations and in certain geographies where treponematosis prevalence is high or endemic (e.g. syphilis, yaws, bejel or pinta). • **Clear messages**: Individuals need to be provided with clear information about their test results so they may be able to access further testing, treatment and care as needed. It is important that all those with test results that indicate an active infection are informed and promptly linked to care services. STI partner services should be discussed and offered as part of case management and public health interventions. • **Integration**: Dual treponemal/non-treponemal RDTs should be integrated into existing testing strategies and algorithms, and provided as part of a package of services, including immediate access to treatment. • **Quality-assured products**: Dual treponemal/non-treponemal RDTs, as with all testing approaches, should be conducted using quality-assured products.	**Strong recommendation**, low certainty in evidence of effects *(new 2023)*

Recommendations	Strength of recommendation and certainty of evidence
Syphilis self-testing	
WHO suggests offering syphilis self-testing as an additional syphilis testing approach. *Remarks:* • **Integration**: Syphilis self-testing, as with all testing approaches, should be offered within a broader programme and package of services, which includes ensuring access and linkage to confirmatory testing (where available) and immediate treatment initiation. Opportunities to integrate syphilis self-testing into and/or to expand existing services should be a priority. • **Quality-assured products**: Syphilis self-testing may include products such as dual HIV/syphilis self-tests, treponemal self-tests and dual treponemal and non-treponemal self-tests. As with all testing approaches, syphilis self-testing should be conducted using quality-assured products. • **Epidemiology and context**: Policy-makers and implementers need to have a clear understanding that syphilis self-testing can be reactive with any current or prior infection by any treponematosis (e.g. syphilis, yaws, bejel or pinta) when determining how and where to deliver self-testing to specific populations and in certain geographies. • **Clear messages**: Self-testers need to be provided with clear guidance about when they should test themselves, how to interpret their self-test results and, if needed, where to go for confirmatory testing and treatment. These further services are particularly critical when single treponemal self-tests are used that cannot differentiate previously treated infections from current infections. In endemic areas, it is critical to clarify that reactive serologic tests cannot differentiate between syphilis and other treponematosis (e.g. yaws). Self-testers may also need support tools to ensure they know how to self-test, and this can include instructions for use, videos, in-person demonstrations and support from peers or community health workers. Information about testing with a partner should also be provided, when appropriate, to encourage use of partner services.	**Conditional recommendation**, low certainty in evidence of effects *(new 2023)*

Table 5. Summary of the new recommendation on STI partner services (see further detail in Chapter 5)

Recommendations	Strength of recommendation and certainty of evidence
STI partner services	
WHO recommends that STI partner services should be offered to people with STIs as part of a range of options based on their needs and preferences and within a comprehensive package of voluntary STI testing, care and prevention. *Remarks:* • **Human rights**: STI partner services must always be voluntary and never mandatory. Coercive or forced testing is never warranted. All consenting patients should have their privacy protected and personal information should be kept confidential. • **Important to offer options**: There are a range of STI partner services that should be offered based on patient preferences, feasibility and resources available. Partner services include several options, such as simple patient referral, enhanced patient referral, delayed provider referral, provider–patient referral, provider-assisted referral and social network approaches. Approaches with provider (health worker) support are particularly effective and can be prioritized or encouraged where feasible. Expedited partner therapy (EPT) could also be considered as part of partner services for some curable STIs, such as chlamydia or gonorrhoea. • **Linkage**: Linkage to STI management services for sexual partners is an essential component of STI services. • **Integration**: STI partner services should be based within a broader programme and package of services. It is important to build on existing services (e.g. sexual and reproductive health services and family planning services), and integrated delivery across disease areas (e.g. HIV and viral hepatitis).	**Strong recommendation**, low certainty in evidence of effects *(new 2023)*

1. Introduction



1. Introduction

1.1 Epidemiology and global targets

Sexually transmitted infections (STIs) are a major public health problem worldwide, reducing quality of life and causing serious morbidity and mortality. STIs directly affect reproductive and child health by causing infertility, cancers and pregnancy complications, and have further indirect impacts through their role in facilitating sexual transmission of HIV; therefore, in addition to impacts on health, STIs also affect national economies and individual finances.

Chlamydia, caused by *Chlamydia trachomatis*, and gonorrhoea, caused by *Neisseria gonorrhoeae*, are the two most common bacterial STIs and result in substantial morbidity and economic cost worldwide. The World Health Organization (WHO) estimates that, in 2020, 128.5 million (90.0–173.8 million) new cases of chlamydia and 82.4 million (47.7–130.4 million) new cases of gonorrhoea occurred among adolescents and adults aged 15–49 years worldwide *(1)*. The burden of chlamydia falls primarily on women, who have higher rates of this disease than men and in whom it causes pelvic inflammatory disease, tubal factor infertility and poor birth outcomes *(2, 3)*. The three biovars of *C. trachomatis*, each consisting of several serovars or genotypes, cause genital infections, lymphogranuloma venereum (LGV) and trachoma (eye infection). As for gonococcal infection, while there are higher rates among men, the complications disproportionally affect women and include pelvic inflammatory disease, ectopic pregnancy, infertility and increased HIV acquisition *(4-6)*.

Syphilis is a bacterial STI caused by *Treponema pallidum* that results in substantial morbidity and mortality. WHO estimates that, in 2020, 7.1 million (2.4–11.5 million) new cases occurred among adolescents and adults aged 15–49 years worldwide *(1)*. Syphilis is transmitted through sexual contact with infectious lesions of the mucous membranes or abraded skin, via blood transfusion, or trans-placentally during pregnancy. Without treatment, syphilis may cause serious health complications, including neurological problems. Congenital syphilis causes a wide range of adverse birth outcomes; global estimates of adverse birth outcomes based on data for 2016 include 143 000 early fetal deaths and stillbirths, 61 000 neonatal deaths and 41 000 preterm or low-birth-weight births *(7)*. The fetus can be easily cured with treatment and the risk of adverse outcomes to the fetus is minimal if infection is detected and treated sufficiently early in pregnancy.

Population groups that are especially vulnerable to STIs include sex workers and their clients, gay men and other men who have sex with men, transgender people, people who inject drugs, people in prisons, young people, mobile populations and people affected by conflict and civil unrest *(1)*.

WHO has set ambitious targets within the recent publication Global health sector strategies on *HIV, viral hepatitis and STIs for the period 2022–2030*, including a 90% reduction in both gonorrhoea and syphilis infections and the elimination of congenital syphilis as a public health problem (defined as less than 50 cases per 100 000 live births) by 2030 *(8)*. To achieve these targets, the strategy on STIs (Chapter 6) highlights the importance of making it easier for people with STIs or at risk of STIs to access prevention, diagnosis, treatment and care.

1.2 Rationale for updating the STI treatment recommendations

Effective, accessible and affordable antimicrobial medication is imperative for managing gonorrhoea, chlamydia and syphilis infections. To address the evolving landscape of antimicrobial resistance (AMR) and antimicrobial susceptibility patterns, it is crucial to keep treatment guidelines up to date to ensure optimal therapeutic outcomes and to counter the escalating risk of AMR. For gonococcal infections in

particular, increased resistance to most antibiotics has been reported worldwide, raising concerns about the eventual development of untreatable gonococcal infections with serious sexual and reproductive health consequences *(4-6)*.

Antimicrobial resistance in *N. gonorrhoeae* has emerged for all medicines used for empirical first-line treatment. In 2019–2020, 20 out of 59 countries (34%) reported isolates with reduced susceptibility or resistance to ceftriaxone (up from 31% of reporting countries in 2017–2018) and 11 of 41 countries (27%) reported reduced susceptibility or resistance to cefixime (down from 47% in 2017–2018) *(9)*. Isolates with resistance to azithromycin were reported by 42 of 47 countries (89%; up from 84% in 2017–2018) and resistance to ciprofloxacin was reported by all 58 reporting countries (100%; also 100% in 2017–2018) *(9)*.[1]

The extended-spectrum cephalosporin, ceftriaxone, is the last option for empirical first-line gonorrhoea monotherapy in most countries. Sporadic treatment failures with the recommended dual therapy (ceftriaxone plus azithromycin), and ceftriaxone monotherapy in particular, have also been confirmed internationally *(6)*. Since 2015, the international spread of ceftriaxone-resistant gonococcal strains has been confirmed *(10)* and, in 2018, the first strain with ceftriaxone resistance plus high-level resistance to azithromycin was isolated in the United Kingdom of Great Britain and Northern Ireland and Australia *(11)*. Recently, the global transmission of *N. gonorrhoeae* strains linked to the high-level ceftriaxone-resistant FC428 clone, or those acquiring its primary ceftriaxone resistance factor (penA allele 60.001), has led to ceftriaxone treatment failures in several instances *(12)*. The actual level of AMR and treatment failure is mostly unknown, especially in lower-resource settings with the largest gonorrhoea burden; however, the pattern and proportion of resistant genotypes as recently evidenced in Cambodia may be indicative of the situation elsewhere *(13)*.

With increasing resistance to azithromycin and extended-spectrum cephalosporins *(6, 12)*, it is necessary to update these guidelines to reduce the risk of further development of AMR. The treatment recommendations for gonorrhoea must be updated urgently to reflect the actual AMR patterns, to delay the further development of resistance to cephalosporins and to include treatment options for cases of cephalosporin treatment failure.

For chlamydia, the updates to the treatment recommendations aim to highlight the efficacy of doxycycline, while reserving use of azithromycin for other infections, such as *Mycoplasma genitalium*.

There is also a need for clarity regarding the efficacy of treatment for syphilis infection, especially during pregnancy. Many countries have shown a preference for alternative treatments, instead of benzathine penicillin G. The updated recommendations in this guidance aim to clarify and highlight the effects of benzathine penicillin G and other treatment options. Additionally, the updated treatment recommendations aim to specifically address the management of pregnant women with syphilis who are allergic to penicillin, which is a critical area of concern.

1.3 Rationale for the new recommendations for syphilis testing and STI partner services

In recent years, there have been important innovations in both diagnostic technologies and service delivery of syphilis testing. WHO previously issued guidelines that addressed STI testing in 2003 *(14)*, and more recently (2017) issued detailed guidance on syphilis testing and diagnosis during pregnancy *(15)*. This has been further complemented by recent WHO guidance encouraging the use of dual HIV/syphilis rapid diagnostic tests (RDTs) among pregnant women and key populations (men who have sex with men, people who inject drugs, people in prisons and other closed settings, sex workers and transgender people), in 2019 and 2022 respectively *(16, 17)*, as well as the broader consolidated guidelines issued in 2021 on the management of symptomatic STIs *(18)*.

1 Additional reference: unpublished data from the WHO Global Antimicrobial Resistance Surveillance Programme (GASP) for *Neisseria gonorrhoeae* 2019–2020. These data will be published at: https://www.who.int/data/gho/data/themes/topics/who-gonococcal-amr-surveillance-programme-who-gasp

Considering the renewed global commitment to end syphilis and congenital syphilis as public health problems by 2030, it is critical to increase access to testing, including self-testing, that can provide rapid results and facilitate linkage to treatment and care services. Additionally, strategic testing approaches to support diagnosis of acute syphilis, such as the use of RDTs that detect both treponemal and non-treponemal antibodies, are needed where laboratory resources are limited.

Scale-up of effective and acceptable STI partner services is also essential as programmes need ways to prioritize and connect those most affected by STIs with the treatment and clinical care services they need to avoid complications of an untreated STI and to stop the chain of transmission. This can include identifying, locating and linking partners to STI services. STI partner services can prevent new and repeat infections, as well as treat existing infections, and thus help programmes focus their service delivery on those at greatest risk.

Currently, most services providers limit partner referral or management to passive notification of cases, such as when a health worker asks a patient with an STI to inform their sexual partner(s) about their exposure. Countries need guidance and innovative tools to help support strategic scale-up and prioritization of active partner notification, including offering patients a range of effective options based on the types of relationships they have with different sexual partners, as well as offering different options as appropriate for different populations and epidemiological settings.

To overcome these challenges and build on existing services, these guidelines present new evidence and recommendations on the use of treponemal/non-treponemal syphilis RDTs and syphilis self-testing, and STI partner services. Countries introducing these new recommendations may need to assess whether they have the required resources to scale up effective partner services, adapt national testing policies, and update policies relating to product regulation and registration, to ensure the availability of affordable quality-assured test kits.

1.4 Objectives

The objectives of these guidelines are:

- to provide evidence-informed guidance on treating infection with *N. gonorrhoeae and C. trachomatis,* and infection with *T. pallidum* (syphilis) during pregnancy;
- to provide new recommendations on syphilis testing, specifically on syphilis self-testing and the use of dual treponemal/non-treponemal RDTs;
- to provide new recommendations on STI partner services; and
- to support countries and national programmes in updating their national guidelines with a view to reaching the 2030 targets of the global health sector strategy on STIs.

1.5 Target audience

These guidelines are intended for STI prevention and control programme managers at the national level and for frontline health workers in primary, secondary and tertiary health facilities involved in diagnosing, treating and managing people with STIs. The recommendations and guidance are also important for health workers, including lay providers and community health workers, responsible for offering and performing STI partner services. These guidelines will be relevant for implementers of STI and HIV services (including providers of pre-exposure prophylaxis [PrEP] for HIV), sexual and reproductive health (SRH) services and maternal and child health (MCH) services. They will also be relevant to nongovernmental and community-based organizations, including those working with or led by key populations for the HIV epidemic. These guidelines can be used to support the planning, implementation, and monitoring and evaluation of such services, and can also be used as an advocacy tool in seeking the financial and human resources required to deliver adequate, acceptable and equitable STI services and care for everyone who needs them.

The recommendations are also important for persons with or at greater risk of acquiring STIs, including HIV, such as members of key populations, people who use PrEP for HIV, and other vulnerable population groups, such as pregnant women, adolescents in high HIV/STI burden settings, Indigenous populations, refugees and people in humanitarian settings.

1.6 Guiding principles

The following principles have informed the development of these guidelines and should guide the implementation of the recommendations.

- These guidelines will contribute to the achievement of key global goals, including the Sustainable Development Goals, and relevant national-level goals and targets.
- The guidelines are based on a public health approach to scaling up the provision of services and care for people with STIs, with the aim of reaching everyone, including vulnerable populations and key populations, with relevant interventions, including, for example, targeted screening for *N. gonorrhoeae* and antimicrobial resistance monitoring (in accordance with WHO guidance).
- The adaptation and implementation of the guidelines should be accompanied by efforts to promote and protect the human rights of people receiving STI services, including preventing stigma and discrimination, promoting gender equity, and ensuring that the use of services is always voluntary and never mandatory or coerced.
- The implementation of the recommendations in these guidelines should be informed by the local context, including the epidemiology of STIs, the availability of resources and commodities for diagnosis and treatment of STIs, the capacity of the health system and anticipated cost–effectiveness of the various interventions.
- The adaptability built into these guidelines is intended to promote accessibility, acceptability and effectiveness of STI services through public and private health-care systems, including at community health centres and other primary care facilities providing services for STIs, such as clinics for maternal and child health, antenatal care, family planning and other sexual and reproductive health services. As such, these guidelines should form part of a broader package of service-delivery approaches, including linkage to prevention, testing, treatment and care services.
- The guidelines provide direction for acceptable and effective STI services for populations identified as being especially vulnerable to or at higher risk of STIs, including those living with HIV infection, and aim to improve health outcomes at the population level.
- The guidelines also followed the guiding principles of the WHO Model List of Essential Medicines (known as the Essential Medicines List or EML), including to prevent the emergence and spread of antimicrobial resistance, as well as the principles of parsimony, feasibility and alignment with the WHO List of Critically Important Antimicrobials for Human Medicine, including the WHO Access, Watch and Reserve (AWaRe) antibiotic categorization *(19, 20)* (Table 1.1).

Table 1.1 The WHO Access, Watch and Reserve (AWaRe) antibiotic categorization

Access group	Watch group	Reserve group
• first or second choice antibiotics • offer the best therapeutic value, while minimizing the potential for resistance	• first or second choice antibiotics • only indicated for specific, limited number of infective syndromes • more prone to be a target of antibiotic resistance and thus prioritized as targets of stewardship programmes and monitoring	• "last resort" • highly selected patients (life-threatening infections due to multidrug-resistant bacteria) • closely monitored and prioritized as targets of stewardship programmes to ensure their continued effectiveness

Source: adapted from AWaRe – the WHO antibiotic categorization website *(20)*.

1.7 Structure of the guidelines

These guidelines are structured into three parts to provide evidence-informed recommendations for STI treatment, syphilis testing and partner services, respectively, which are intended to become subsections of the forthcoming edition of consolidated guidelines for the prevention, diagnosis, treatment and care of STIs.

The first section provides updated treatment recommendations, based on the most recent evidence, for the most important conditions caused by *N. gonorrhoeae*, *C. trachomatis* and *T. pallidum*; these are presented in Chapter 3. While these guidelines and recommendations provide direction for countries as they develop and update their national treatment guidelines and recommendations, countries should also consider the local pattern of antimicrobial resistance as well as health service capacity and resources. Recommendations were not updated for rare conditions and other conditions for which no new information has become available since the previous WHO treatment guidelines for these infections were published in 2016 and 2017 *(15, 21-23)*.

Treatment recommendations for the following conditions caused by *N. gonorrhoeae* are included in these guidelines:

- uncomplicated genital, anorectal and oropharyngeal infections; and
- infections that persist after treatment failure (retreatment).

Treatment recommendations for the following conditions caused by *C. trachomatis* are included in these guidelines:

- uncomplicated chlamydial infections (genital, anorectal and oropharyngeal); and
- uncomplicated chlamydial infections in pregnant and breastfeeding women.

Treatment recommendations for the following conditions caused by *T. pallidum* during pregnancy are included in these guidelines:

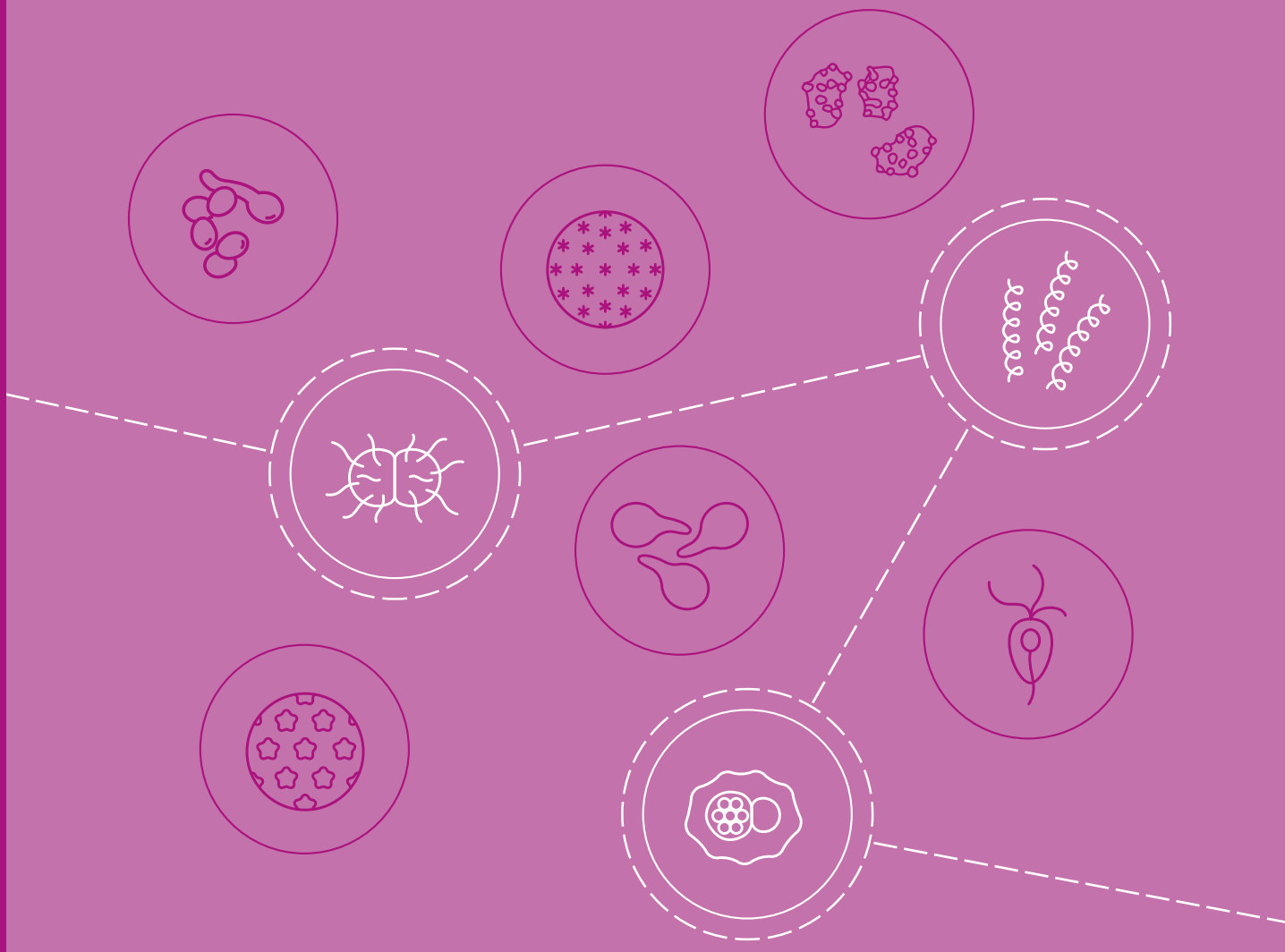
- early syphilis (primary, secondary and early latent syphilis of not more than two years' duration); and
- late syphilis (syphilis of more than two years' duration without evidence of treponemal infection), latent syphilis and syphilis infection of unknown duration.

The second section (presented in Chapter 4) focuses on syphilis testing services and adds to existing WHO recommendations for syphilis diagnosis *(15, 18)*. This includes summaries of evidence towards new recommendations and implementation considerations for the:

- use of dual treponemal/non-treponemal syphilis RDTs; and
- offer of syphilis self-testing as an additional syphilis testing approach.

The third and final section provides a new recommendation and updated guidance on STI partner services (presented in Chapter 5). This guidance adds to existing guidance that recommends partner services approaches across different disease areas *(16, 17, 24-28)*, providing further advice for STI programmes on the most efficient and effective approaches to consider for their settings.

2. Methods



2. Methods

2.1 Overview

These guidelines were developed in accordance with procedures in the *WHO handbook for guideline development (29)*.

In 2016, WHO published a series of three guideline documents for the treatment of *N. gonorrhoeae*, *C. trachomatis* and *T. pallidum*, and, in 2017, published another guideline on syphilis screening and treatment during pregnancy, taking into consideration the latest evidence available at the time. The four publications were:

- WHO guidelines for the treatment of *Neisseria gonorrhoeae (21)*
- WHO guidelines for the treatment of *Chlamydia trachomatis (22)*
- WHO guidelines for the treatment of *Treponema pallidum* (syphilis) *(23)*
- WHO guideline on syphilis screening and treatment for pregnant women *(15).*

Although some recommendations within these guidelines still remain current and relevant, the Guideline Development Group (GDG; see section 2.2) in 2020 identified key questions about treatment to be updated from these four previously published guidelines and new questions related to service delivery and syphilis testing. Systematic reviews were conducted or updated to develop evidence summaries for each key question and evidence was assessed according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach *(29)*.

The GDG updated the recommendations considering the certainty of evidence for the effects, the balance between desirable and undesirable effects, values and preferences, acceptability, feasibility and resource needs across a variety of settings. Information on each of these aspects was included in evidence-to-decision tables, which were shared in advance with the GDG members and used at the meetings to support the judgements of the GDG in making WHO recommendations. Consistent with previous WHO guidelines, these guidelines are based on a public health approach. Since there were updated recommendations that had an impact on other existing recommendations, these were edited for clarity and the revised wording has also been included in these guidelines.

The following sections provide further details on each aspect of the guideline development process.

2.2 Roles of groups involved in developing the guidelines

Five main groups were formed to guide and implement the guideline development process, coordinated by the WHO Secretariat. Each group played a specific role, as described below. Annex 1 lists the members of these groups and other contributors and their affiliations.

- **WHO Steering Committee.** This group, which is responsible for the overall coordination of the guideline development process, was led by the Department of Global HIV, Hepatitis and Sexually Transmitted Infections Programmes (HHS). Participants included WHO staff members from the HHS Department and from the Department of Sexual and Reproductive Health and Research, the Department of Surveillance, Prevention and Control and the Department of Access to Medicines and Health Products. The Steering Committee also included WHO technical staff members from every WHO region.

- **Guideline Development Group (GDG).** This group comprised non-United Nations/non-WHO experts, health professionals and representatives of groups most affected by the recommendations in the guidelines. The 34 GDG members formulated the WHO recommendations and good practice statements, including any implementation and service-delivery considerations. They also reviewed and approved the final content of these guidelines. The composition of the GDG represented all six WHO regions and was balanced across gender and backgrounds, including academia and research, programme implementation and policy and community organizations and networks. The group members were selected in coordination with the WHO Steering Committee and WHO country and regional offices. The Steering Committee reviewed curricula vitae, declarations of interests and confidentiality agreements. The proposed membership list was posted for public review and comment, and then finalized.
- **External Review Group (ERG).** The members were responsible for peer reviewing these guidelines, including the updated and new recommendations. This group was selected in consultation with the WHO Steering Committee to assure geographical and gender balance. It comprised 15 peer reviewers from academia, policy and research institutions, programme implementation and community organizations, and representatives of networks of key and vulnerable populations.
- **External evidence reviewers, led by a methodologist**. With oversight by the guideline methodologist and with input from members of the WHO Steering Committee and GDG, an independent team of external experts conducted systematic reviews of the effects of interventions based on the selected key questions for the guidelines. In addition, evidence on values and preferences, feasibility and cost–effectiveness was compiled and summarized for each question.
- **External observers**. Representatives of the Global Antibiotic Research and Development Partnership (GARDP), Unitaid, the United Nations Population Fund (UNFPA) and the United States Centers for Disease Control and Prevention (CDC) attended the GDG meeting as observers. These organizations have a long history of collaboration with WHO's HHS Department.

All members of the GDG, ERG and other non-WHO staff participating in the meetings and/or other guideline development processes submitted declaration of interests forms and confidentiality statements to WHO. All of the declarations were reviewed by WHO and no conflicts of interest sufficient to preclude any GDG member from participating fully in the development of the guidelines were found. Annex 2 provides a full compilation and a summary of the declarations of interests.

2.3 Scope and key questions

In December 2013, the first GDG meeting was held to identify and agree on the key questions of potential importance for these guidelines, including specification of the population, intervention, comparator(s) and outcome(s) (PICO questions). Following this meeting, a survey of GDG members was conducted to set priorities among the selected questions and outcomes of interest, based on clinical relevance and importance.

PICO questions were prioritized if they pertained to adults and other special populations: adolescents, pregnant women, people living with HIV and populations disproportionately affected by STIs, including key populations. The GDG also agreed to prioritize treatment questions related to gonorrhoea, chlamydia and syphilis.

In 2016–2017, the four WHO guideline documents were published, as listed in section 2.1 *(15, 21-23)*. However, in 2020, with increasing resistance to azithromycin and extended-spectrum cephalosporins, and the inappropriate treatment of maternal syphilis to prevent congenital syphilis (i.e. inappropriate or non-optimal choice of drug, dose, regimen), the need to review the recommendations was considered. In September 2020, the GDG agreed to update treatment recommendations for gonorrhoea, chlamydia and syphilis.

Subsequently, PICO questions were developed to determine whether:

1. increased doses in single or dual therapy (compared with the 2016 WHO treatment recommendations on *N. gonorrhoeae*) should be used for adults and adolescents with uncomplicated genital, anorectal or oropharyngeal gonococcal infections;
2. multi-dose doxycycline (compared with single-dose azithromycin as recommended in the 2016 WHO treatment recommendations on *C. trachomatis*) should be used for adults and adolescents with uncomplicated genital, anorectal or oropharyngeal chlamydial infections; and
3. other antibiotics (compared with benzathine penicillin as recommended in the 2016 WHO treatment guidelines on syphilis) should be used for pregnant women with early or late syphilis.

The critical and important outcomes identified for the 2016–2017 guidelines were used again for these new guidelines: microbiological cure and adverse effects (including maternal and fetal effects).

To assess the need for the new edition of the guidelines to include recommendations relating to STI testing and partner services (see Glossary), the WHO Secretariat convened scoping meetings in 2021 with the WHO Steering Committee. Based on the outcomes of these meetings, and in consultation with the GDG members, a PICO question for STI partner services was finalized and new PICO questions for the use of dual treponemal and non-treponemal rapid diagnostic tests (RDTs) and syphilis self-testing within testing strategies were developed. Given that these were new questions, the GDG identified outcomes that were rated by importance in an electronic survey according to the GRADE suggested rating scale of 1–9 (0–3: not important; 4–6: important; 7–9: critical) *(29)*.

The PICO components of all PICO questions addressed in these guidelines are provided in Table 2.1.

Table 2.1 Population, intervention, comparator and outcome (PICO) components of all PICO questions prioritized for these guidelines

	Population	Intervention	Comparator(s)	Critical outcomes
Updates to existing treatment recommendations				
***Neisseria gonorrhoeae* treatment**	Adults and adolescents (including pregnant women) with uncomplicated genital, anorectal or oropharyngeal gonococcal infections	Increased doses in single or dual therapy	2016 WHO recommended treatments *(21)*	Microbiological cure Adverse effects (including maternal and fetal effects)
***Chlamydia trachomatis* treatment**	Adults and adolescents with uncomplicated genital, anorectal or oropharyngeal chlamydial infections	Multi-dose doxycycline	Single-dose azithromycin	Microbiological cure Adverse effects (including maternal and fetal effects)
***Treponema pallidum* treatment**	Pregnant women with early or late syphilis	Other antibiotics	Benzathine penicillin and procaine penicillin	Microbiological cure Adverse effects (including maternal and fetal effects)

	Population	Intervention	Comparator(s)	Critical outcomes
New recommendations on testing and partner services				
Dual treponemal/ non-treponemal rapid diagnostic tests (T/NT RDTs)	Population receiving syphilis testing	Syphilis testing services with dual T/NT RDTs	Standard laboratory-based syphilis testing services without dual T/NT RDTs or no intervention	Test accuracy Usability Feasibility Uptake Acceptability Appropriate treatment following testing
Syphilis self-testing	Population receiving syphilis testing	Syphilis testing services that include the option for self-testing	Standard laboratory-based syphilis testing or no intervention	Test accuracy Usability Uptake Reactivity Linkage to confirmatory testing, treatment or other sexual health services Social harm or adverse events
STI partner services	Population receiving STI testing or screening	STI testing services that include any partner services approach	STI testing services that include standard testing, different partner service methods or no intervention related to partners	Reinfection in index patient Partners elicited Partners notified Partners presenting for testing and care Partners testing positive Partners treated Social harm or adverse events

*RDT: ra*pid diagnostic test; STI: sexually transmitted infection; T/NT: treponemal/non-treponemal.

2.4 Review of the evidence

Comprehensive searches were conducted to gather existing systematic reviews, including those conducted for the previous WHO guidelines, and to gather randomized and non-randomized studies addressing the benefits and harms, the values and preferences of service users, resource use, acceptability, equity and feasibility of the interventions. The searches were performed from the date of the last search conducted for each of the previous treatment guidelines up to August 2023. Detailed methods of the systematic reviews are available for the updated recommendations for gonorrhoea (Web Annex A), chlamydia (Web Annex B) and syphilis (Web Annex C).

The literature search for dual treponemal and non-treponemal syphilis testing was performed from 2010 to July 2022 (Web Annex D); for syphilis self-testing, from 2000 to October 2022 (Web Annex E); and for STI partner services up to February 2020 (Web Annex F). These searches encompassed studies that reported on values and preferences, costs, feasibility, acceptability and equity.

Since there were limited data directly comparing dual treponemal/non-treponemal RDTs with standard laboratory-based serologic tests for syphilis, and limited data comparing their effects on important outcomes, a modelling study was conducted to provide evidence (see Web Annex D).

Evidence for the effects of interventions was synthesized statistically when possible, and was assessed using the GRADE approach based on the domains for risk of bias, inconsistency, indirectness, imprecision, publication bias, effect size, dose response and opposing confounding *(29)*.

Certainty of the evidence for effects was assigned to one of the four grades of evidence defined by the GRADE Working Group:

- High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
- Moderate certainty: We are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- Low certainty: Our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
- Very low certainty: We have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

Evidence summary-of-findings tables (also called evidence profiles) and the evidence-to-decision frameworks (i.e. tables to facilitate decision-making for the updated recommendations) were drafted in advance of the GDG meeting using the GRADEpro software *(30)* (see the first section of Web Annexes A–F for the evidence-to-decision frameworks for each recommendation).

2.5 Making recommendations

A virtual GDG meeting was held in November 2022 to support the development of updated and new recommendations. The GDG reviewed the tables in the evidence-to-decision frameworks and evidence profiles and made judgements about the effects of treatment. Based on the discussions, the GDG made decisions on whether to make strong or conditional recommendations (see descriptions below) for or against an intervention. The GDG members arrived at agreement by consensus and so there was no need for voting. The recommendations and evidence-to-decision frameworks were finalized electronically via email and presented during a follow-up GDG meeting on 30 May 2023.

According to the GRADE approach, the strength of each recommendation was rated as either strong or conditional. The strength of the recommendations reflects the degree of confidence of the GDG that the desirable consequences (e.g. beneficial health outcomes) of the recommendations outweigh the undesirable consequences (e.g. adverse effects) and takes into account other criteria, such as resources, acceptability, equity and feasibility. According to this assessment, the strength of recommendations is graded into two categories:

1. A strong recommendation is one for which the GDG was confident that the desirable consequences of adhering to the recommendation outweigh the undesirable consequences.
2. A conditional recommendation is one for which the GDG concluded that the desirable consequences of adhering to the recommendation probably outweigh the undesirable consequences but was not confident about these trade-offs *(29)*.

Table 2.2 explains the implications of the differing strengths of recommendations for patients, clinicians and policy-makers.

Good practice statements were made when the GDG agreed that it was necessary to provide guidance but a review of the literature was not warranted because the balance of desirable and undesirable consequences of an intervention was unequivocal and no other criteria would lead to a different assessment. Remarks were added to the recommendations or good practice statements to explain the recommendation and/or describe any relevant conditions. Implementation considerations were added to provide further information for the possible application of the recommendation.

WHO then drafted the full guidelines and circulated them electronically to the WHO Steering Committee, the GDG and the ERG for comments and feedback in September 2023. All the input was then considered and addressed as appropriate in the revised draft, followed by submission to the WHO Guidelines Review Committee for approval. Final editing prior to publication did not affect the recommendations that had been formulated.

Table 2.2 Implications of differing strengths of GRADE recommendations

Implications	Strong recommendation WHO recommends…	Conditional recommendation WHO suggests…
For patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guidelines could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Clinicians should recognize that different choices will be appropriate for each individual, and that clinicians must help each individual arrive at a management decision consistent with the individual's values and preferences. Decision aids may be useful to help individuals make decisions consistent with their values and preferences.
For policy-makers	The recommendation can be adopted as policy in most situations.	Policy-making will require substantial debate and the involvement of various stakeholders.

GRADE: Grading of Recommendations Assessment, Development and Evaluation.

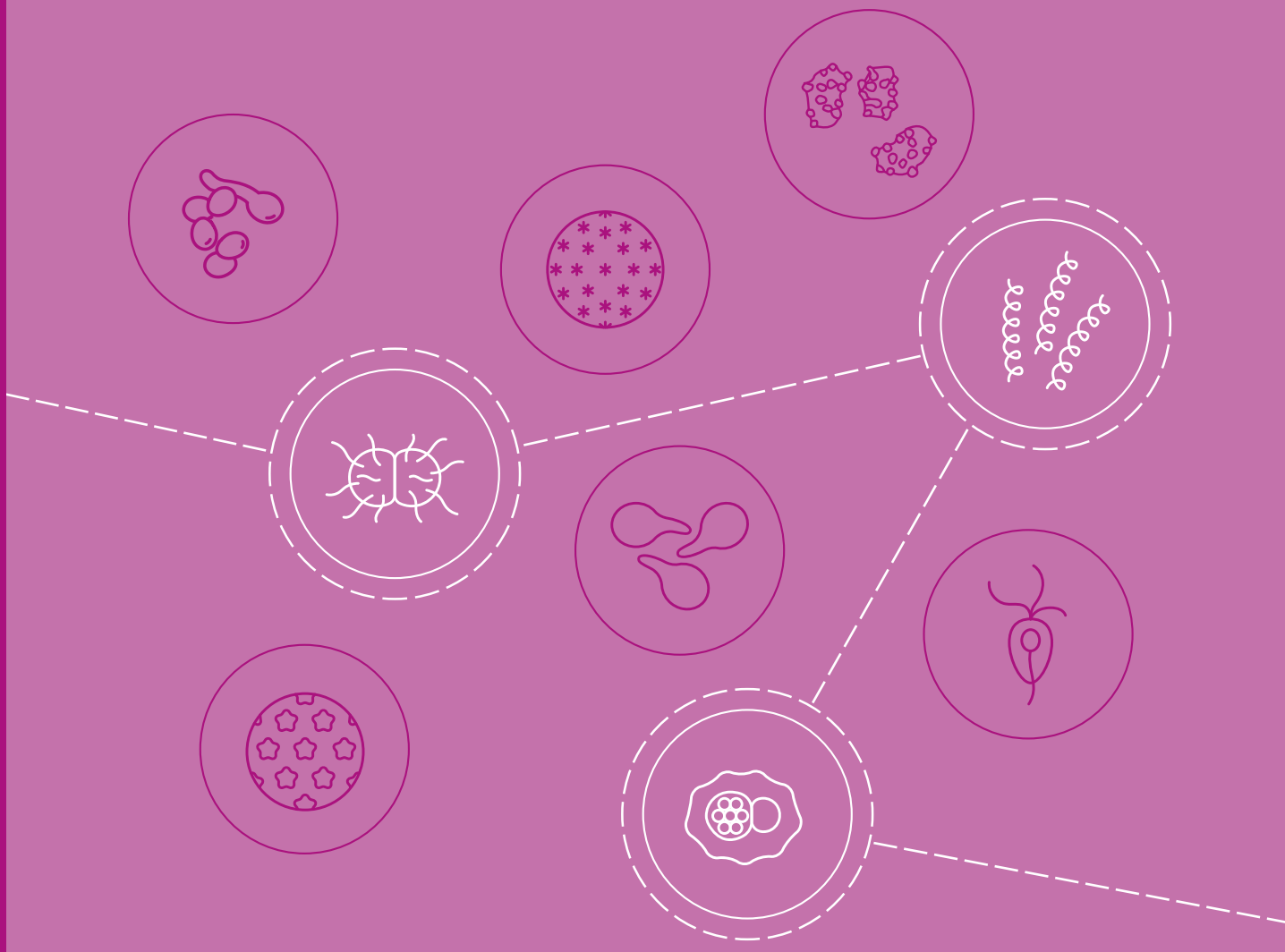
Source: WHO, 2014 *(29)*.

2.6 Managing conflicts of interest

Managing conflicts of interest was a key priority throughout the process of developing the guidelines. WHO guidelines for declaration of interests (DOI) by WHO experts were implemented. DOI statements were obtained from all members of the GDG and the ERG before they assumed their roles. At the beginning of the GDG meetings, including subgroup meetings, the members disclosed their declared interests and any new ones. The DOI statements are summarized in Annex 2.

Eleven members of the GDG declared interests. One member was excluded from discussions related to treatment of *N. gonorrhoeae* because they were involved in a study on that subject. Others were approved for full participation in all discussions as the declared conflict of interest was not related to treatment for *N. gonorrhoeae*, *C. trachomatis* or *T. pallidum*, or related diagnostics.

3. Updated treatment recommendations



3. Updated treatment recommendations

This section provides treatment recommendations and good practice statements for specific conditions caused by *N. gonorrhoeae, C. trachomatis* and *T. pallidum*. The recommendations for treating gonococcal and chlamydial infections (sections 3.1 and 3.2) apply to all adults and adolescents, including during pregnancy, and including people living with HIV and key populations (see Glossary). A separate recommendation on treating uncomplicated chlamydial infections applies specifically to pregnant and breastfeeding women. The updated treatment recommendations for syphilis infections (section 3.3) apply only to pregnant and breastfeeding women.

3.1 Treatment of gonococcal infections

The following recommendations apply to adults and adolescents, including during pregnancy, and including people living with HIV and key populations.

Good practice statement on treatment of gonococcal infections (updated 2023)

WHO recommends that national or local antimicrobial resistance data should determine the choice of therapy when available.

Recommendation on treatment of gonococcal infections (updated 2023)

For adults and adolescents (including pregnant women) with genital, anorectal and/or oropharyngeal gonococcal infections, **WHO suggests:**

- ceftriaxone 1 g intramuscularly as a single dose.

If ceftriaxone is not available or refused, **WHO suggests:**

- cefixime 800 mg orally and performing test of cure.

If test of cure is not possible or when oropharyngeal infection is diagnosed or is a potential concern, **WHO suggests:**

- cefixime 800 mg orally plus azithromycin 2 g orally.

When resistance, allergy or availability of cephalosporins is a concern, **WHO suggests** one of the following options:

- spectinomycin 2 g intramuscularly as a single dose plus azithromycin 2 g orally; or
- gentamicin 240 mg intramuscularly as a single dose plus azithromycin 2 g orally.

Conditional recommendation, low certainty in evidence of effects

Remarks:

- Ceftriaxone 1 g intramuscularly may be painful; discuss with the individual the option of using lidocaine as diluent with the injection.
- Azithromycin 2 g may cause gastrointestinal side-effects, especially on an empty stomach. To reduce side-effects, consider azithromycin 1 g taken at 6- to 12-hour intervals.
- Sexual abstinence, condom use and partner treatment should be discussed.
- WHO guidance on surveillance of antimicrobial resistance in *N. gonorrhoeae* and test of cure is available *(31)*.
- Pregnant women should be closely monitored for adverse reactions (e.g. allergic reactions including anaphylactic shock, premature delivery and premature rupture of membranes).

3.1.1 Genital, anorectal and oropharyngeal gonococcal infections

Rationale for making the recommendations

The evidence for moderate benefits and negligible harm of higher doses of ceftriaxone and cefixime mainly comes from non-comparative studies conducted before changes in resistance, and therefore the certainty is low. Surveillance data indicate a possible decrease in resistance to ceftriaxone and cefixime in some countries and a possible increase in others, while they also indicate increasing resistance to azithromycin globally. Pharmacodynamic data suggest that ceftriaxone 1 g could eradicate most strains (except highly resistant strains causing oropharyngeal infections). Because evidence found fewer cures with cefixime (even at 800 mg), a test of cure could be performed to ensure cure, or – if not possible – combining therapy with a higher dose of azithromycin (2 g) may ensure cure. Therefore, the GDG increased the dose of ceftriaxone to 1 g without azithromycin; the dose of cefixime was increased to 800 mg (with or without azithromycin depending on whether a test of cure is performed), and the dose of spectinomycin and gentamicin were unchanged with the addition of azithromycin 2 g to ensure cure.

Summary of the evidence

Effects

Overall, the certainty of evidence for the effects of treatment on gonococcal infections is low, due to most studies not being recent, changes in antimicrobial resistance and small sample sizes in comparative studies. The evidence-to-decision framework in Web Annex A provides a detailed description of the evidence summarized below, with references. In the updated systematic review of the literature, there were 15 new studies (3 randomized controlled trials [RCTs] and 12 non-randomized and non-comparative studies) in addition to the 41 studies reviewed in 2016 (see Web Annex A). The studies primarily involved individuals with confirmed gonorrhoea. Higher doses of ceftriaxone or cefixime may result in slightly greater cure rates (1–3 percentage points more), but cefixime may provide fewer cures. Combining ceftriaxone with azithromycin (dual therapy) probably does not increase cures. Data from systematic reviews of the literature and from the WHO Gonococcal Antimicrobial Surveillance Programme (GASP) found that ceftriaxone resistance is increasing in most countries, except in Europe, where introducing a ceftriaxone 500 mg dose in 2013 and subsequently increasing to ceftriaxone 1 g was associated with a decrease in reported ceftriaxone resistance *(6, 9, 12, 32)*. Treatment failure after use of ceftriaxone and azithromycin dual therapy is increasingly being reported globally, and there are indications that the determinants of ceftriaxone antimicrobial resistance are spreading. Pharmacodynamic data suggest that ceftriaxone 1 g could eradicate most strains except oropharyngeal infections caused by highly resistant strains. Providing ceftriaxone 1 g will cure most cases of gonorrhoea, thus delaying the emergence and spread of multi-drug resistance and particularly ceftriaxone resistance. The evidence was inconsistent regarding undesirable effects and did not show a pattern of greater adverse events with higher doses of ceftriaxone or cefixime. However, higher doses of intramuscular ceftriaxone may be more painful, and azithromycin 2 g can result in gastrointestinal side-effects, especially when taken on an empty stomach.

Values and preferences

Although no studies assessing patient values were found, the Guideline Development Group (GDG) agreed that reducing treatment failures to reduce the spread of *N. gonorrhoeae* and prevent resistant strains was more highly valued than reducing adverse effects. The GDG also noted that ceftriaxone 1 g intramuscularly is painful and potentially less acceptable, and some individuals may prefer to use lidocaine to mitigate the pain. To reduce the gastrointestinal side-effects, azithromycin can be taken in two divided doses at 6- to 12-hour intervals. In many countries, clinicians are already providing ceftriaxone 500 mg or 1 g, and ceftriaxone 1 g ampules are available in most countries.

Costs and feasibility

Evidence for cost-effectiveness was also compiled, but these models were unlikely to account for changing antimicrobial resistance. The cost differences between lower and higher doses of ceftriaxone or cefixime are likely to be negligible since the packages dispensed typically include higher/more doses than needed. Moreover, higher doses are already provided in many countries, indicating feasibility of use.

3.1.2 Gonococcal infections after treatment failure

Good practice statement on retreating gonococcal infections after treatment failure (new 2023)

For adults and adolescents (including pregnant women) with gonococcal infections for whom treatment has failed as evidenced by persistent symptoms or a positive test of gonococcal infection, **WHO recommends** that the possibility of reinfection or antimicrobial resistance be considered to determine the choice of therapy.

Recommendation on retreating gonococcal infections after treatment failure (updated 2023)

If treatment failure occurred after a non-WHO-recommended treatment, **WHO suggests** retreating with a WHO-recommended therapy.

If reinfection is suspected, **WHO suggests** retreating with a WHO-recommended therapy, reinforcing the need for sexual abstinence, condom use and partner treatment.

If treatment failure occurred and antimicrobial susceptibility testing data are available, **WHO suggests** retreating according to susceptibility profile.

If treatment failure occurred after a WHO-recommended therapy and reinfection is assessed to be unlikely, **WHO suggests** retreating with a regimen not used previously from one of the following options and performing test of cure:

- ceftriaxone 1 g intramuscularly as a single dose plus azithromycin 2 g orally, only if ceftriaxone was not used previously;
- spectinomycin 2 g intramuscularly as a single dose plus azithromycin 2 g orally; or
- gentamicin 240 mg intramuscularly as a single dose plus azithromycin 2 g orally.

Conditional recommendation, very low certainty in evidence of effects

Remark:

- Retreatment should not be delayed. If an individual does not respond to these treatment failure recommendations, refer the individual to a specialist for further assessment and management.

Rationale for making the recommendations

As indicated in the summary of the evidence for the recommendations for treatment of gonococcal infections (in section 3.1.1) and also in Web Annex A, azithromycin resistance is increasing, and doses higher than azithromycin 1 g may therefore be more effective. The GDG also agreed that adding azithromycin to treatment for men who have sex with men may delay the spread of ceftriaxone resistance. The GDG therefore agreed that treatment should be built on the recommendations for treating gonococcal infections, including ceftriaxone and alternative options, but that azithromycin 2 g should be added. In addition, these recommendations were edited to align with the recommendations for the initial treatment of genital, anorectal and oropharyngeal gonococcal infections (in section 3.1.1).

Summary of the evidence

Effects

Overall, the certainty of the evidence in effects is very low. No new evidence was found with which to update the literature review for this question, and therefore the same evidence used to develop the 2016 recommendations was used. There were 34 randomized and non-randomized studies that evaluated a single treatment or many treatments and then reported on retreatment of individual cases of treatment failure. No studies specifically recruited people who had treatment failure. Most studies gave reports regarding cases of treatment failure or reinfection (often not distinguished from each other). These studies also reported the medicine used for initial treatment and the medicine used for retreatment and sometimes reported whether or not the case was cured. Cure rates for different medicines were not consistent across the studies. Case reports of treatment failure indicated cure was achieved by increasing dosages of ceftriaxone to 1 g and azithromycin to 2 g.

3.2 Treatment of chlamydial infections

The following recommendations apply to adults and adolescents, including people living with HIV and key populations. Separate recommendations are provided specifically for pregnant and breastfeeding women.

3.2.1 Uncomplicated chlamydial infections (genital, anorectal and oropharyngeal)

Recommendation on treatment of chlamydial infections (updated 2023)

For adults and adolescents with uncomplicated chlamydial infections (genital, anorectal and/or oropharyngeal), **WHO suggests:**

- doxycycline 100 mg orally twice a day for 7 days.

If doxycycline is not available or adherence to multiple doses is a serious concern, **WHO suggests:**

- azithromycin 1 g orally as a single dose.

If doxycycline and azithromycin are not available, **WHO suggests** one of the following options:

- erythromycin 500 mg orally four times a day for 7 days;
- ofloxacin 200–400 mg orally twice a day for 7 days; or
- tetracycline 500 mg orally four times a day for 7 days.

Conditional recommendation, moderate certainty in evidence of effects

Remarks:

- Doxycycline extended release (ER) may be an alternative to twice daily dosing of doxycycline, but the high cost may prohibit its use.
- If using an alternative treatment for gonococcal infection (cefixime 800 mg plus azithromycin 2 g), maintain the 2 g dosage of azithromycin to cover chlamydial infection.
- Note that doxycycline, tetracycline and ofloxacin are contraindicated in pregnant and breastfeeding women (see separate recommendations for pregnant and breastfeeding women).

Recommendations on treatment of chlamydial infections in pregnant and breastfeeding women (edited 2023)

For pregnant and breastfeeding women with uncomplicated chlamydial infection, **WHO recommends:**

- azithromycin 1 g orally as a single dose.

Strong recommendation, moderate certainty in evidence of effects

When azithromycin is not available, **WHO suggests** one of the following options:

- amoxicillin 500 mg orally three times a day for 7 days; or
- erythromycin 500 mg orally four times a day for 7 days.

Conditional recommendation, low certainty in evidence of effects

Remark:

- If using an alternative treatment for gonococcal infection (cefixime 800 mg plus azithromycin 2 g), maintain the 2 g dosage of azithromycin to cover chlamydial infection.

Rationale for making the recommendations

While it was generally agreed that use of either medicine is feasible, the GDG emphasized the need for special consideration in addressing the concerns of adolescent girls and other vulnerable populations. Overall, the recommendation for the primary treatment for adults and adolescents for uncomplicated genital chlamydial infections was changed to doxycycline instead of azithromycin, making it similar to recommendations for anorectal or oropharyngeal chlamydial infections, and therefore all recommendations were combined.

The GDG did not identify the recommendation for pregnant and breastfeeding women as needing an update. In 2017, an updated Cochrane systematic review was published on this topic with a literature search including publications up to June 2017 and no new RCTs comparing different medications were found at that time. The GDG agreed that the recommendations for pregnant and breastfeeding women did not need to be revised but instead could be edited to align with the format and language of the recommendation for adults and adolescents, and therefore the edited recommendation is presented here.

Summary of the evidence

Effects

Overall, the certainty of evidence in adults and adolescents for the effects of azithromycin compared with doxycycline for chlamydial infections is moderate. A Cochrane systematic review was updated to include evidence published up to August 2023 *(33)*, but no additional studies were found that met the eligibility criteria (Web Annex B). The 11 RCTs found similar cure rates with both medicines (92.5% with azithromycin and 94.4% with doxycycline) and similar rates of adverse events (18% with azithromycin and 21.8% with doxycycline).

Although, there are minor differences between benefits and harms of the different medication regimens, the GDG agreed that there may be greater harm when using azithromycin. There is increasing resistance in *N. gonorrhoeae* to azithromycin (see section 3.1). Continued use of azithromycin will select for strains with increased resistance. A systematic review of 59 studies found that the prevalence of mutations linked to macrolide resistance rose from 10% to 51% between the years prior to 2010 and the years 2016–2017 in *Mycoplasma genitalium (34)*. There are limited treatment options for *M. genitalium*, therefore there is a need to conserve the use of azithromycin for treatment of *M. genitalium*. Moreover, research has shown that doxycycline may have the added benefit of reducing the bacterial load of *M. genitalium* before administering azithromycin *(35)*.

Costs, feasibility and equity

Estimations of costs were based on dosing and pre-packaging, which may vary across countries, and cost-effectiveness likely depends on the prevalence of chlamydia. Equity issues in treatment distribution were explored, with some studies pointing to gender-related treatment disparities. A systematic review found that simpler medication regimens (e.g. single-dose azithromycin) may improve adherence *(36)*. However, a comparison of studies indicates similar cure rates between the azithromycin and doxycycline, even in cases of potential non-adherence. The importance of sexual abstinence during treatment to prevent reinfection was noted, particularly for azithromycin (which is a single-dose treatment); however, evidence supporting this is lacking. In summary, although both medication regimens have similar costs, and are acceptable and feasible, the GDG agreed that the benefits of doxycycline outweigh the benefits of azithromycin for chlamydia treatment, when considering the growing resistance to azithromycin.

3.3 Treatment of *Treponema pallidum* (syphilis) during pregnancy

The following recommendations apply to pregnant women, and differ based on the duration of infection. This includes early syphilis (primary, secondary and early latent syphilis of not more than two years' duration), late syphilis (late latent and tertiary syphilis of more than two years' duration without evidence of treponemal infection) or unknown duration of syphilis infection.

3.3.1 Syphilis (early and late) in pregnant women

Recommendations for treatment of early syphilis in pregnant women (updated 2023)

In pregnant women with early syphilis, **WHO recommends:**

- benzathine penicillin G 2.4 million units once intramuscularly.

Strong recommendation, very low certainty in evidence of effects

If benzathine penicillin is not available, **WHO suggests:**

- procaine penicillin 1.2 million units intramuscularly once daily for 10 days.

In **rare situations** when benzathine or procaine penicillin cannot be used (e.g. due to confirmed penicillin allergy, which occurs in less than 3% of the population, and where penicillin desensitization is not possible) or are not available (e.g. due to stock-outs), **WHO suggests** one of the following options with caution and enhanced follow-up:

- ceftriaxone 1 g intramuscularly once daily for 10–14 days; or
- erythromycin 500 mg orally four times daily for 14 days.

Conditional recommendation, very low certainty in evidence of effects

Remarks:

- If the stage of syphilis is unknown, follow recommendations for pregnant women with late syphilis.
- Although erythromycin treats the pregnant woman, it does not cross the placental barrier completely and as a result the fetus is not treated. It is therefore necessary to treat the newborn infant soon after delivery (see recommendations in the WHO guidelines referring to congenital syphilis *[15, 23]*).
- Doxycycline is contraindicated during pregnancy.

Recommendations for treatment of late syphilis or unknown duration of infection in pregnant women (updated 2023)

In pregnant women with late syphilis or an unknown duration of infection, **WHO recommends:**

- benzathine penicillin G 2.4 million units intramuscularly once weekly for three consecutive weeks.

Strong recommendation, very low certainty in evidence of effects

Remark:

- The interval between consecutive doses of benzathine penicillin G should not exceed 14 days.

If benzathine penicillin is not available, **WHO suggests:**

- procaine penicillin 1.2 million units intramuscularly once daily for 20 days.

In **rare situations** when benzathine or procaine penicillin cannot be used (e.g. due to confirmed penicillin allergy, which occurs in less than 3% of the population, and where penicillin desensitization is not possible) or are not available (e.g. due to stock-outs), **WHO suggests** using, with caution and enhanced follow-up:

- erythromycin 500 mg orally four times daily for 30 days.

Conditional recommendation, very low certainty in evidence of effects

Remarks:

- Although erythromycin treats the pregnant woman, it does not cross the placental barrier completely and as a result the fetus is not treated. It is therefore necessary to treat the newborn infant soon after delivery (see recommendations in the WHO guidelines referring to congenital syphilis *[15, 23]*).
- Doxycycline is contraindicated during pregnancy.

Rationale for making the recommendations

Penicillin continues to be the treatment with the greatest benefits compared with other antibiotics used for syphilis during pregnancy, and while there is little data for azithromycin the available data indicate that this treatment has the greatest potential for harm. There continue to be concerns about penicillin allergy, but it is likely that fewer than 3% of pregnant women are allergic to penicillin. The GDG therefore emphasized the need for increased public awareness about the low risk of penicillin allergy and that alternatives only rarely need to be used. Overall, the recommendations for penicillin use were not changed, but edits were made to delete azithromycin as an alternative and to emphasize the low risk of penicillin allergy.

Summary of the evidence

Effects

Overall, the certainty of evidence for the effects of treatment for syphilis during pregnancy is very low. The evidence-to-decision framework in Web Annex C provides a detailed description of the evidence summarized below, and includes all the references. Since the systematic review was conducted for the previous WHO treatment guidelines published in 2016, six non-randomized comparative studies comparing benzathine penicillin G with other antibiotics, two non-randomized trials comparing amoxicillin versus azithromycin, and three single-arm studies of non-penicillin antibiotics have been published (Web Annex C). As most studies did not report whether pregnant women had early or late syphilis, the evidence from these studies could not be separated for analysis as the basis for making the recommendations. The majority of the data (representing over 5000 participants) are from studies assessing penicillin and prevention of transmission of syphilis to babies, with reported effectiveness ranging from 96% to 100%. There is less data for erythromycin (about 70 participants) and ceftriaxone (about 30 participants), showing 96% and 70% effectiveness at preventing transmission, respectively. There is a very small amount of data for the use of azithromycin: in all five participants vertical transmission occurred, which may be because azithromycin does not cross the placental barrier. Adverse events may also be similar across medication regimens, although azithromycin likely results in greater adverse events. While both benzathine penicillin G (benzathine benzylpenicillin) and procaine penicillin (procaine benzylpenicillin) are categorized as "Access" on the WHO AWaRe list, the alternative treatments, such as azithromycin, are typically categorized as "Watch" (see Table 1.1 in section 1.6) *(19, 20)*.

Concerns were raised about penicillin allergy, but a review found that while allergic responses are often reported (ranging from 6% to 25% across various treatment populations), only a small proportion of pregnant women, or indeed of people in general (likely less than 3%), truly has a penicillin allergy *(37)*. In the absence of benzathine penicillin G, use procaine penicillin; this would provide greater benefits than other antibiotics since it can cross both the placental and blood–brain barriers.

Costs, feasibility and equity

Costs and feasibility are probably similar across medication regimens. Estimates of the costs of both medicines were based on the UNICEF Supply Catalogue and judged to be similar *(38)*. Three studies explored equity issues in different contexts, including barriers to immediate treatment due to lack of awareness and concerns about adverse reactions.

3.4 Implementation considerations

3.4.1 Adapting, implementing and monitoring

These guidelines provide recommendations for treatment of gonorrhoea, chlamydia and syphilis based on the best available evidence at the time of compilation. However, the epidemiology and the patterns of AMR vary geographically and need to be monitored, in particular for *N. gonorrhoeae*. In areas lacking local, national or regional data as a basis for adaptation, the recommendations in these guidelines can be adopted as presented since they have been assessed globally before being included in these guidelines and were developed with a view to being applicable to most settings.

When the guidelines are adapted for national use, the STI medication regimens that are included should have an efficacy of at least 95% and should also meet as many of the other criteria listed in Box 3.1 as possible. The selected medicines also need to be locally available, and the competencies and experience of local health workers should be considered.

Box 3.1 Criteria for selecting medicines for treating STIs to include in national guidelines

- High efficacy (at least 95% cure rate)
- High quality (potent active ingredient)
- Low cost
- Low toxicity levels
- Organism resistance unlikely to develop or likely to be delayed
- Single-dose regimen
- Oral administration
- Not contraindicated for pregnant or lactating women

Appropriate medicines should also be included in national lists of essential medicines.

3.4.2 Identifying and procuring STI medicines

Identifying the medicines that will be recommended as first-line treatment for STIs is important but so are the estimated quantities of the medicines that will be required. Quantifying medicine needs is an important part of estimating costs, to reconcile financial requirements with the available budget. Budgeting appropriately for medicines is critical. If the national health ministry does not provide medicines without user charges and the people who need the medicines cannot afford them, then there will essentially be no way to curtail the spread of infection and the occurrence of complications, which put more strain on the health system and national economy. Decision-makers, politicians and fiscal controllers at the national level should therefore understand the need to subsidize STI medicines.

Estimation of quantities is also key information as a basis for placing advance orders of medicines, with a view to minimizing the unit and freight costs. Estimating the quantity of medicines needed requires reviewing the recommended medicines, their unit prices, the quantity required per treatment and the epidemiological information on the prevalence of infection. Medicine needs can be estimated by multiplying the estimated number of cases by the average quantity of medicine required for treating one case. These figures can be derived from health centres providing care but must be verified to avoid waste caused by excessive ordering (considering the limitations of shelf life and storage requirements).

Low-cost STI medicines can be obtained through international vendors of generic products and non-profit organizations with procurement schemes such as UNICEF, UNFPA and the United Nations High Commissioner for Refugees (UNHCR). In addition, through joint medicine procurement schemes, national programmes from two or more countries can agree to jointly procure medicines, thus reducing the overall costs by sharing the overhead costs and taking advantage of discounts for purchasing in bulk.

Placing STI medicines on national lists of essential medicines increases the likelihood of achieving a supply of these medicines at low cost.

3.4.3 STI services for key populations

Adaptation and implementation of these guidelines should be accompanied by efforts to promote and protect the human rights of people who need services for STI care. This includes ensuring that stigma and discrimination are prevented in providing such services, while promoting gender equity, and ensuring that the use of services is voluntary. As key populations are disproportionately affected by STIs, it is critical to increase access to STI services, including treatment for specific STIs, for people living with HIV and key populations. Recommendations and guidance are provided in WHO's 2022 *Consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment and care for key populations (17)*. In addition, the following WHO guidance documents provide additional implementation considerations for increasing access to and effectively delivering STI services for key populations.

- *Implementing comprehensive HIV and STI programmes with sex workers: practical approaches from collaborative interventions (39)*
- *Implementing comprehensive HIV and STI programmes with men who have sex with men: practical guidance for collaborative interventions (40)*
- *Implementing comprehensive HIV and STI programmes with transgender people: practical guidance for collaborative interventions (41)*
- *Implementing comprehensive HIV and HCV programmes with people who inject drugs: practical guidance for collaborative interventions (42)*.

3.5 Research needs

3.5.1 Research needs relating to treatment for gonococcal infections

Although surveillance data should be collected – including break points for resistance, frequency of collection, number of isolates and interpretation of local data – research on current and new medicine options is needed for genital, anorectal and oropharyngeal infections. This research is essential given the increasing antimicrobial resistance (AMR) to currently recommended treatments. Appropriately designed RCTs should be conducted on new medicine options, dual therapy and other alternatives (e.g. gentamicin). Specifically, studies should compare different combinations of dual therapy (e.g. combinations of gentamicin, ceftriaxone, cefixime, zoliflodacin, gemifloxacin or azithromycin), and should evaluate how dual therapy as the first line of treatment affects decreasing resistance rates to ceftriaxone and how dual therapy influences the emergence of resistance.

Continued surveillance and trials are necessary to monitor and investigate resistance to ceftriaxone, cefixime, azithromycin, doxycycline and other treatments for *N. gonorrhoeae*. Trials should include both men and women, and members of key populations. In addition to commonly reported outcomes (e.g. cure and side-effects), other important outcomes should be evaluated, including transmission of gonorrhoea to partners, HIV transmission and acquisition, quality of life, cost–effectiveness (including an assessment of the cost of resistance) and gonorrhoea AMR in vitro.

Treatment failure has been poorly researched. Although recruiting an entire study population who have all experienced treatment failure is difficult, studies that follow up with patients who have had treatment failure should improve the reporting of results. Studies should distinguish between cases of treatment failure and reinfection and should report the first treatment, the follow-up treatment and the outcome. Studies should also explore and report the susceptibility of the organism for those who have experienced treatment failure.

Low-cost point-of-care tests to diagnose gonorrhoea and to determine antibiotic susceptibility are needed to ensure good antibiotic stewardship that conserves treatment options for those with confirmed gonorrhoea and delays the emergence of resistance. Studies on molecular AMR determinants should be pursued to inform the development of antimicrobial susceptibility testing in *N. gonorrhoeae* to inform targeted treatment.

There is little research on the risk of resistance to medicines that are currently available for treating ophthalmia neonatorum. The state of resistance to the medicines should be explored, and it should be established whether these organisms would be killed by ocular prophylaxis despite resistant strains being present. The prevalence of gonococcal ophthalmia in newborns should be determined given the high prevalence of maternal gonorrhoea in some settings.

There is very little research on the values people place on outcomes such as cure, burden of disease, reducing future antibiotic resistance or risk of transmission. There is also little research specifically on people with gonococcal infections and their preferences for treatments, especially their preference for injection versus oral administration of medicine. Additional studies are needed to evaluate the impacts of intramuscular injections of ceftriaxone 1 g on acceptability of treatment.

3.5.2 Research needs relating to treatment for chlamydial infections

For chlamydial infections, the potential for resistance to doxycycline, azithromycin and other treatment options should be investigated further as additional studies are needed for monitoring purposes. RCTs are needed which compare these treatments and different dosages, while assessing clinical and microbiological cure, complications, side-effects (including allergy, toxicity and gastrointestinal effects), compliance, quality of life, and implications for HIV transmission and acquisition, as well as partner transmission of chlamydia. The outcomes should be assessed in both men and women, and in key populations.

Further research is also needed in pregnant women, comparing treatment options and the recommended dosages. Although these recommended medicines are generally safe to use during pregnancy, monitoring and analysis of maternal and fetal complications (e.g. adverse pregnancy outcomes and fetal defects) arising from the use of these treatments for STIs and other infections are important to inform future updates to recommendations. Cost and treatment acceptability should also be assessed.

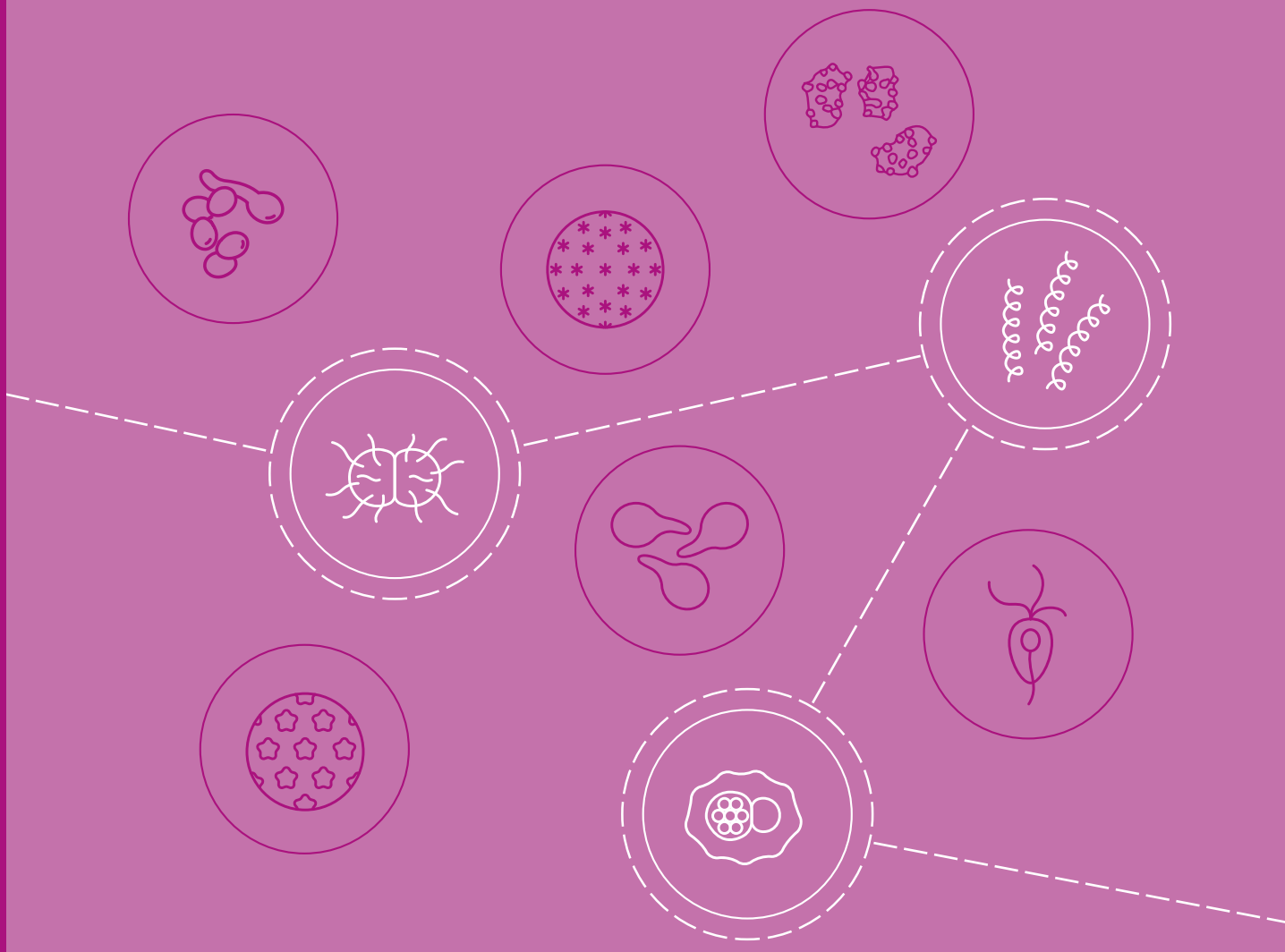
3.5.3 Research needs relating to treatment for syphilis in pregnant women

An urgent need exists to develop a new treatment for syphilis during pregnancy, preferably an effective short-term orally administered course. Such treatment should have the capacity to cross the blood–brain and placental barriers, to prevent vertical transmission of syphilis (congenital syphilis).

Considering the requirement for health workers to administer benzathine penicillin G and related penicillins via injection, in addition to effective oral alternatives, research should explore the safety of self-injection. Dosage considerations for late syphilis (e.g. single-dose options versus multiple doses) should also be studied to inform treatment recommendations.

Further research is needed in pregnant women, comparing treatment options and the recommended dosages. Although these recommended medicines are generally safe to use during pregnancy, monitoring and analysis of maternal and fetal complications (e.g. adverse pregnancy outcomes and fetal defects) arising from the use of these treatments for STIs and other infections are important to inform future updates to recommendations. Cost and treatment acceptability should also be assessed.

4. Recommendations for syphilis testing services



4. Recommendations for syphilis testing services

4.1 Background on syphilis transmission and diagnosis

Syphilis is a bacterial STI caused by *Treponema pallidum*, which is transmitted through sexual or direct contact with infectious lesions and organism penetration of intact mucous membranes or abraded skin, via blood transfusion, or trans-placentally (vertically) from a pregnant woman to her fetus (congenital syphilis). Vertical transmission can be devastating to the fetus in cases where maternal infection is not detected and treated sufficiently early in pregnancy. Syphilis results in substantial morbidity and mortality. Syphilis in pregnancy, if untreated, can lead to stillbirth, neonatal death, prematurity, low birth weight, malformations in bones and neurological issues, among others. When untreated in sexually active people, the disease lasts many years and is divided into stages. Early syphilis consists of primary syphilis, secondary syphilis and early latent syphilis, while late syphilis consists of late latent syphilis and tertiary syphilis (neurosyphilis, ocular syphilis and gumma). Sexual transmission typically occurs during early syphilis. Syphilis also increases the risk of HIV infection, which is facilitated by syphilitic ulcers *(43)*.

Syphilis diagnosis is complex. It is usually based on a combination of clinical history, physical examination, laboratory testing and sometimes radiology. Although other laboratory tests exist, serological tests are the most commonly used to support diagnosis. Serological tests include treponemal tests that detect antibodies to *T. pallidum* infection and non-treponemal tests that use indirect markers of infection.

Types of serological treponemal tests include the fluorescent treponemal antibody absorbed (FTA-ABS), *T. pallidum* haemagglutination assay (TPHA), microhaemagglutination assay for *T. pallidum* (MHA-TP), *T. pallidum* passive particle agglutination assay (TPPA), enzyme immunoassay (EIA), chemiluminescence immunoassay (CIA) and several rapid syphilis tests (also known as RSTs), which are treponemal tests. Treponemal tests usually remain positive (85%) for the rest of one's life, regardless of treatment. Thus, a positive treponemal test does not distinguish between active infection and infection that has been previously treated. Treponemal tests also do not differentiate between sexually transmitted syphilis and endemic, non-sexually transmitted forms of syphilis (including yaws, bejel and pinta), which are caused by a subspecies of *T. pallidum* and mostly affect children living in poor communities.

The most widely available non-treponemal tests are the microscopic Venereal Diseases Research Laboratory (VDRL) and the macroscopic rapid plasma reagin (RPR) tests. These tests detect anti-lipid immunoglobin M or G (IgM or IgG) antibodies. Since these antibodies can also be produced in other diseases, non-treponemal tests are not highly specific for syphilis and can give false-positive results in people with conditions such as acute febrile viral infections and some chronic autoimmune diseases. Non-treponemal tests may be qualitative or quantitative. Quantitative non-treponemal test titres can be used to monitor response to treatment (e.g. RPR and VDRL). Titres are expected to decrease following effective treatment and increase in untreated active infection. However, in some patients, titres may not decrease to become non-reactive after treatment and may remain persistently reactive *(44)*. This is known as a serofast state and is most common in persons treated one or more years after infection *(44, 45)*.

Treponemal and non-treponemal rapid diagnostic tests (RDTs) work on the same principle as other treponemal tests (TPHA/TPPA equivalent) and non-treponemal tests (RPR/VDRL equivalent). Several treponemal RDTs, single or in combination with HIV in the same device (dual syphilis/HIV RDTs), are available on the global market, and some are quality assured as they have received WHO prequalification status. Currently, no non-treponemal RDTs have WHO prequalification, either alone or in combination with treponemal or other diagnostic tests.[2]

2 For the most up-to-date list of WHO prequalified syphilis tests, please see the WHO prequalification website: https://extranet.who.int/prequal/vitro-diagnostics.

If serological tests are used, a presumptive diagnosis of syphilis requires a positive result from a single treponemal or non-treponemal test. For most cases, a confirmed diagnosis of syphilis requires positive results from both types of serological tests. It is important to note, however, that for both types of tests the performance varies according to the stage of infection. The presence of signs of syphilis, such as condyloma lata, provides support for confirming diagnosis. The interpretation of test results, independent of which tests are used, needs to be understood and clearly communicated. Further information about syphilis diagnosis can be found in WHO's updated manual titled, *Laboratory and point-of-care diagnostic testing for sexually transmitted infections, including HIV (46)*.

WHO has made a range of recommendations on syphilis testing strategies for different settings and populations. They are summarized in Box 4.1.

Box 4.1 Existing WHO recommendations and guidance on syphilis diagnosis

1. *Good practice statement*: Perform serology tests for syphilis, including a rapid plasma reagin (RPR)-equivalent test, if available, to attempt to identify active syphilis and for monitoring the response to treatment *(18)*.
2. *Guidance statement*: Dual HIV/syphilis rapid diagnostic tests (RDTs) can be considered as the first test in HIV testing strategies and algorithms in antenatal care settings as well as in key population programmes *(16, 17)*.

Syphilis in pregnancy *(15)*

- *Recommendation*: All pregnant women should be tested for syphilis at least once and as early as possible, ideally at the first antenatal care visit *(strong recommendation, moderate-certainty evidence)*.
- *Recommendation*: In settings with low coverage of syphilis screening and treatment for pregnant women, high loss to follow-up of pregnant women, or limited laboratory capacity, WHO suggests on-site testing rather than the standard off-site laboratory-based screening and treatment strategy *(conditional recommendation, low-certainty evidence)*.
- *Recommendation*: In settings with a low prevalence of syphilis (below 5%), a single on-site rapid syphilis test can be used to screen pregnant women rather than a single on-site RPR test *(conditional recommendation, low-certainty evidence)*.
- *Recommendation*: In settings with a high prevalence of syphilis (5% or greater), on-site rapid testing and, if positive, provision of a first dose of treatment and an RPR test, and then, if the RPR test is positive, provision of treatment according to duration of syphilis. This sequence of tests and treatment should be considered rather than a single on-site syphilis RDT or a single on-site RPR test *(conditional recommendation, low-certainty evidence)*.

  Remarks related to the recommendations on syphilis in pregnancy:

  - These recommendations do not apply to countries that can provide appropriate or high-quality laboratory-based screening and treatment strategies. However, in some settings there may be challenges providing such strategies and/or a sequence of tests.
  - When resources do not permit the use of a sequence of tests, a single on-site syphilis RDT is suggested to ensure greater screening coverage despite the number of pregnant women who will be overtreated due to the high rate of false-positive results.
  - Treatment is based on duration of syphilis, according to WHO guidelines *(23)*.

Key populations *(17)*

- *Recommendation*: Offering periodic serological testing for asymptomatic syphilis infection to men who have sex with men and trans and gender-diverse people is strongly recommended over not offering such screening *(strong recommendation, moderate certainty of evidence)*.

Countries are increasingly utilizing treponemal RDTs to scale-up syphilis testing coverage because they are quick, simple and effective. With the WHO guidance for use of dual HIV/syphilis RDTs, their use has increased globally, with a growing number of countries reporting supportive policies and implementation *(47)*. In 2023, WHO stated that 67 countries reported using dual testing in antenatal care and 56 countries reported using dual testing among key populations; that is 63% and 52%, respectively, out of 107 countries that provided data to the Joint United Nations Programme on HIV/AIDS (UNAIDS)–WHO Global AIDS Monitoring platform that year *(48)*. As a result, some countries are starting to see important gains in terms of greater uptake of syphilis testing and increased treatment coverage *(49)*.

4.2 Dual treponemal/non-treponemal syphilis rapid diagnostic tests

While traditional syphilis serological tests, including those to identify both non-treponemal and treponemal infection, are relatively inexpensive, they must be performed in laboratory settings with electricity, equipment and supplies (e.g. specialized slides), and technicians who carefully follow standardized procedures. Laboratories with such trained personnel, equipment and supplies are increasingly constrained, especially in resource-limited settings, and non-treponemal and treponemal serological testing is often only available in larger, specialized laboratories (e.g. national or regional laboratories or large hospitals) *(50)*. Additionally, some of these tests require cold chain capacity and trained laboratory technicians, further limiting the accessibility of syphilis testing. This is particularly problematic because people seeking STI services or those who should be regularly tested (e.g. pregnant women or members of key populations) receive care in decentralized health facilities without on-site laboratories capable of conducting these types of tests. As a result, service users are either referred to a laboratory with the capacity for serologic testing, or have their blood drawn at the facility and sent to a laboratory. Such referrals have been shown to decrease access to testing services and increase the risk of service users being lost to follow-up *(51)*.

Dual treponemal/non-treponemal rapid diagnostic tests (RDTs) can identify the presence of both treponemal and non-treponemal components and so they can support differentiation between a current/active syphilis infection and one that has been previously treated/cured. These tests may, therefore, contribute to reductions in overtreatment and an increase in access to testing *(52)*. Also considering their ease of use and no need for refrigeration, the adoption of dual treponemal/non-treponemal RDTs may be particularly beneficial among certain populations and settings, such as: populations where syphilis prevalence and the likelihood of having been previously infected and treated are high (e.g. key populations and people using or who could benefit from using PrEP for HIV); people with high risk of loss to follow-up (e.g. migrants or people who are homeless); and those for whom the consequences of untreated syphilis are very severe (e.g. pregnant women) *(50)*. It is important to note that these dual treponemal/non-treponemal RDTs are qualitative in nature and only give an indication of infection (reactive or non-reactive), such that they cannot be used to monitor treatment effectiveness, as this requires a test that can measure the quantity (titre) of antibodies in the blood, such as RPR and VDRL testing. Therefore, it is important to understand how best to use dual treponemal/non-treponemal RDTs to scale up syphilis testing strategically.

Although WHO provides guidance to countries pursuing the eradication of yaws on the use of dual treponemal/non-treponemal RDTs *(52-54)* as a critical intervention, no recommendation existed for the use of such tests to support syphilis diagnosis.

The following sections present the recommendation on the use of dual treponemal/non-treponemal RDTs and summarize the findings of the systematic review (see Web Annex D for full details).

4.2.1 Offering dual treponemal/non-treponemal RDTs within syphilis testing strategies

Recommendation on dual treponemal/non-treponemal RDTs (new 2023)

WHO recommends offering dual treponemal/non-treponemal rapid diagnostic tests as an additional approach within syphilis testing strategies.

Strong recommendation, low certainty in evidence of effects

Remarks:

- **Epidemiology and context:** Dual treponemal/non-treponemal rapid diagnostic tests (RDTs) can be incorporated into syphilis testing strategies and algorithms based on the needs of different populations, epidemiology and settings. Policy-makers and implementers need to have a clear understanding of how to use and interpret reactive results based on their context, particularly when determining how to deliver the test to specific populations and in certain geographies where treponematosis prevalence is high or endemic (e.g. syphilis, yaws, bejel and pinta).
- **Clear messages:** Individuals need to be provided with clear information about their test results so they may be able to access further testing, treatment and care as needed. It is important that all those with test results that indicate an active infection are informed and promptly linked to care services. STI partner services should be discussed and offered as part of case management and public health interventions.
- **Integration:** Dual treponemal/non-treponemal RDTs should be integrated into existing testing strategies and algorithms, and provided as part of a package of services, including immediate access to treatment.
- **Quality-assured products:** Dual treponemal/non-treponemal RDTs, as with all testing approaches, should be conducted using quality-assured products.

Rationale for making the recommendation

Considering the evidence on effectiveness of dual RDTs, its acceptability to stakeholders, feasibility to implement, potential for improved cost-effectiveness, cost-savings and equity, the Guideline Development Group (GDG) determined that the overall benefits outweighed potential harms. The GDG also noted that given the ability of dual RDTs to support same-day diagnosis and treatment, these tests are a priority for addressing gaps in syphilis testing and treatment coverage. Additionally, the GDG noted that countries with endemic treponematosis will need to consider where and how to use dual RDTs. By consensus, the GDG decided to recommend dual treponemal/non-treponemal RDTs to be used within syphilis testing strategies and algorithms, with additional remarks. Because of the high levels of acceptability and feasibility, as well as the presence of some moderate-certainty evidence for critical outcomes, the GDG opted to make a strong recommendation.

Summary of the evidence

Effects

Evidence on the effectiveness and diagnostic accuracy of dual treponemal/non-treponemal RDTs was derived from a systematic review directly comparing dual treponemal/non-treponemal RDTs with laboratory-based syphilis tests as standard. The review also summarized values and preferences and resource use. The review included 25 studies, among which there were no RCTs related to syphilis. The studies covered a range of diverse populations and settings, including key populations, pregnant women and children from high-, low- and middle-income settings *(52)*.

The evidence reviewed showed that dual treponemal/non-treponemal RDTs had good performance and accuracy when compared with standard laboratory-based syphilis testing *(52)*. Using laboratory-based serology testing as the reference standard, the pooled sensitivity of the treponemal component (i.e. any infection, including previously treated cases) was 93% (95% CI: 86–97%) and the pooled specificity was 98% (95% CI: 96–99%), respectively. The pooled sensitivity and specificity of the non-treponemal component (i.e. active infection) was 90% (95% CI: 82–95%) and 97% (95% CI: 92–99%), respectively.

Concordance between dual treponemal/non-treponemal RDTs and standard syphilis laboratory tests was also high compared with laboratory-based serology testing *(52)*. The evidence review thus indicates good performance, and shows that only a small number of syphilis cases would be missed by dual treponemal/non-treponemal RDTs compared with standard testing approaches. Further, when assessing the impact of treponemal/non-treponemal RDTs compared with standard syphilis testing approaches, the performance and accuracy information was modelled and the results showed that dual treponemal/non-treponemal RDTs could reduce overtreatment by more than half *(52)*. This would not only improve the efficiency and effectiveness of syphilis testing programmes, but also help programmes to optimize their use of resources.

Dual treponemal/non-treponemal RDTs were also found to improve the ability to provide same-day treatment, thus reducing loss to follow-up and time to treatment, which supports better case management and decreases potential transmission; these improvements could ultimately assist with reaching global targets *(52)*. In one study among pregnant women in sub-Saharan Africa, when laboratory-based syphilis testing was used instead of dual treponemal/non-treponemal RDTs, treatment rates declined substantially (from 100% to 67%), indicating that a large proportion of service users were lost to follow-up due to delays with the provision of test results *(55)*.

No social harms were identified or reported by any studies. However, further implementation research and engagement with community-led systems may be needed to improve monitoring.

Values and preferences

Overall, dual treponemal/non-treponemal RDTs were acceptable to both individuals and health workers as an easy and reliable testing method. Many health workers (98%) preferred it over standard syphilis laboratory-based testing methods, particularly because the standard methods require venepuncture and do not provide same-day results and treatment. Most health workers also found the RDTs simple and felt this method would reduce errors that often occur when using laboratory-based syphilis testing and other confirmatory assays. Because of the need to provide testing in a range of different settings, dual treponemal/non-treponemal RDTs were also considered more feasible because they could be used outside of laboratories and without the need for specialized staff, and they could also be more widely used in service-delivery settings without electricity, bringing testing services closer for individuals in greatest need.

Resource use

Two studies reporting on cost–effectiveness were identified by the evidence review and reported that RDTs were more cost-effective and potentially cost saving if used in settings providing antenatal care *(55, 56)*. User values and preferences also suggested that dual RDTs would reduce the opportunity costs for service users by making it possible to further decentralize testing services, avoiding long trips to or delays at the clinic, and the need to return for test results.

For a summary of key finding of this systematic review, see Box 4.2.

Equity and human rights

In light of the evidence reviewed, the GDG noted that dual treponemal/non-treponemal RDTs will enable more people to get accurate and reliable testing for active syphilis and will provide important information on the need for treatment. The availability of these tests will make it possible not only to diagnose and promptly treat more people with syphilis, but also to reduce overtreatment. While the evidence identified about resource use was encouraging, the accessibility and affordability of tests may vary and this may limit their potential positive impact on equity.

Box 4.2 Key findings from a systematic review on dual treponemal/non-treponemal rapid diagnostic tests (RDTs)

Overall, the systematic review found that when compared with standard laboratory-based serological syphilis testing, dual treponemal/non-treponemal RDTs:

- probably achieve good accuracy and performance when using quality-assured products *(moderate-certainty evidence)*;
- may likely be usable and feasible in different settings *(low-certainty evidence)*;
- probably improve the number of people appropriately treated for syphilis *(moderate-certainty evidence)*;
- probably reduce the number of people incorrectly treated for syphilis (overtreatment) *(moderate-certainty evidence)*; and
- are likely to rarely cause social harms, but this is uncertain due to the limitations of existing monitoring systems *(very low-certainty evidence)*.

Additional findings on values and preferences and resource use:

- Dual treponemal/non-treponemal RDTs are **acceptable and feasible** to health workers and service users, as they are simple and easy to use, and they avoid the need for laboratory-based testing methods, venepuncture and the need to return for test results. They can also be used to bring services closer to those in greatest need of testing and treatment.
- Dual treponemal/non-treponemal RDTs **may be more cost-effective or cost saving** compared with laboratory-based testing. They can also reduce opportunity costs for service users and save health worker time.

Source: Zhang et al., 2022 *(52)*.

4.3 Syphilis self-testing

Rapid syphilis self-tests are an emerging technology with the potential to support syphilis detection. Self-testing is a process in which a person collects their own specimen using a simple rapid test kit and then performs the test and interprets the result, at the time and place of their choosing.

Self-care and self-testing are increasingly being recommended and successfully applied across different conditions and disease areas *(16, 57, 58)*. WHO currently recommends self-testing for HIV, hepatitis C virus (HCV), COVID-19 and pregnancy, as well as self-collection of samples for chlamydial infection, gonorrhoea and human papillomavirus (HPV), as lay users can perform these procedures reliably and accurately and achieve performance comparable to that of trained health workers (Box 4.3).

Similar to HIV self-testing, syphilis self-testing can provide a private and convenient option for reaching people with syphilis in need of diagnosis and treatment, who may not otherwise get tested or who may prefer self-care options. This may include key populations at increased risk of HIV, men, sexually active young people and other groups who have increased syphilis risk based on local epidemiology and context. It is also important to reach the sexual partners of pregnant women as scaling up testing access for them can contribute to reductions in cases of congenital syphilis.

These guidelines will be critical for programmes introducing self-testing for the first time as well as those with existing self-testing policies and ongoing implementation. These guidelines will also help programmes to build on existing services and to learn lessons from self-testing implementation to date in different settings. This may be particularly important for innovative diagnostic tools, including dual HIV/syphilis self-tests, and potentially the dual treponemal/non-treponemal syphilis self-tests when sufficient evidence is available.

Box 4.3 Existing WHO recommendations on self-testing and self-collection of samples for STI testing

Self-testing

- HIV self-testing should be offered as an approach to HIV testing services *(strong recommendation, moderate-certainty evidence) (16).*
- HIV self-testing may be offered as an additional option for testing at facilities *(conditional recommendation, low-certainty evidence) (16).*
- HIV self-testing may be used to deliver pre-exposure prophylaxis (PrEP), including for initiation, re-initiation and continuation *(conditional recommendation, low-certainty evidence) (16).*
- Hepatitis C virus (HCV) self-testing should be offered as an additional approach to HCV testing services *(strong recommendation, moderate-certainty evidence) (57).*
- COVID-19 self-testing, using SARS-CoV-2 antigen-detecting rapid diagnostic tests (Ag-RDTs), should be offered in addition to professionally administered testing services *(strong recommendation, low-certainty evidence) (59).*
- Self-testing for pregnancy should be available as an additional option to health worker-led testing for pregnancy, for individuals seeking pregnancy testing *(strong recommendation, very low-certainty evidence) (58).*

Self-collection of samples

- Self-collection of samples for gonorrhoea and chlamydia should be made available as an additional approach to deliver STI testing services *(strong recommendation, moderate certainty evidence) (58).*
- Human papillomavirus (HPV) self-sampling should be made available as an additional approach to sampling in cervical cancer screening services for individuals aged 30–60 years *(strong recommendation, moderate certainty evidence) (58).*

The following sections present the updated recommendation on syphilis self-testing and summarize the findings of the systematic review (see Web Annex E for details).

4.3.1 Offering syphilis self-testing as an additional syphilis testing approach

Recommendation on syphilis self-testing (new 2023)

WHO suggests offering syphilis self-testing as an additional syphilis testing approach.

Conditional recommendation, low certainty in evidence of effects

Remarks:

- **Integration:** Syphilis self-testing, as with all testing approaches, should be offered within a broader programme and package of services, which includes ensuring access and linkage to confirmatory testing (where available) and immediate treatment initiation. Opportunities to integrate syphilis self-testing into and/or to expand existing services should be a priority.
- **Quality-assured products:** Syphilis self-testing may include products such as dual HIV/syphilis self-tests, treponemal self-tests and dual treponemal and non-treponemal self-tests. As with all testing approaches, syphilis self-testing should be conducted using quality-assured products.

- **Epidemiology and context:** Policy-makers and implementers need to have a clear understanding that syphilis self-testing can be reactive with any current or prior infection by any treponematosis (e.g. syphilis, yaws, bejel or pinta) when determining how and where to deliver self-testing to specific populations and in certain geographies.
- **Clear messages:** Self-testers need to be provided with clear guidance about when they should test themselves, how to interpret their self-test results and, if needed, where to go for confirmatory testing and treatment. These further services are particularly critical when single treponemal self-tests are used that cannot differentiate previously treated infections from current infections. In endemic areas, it is critical to clarify that reactive serologic tests cannot differentiate between syphilis and other treponematosis (e.g. yaws). Self-testers may also need support tools to ensure they know how to self-test, and this can include instructions for use, videos, in-person demonstrations and support from peers or community health workers. Information about testing with a partner should also be provided, when appropriate, to encourage use of partner services.

Rationale for making the recommendation

Considering the evidence on the effectiveness of syphilis self-testing overall, its acceptability to stakeholders, feasibility to implement, potential to improve affordability, cost–effectiveness and equity, the GDG deemed that the overall benefits of syphilis self-testing outweighed the potential harms. However, the GDG also noted that while syphilis self-testing could be an important tool to achieve global targets, it may be challenging to implement due to complex procurement and logistics systems, and that there may not be sufficient resources to enable affordable access for different populations. There were also concerns about how syphilis self-testing could be used in settings and among populations with high background prevalence of treponematosis (e.g. syphilis, bejel, pinta and yaws).

Summary of the evidence

Effects

Evidence on the effectiveness of syphilis self-testing was derived from a systematic review which directly compared syphilis self-testing with standard laboratory-based syphilis testing alone. The review also summarized values and preferences and resource use needs *(60)* (also see Web Annex E).

Overall, the review included 12 publications of about seven different studies *(61-72)*, of which two were RCTs *(64, 66)*. All the studies were among key populations (specifically, men who have sex with men, sex workers and transgender people) and were conducted in countries in Asia, Africa and the Americas. Only blood-based self-tests were used, including both single treponemal syphilis self-tests and dual HIV/syphilis self-tests. No studies included self-tests with a non-treponemal syphilis testing component, therefore differentiation between previously treated syphilis and active infections needing treatment could only be made based on clinical history and/or confirmatory testing.

Syphilis self-tests and dual HIV/syphilis self-tests were found to improve uptake of syphilis testing. A meta-analysis of two RCTs *(64, 66)* demonstrated that availability of syphilis self-testing and dual HIV/syphilis self-testing led to more than a four-fold increase in the uptake of syphilis testing compared with standard laboratory-based syphilis testing alone. Some evidence from these two RCTs suggested that uptake could potentially be higher when offering dual HIV/syphilis self-testing versus self-testing only for syphilis *(64, 66)*. Despite these increases, syphilis self-testing may not make a difference to the proportion of people with a reactive syphilis test result compared with the standard testing approach. In the same two RCTs *(64, 66)*, there appeared to be little to no difference between these groups, and the same was true in the pooled analysis combining data from both studies *(64, 66)*.

Syphilis self-testing or dual HIV/syphilis self-testing also did not appear to show different results in terms of linkage to care when compared with standard syphilis testing. In both RCTs, individuals with reactive syphilis

self-testing results who were subsequently confirmed positive received prompt treatment as part of the protocol *(64, 66)*. However, linkage to further testing after a reactive syphilis test result may be higher when using dual HIV/syphilis self-tests compared with self-tests for syphilis alone *(64)*. Across observational studies, linkage to confirmatory testing and treatment after the use of self-testing ranged widely (69.6–100.0%).

Syphilis self-tests and dual HIV/syphilis self-tests can be correctly used by individuals and provide accurate results. Several studies showed that most participants were able to correctly self-test *(62, 64, 66-69)*. Some users had difficulties with the steps to collect and transfer their sample, particularly with finger pricking and using the capillary tube to transfer blood from the finger to the cassette *(62, 66)*. No studies, however, identified or reported user challenges that affected test accuracy or performance. A previous systematic review on HIV self-testing has shown it to be highly reliable and accurate – similar to testing by trained health workers *(73)*. Similar levels of accuracy and usability have also been observed across other self-tests *(74)*.

No social harm or adverse events were identified or reported in the RCT publications *(64, 66)*. Observational studies also suggested that harm related to self-testing was rare overall, but they did indicate that some users felt pressure to test themselves and/or experienced arguments with a partner following syphilis self-testing or dual HIV/syphilis self-testing *(62, 69, 75)*. Findings are similar to those reported in HIV self-testing studies, which indicated high levels of safety and efficacy across self-testing in different disease areas *(76-78)*.

Values and preferences

Syphilis self-testing, including dual HIV/syphilis self-testing, was well accepted and desirable overall *(62, 63, 67-69)*. Many individuals found the approach convenient, private and time saving compared with facility-based testing. Some users also expressed a preference for having self-testing as an option because it was blood-based (rather than using oral fluid), and they trusted the results more. To successfully implement syphilis self-testing, users felt that programmes need to address the lack of general awareness about self-testing and STIs more broadly, and better equip users to correctly self-test and interpret their self-test results. Interpretation of positive test results is particularly critical considering the limitations of using treponemal tests alone. As shown by other self-testing studies, providing demonstrations and support tools can be important to help optimize implementation, particularly for first-time self-testers and those with low literacy and in rural settings *(73)*. Although no harms were identified or reported, community messaging efforts may be needed to address concerns and further mitigate potential risks.

Resource use

Syphilis self-testing, including dual HIV/syphilis self-testing, appeared to be cost-effective and affordable compared with standard laboratory-based syphilis testing. In both China and Zimbabwe, the cost per person tested with syphilis self-tests or dual HIV/syphilis self-tests was less than half the cost of standard syphilis testing *(64, 66)*. Cost per reactive person tested after syphilis self-testing (including the costs of the initial self-test, the confirmatory test and training), however, was slightly higher than standard laboratory-based syphilis testing. This is likely due to the need to improve targeting for self-testing. No studies evaluated the impact of syphilis self-testing or dual HIV/syphilis self-testing on health worker time, but previous studies have shown that there can be significant savings if self-tests are used strategically to optimize the use of health workers' time *(79, 80)*.

For a summary of the findings of the systematic review on syphilis self-testing, see Box 4.4.

Equity and human rights

In light of the evidence reviewed, the GDG noted that syphilis self-testing enabled more people to access syphilis testing services and subsequently also to access treatment and care. The approach may be particularly important for reaching those who may not otherwise get tested and as part of global efforts to increase syphilis testing and treatment coverage. The GDG felt that syphilis self-testing would most likely improve equity by making it easier for different populations to access testing and could also alleviate the burden of testing at facilities and optimize the use of health workers' time, depending on the context.

Box 4.4 Summary of key findings from systematic review on syphilis self-testing

Overall, the systematic review found that, when compared with standard laboratory-based syphilis testing, **syphilis self-testing, including dual HIV/syphilis self-testing**:

- improves uptake of syphilis testing *(high-certainty evidence)*;
- may achieve a similar proportion of reactive syphilis results *(low-certainty evidence)*;
- may achieve comparable rates of linkage to further testing, care and treatment *(low-certainty evidence)*;
- probably achieves good accuracy when using quality-assured products *(moderate-certainty evidence)*; and
- potentially causes no harm (and social harm is rare overall); however, the evidence is uncertain *(very low-certainty evidence).*

Additional findings on values and preferences and resource use:

- Syphilis self-testing, including dual HIV/syphilis self-testing, is well accepted and desirable as a convenient and private approach. Programmes may need to invest in increasing knowledge and awareness of self-testing and STIs overall, as well as developing service-delivery models that include support tools and demonstrations to optimize implementation.
- Syphilis self-testing, including dual HIV/syphilis self-testing, can be cost-effective compared with standard laboratory-based syphilis testing services. Effective prioritization and targeting will be important, however, particularly to reach individuals less likely to access existing testing services, populations at greatest risk for syphilis, and the sexual partners of pregnant women.

Source: Towns et al., 2023 *(60)*.

4.4 Implementation considerations

4.4.1 Implementation considerations for dual treponemal/non-treponemal RDTs

When implementing testing strategies and algorithms that use dual treponemal/non-treponemal RDTs, it is important to first assess the current syphilis testing and treatment approaches used and to understand the epidemiological context and local resources. Country capacity to provide on-site, timely confirmatory testing and treatment varies widely, and in many settings such capacity is low *(50)*. Thus, testing strategies and diagnostic algorithms may need to be adapted for different settings to provide as many affected people as possible with the opportunity for same-day diagnosis and treatment. The strategies and algorithms may need to be tailored to fit into existing service-delivery models, considering the optimal use of self-testing, integrated service sites, community outreach and critical health-care facility entry points, for instance. Further, testing strategies and approaches may need to be adapted based on local or subpopulation syphilis background prevalence, individual history of past treatment, likelihood of loss to follow-up, or other factors – such as the potential risk of missing and not effectively treating syphilis infections during pregnancy.

Settings and populations with a high prevalence of syphilis are likely to benefit most from the introduction of dual treponemal/non-treponemal RDTs. Although settings with limited resources and low syphilis prevalence are unlikely to substantially benefit from these RDTs if offered to the general population, they could be targeted for use among higher-prevalence populations (e.g. gay men and other men who have sex with men and sex workers), individuals with high risk of loss to follow-up (e.g. homeless people), and pregnant women and their sexual partners. Prior to implementation, programmes need to carefully consider the trade-offs of introducing these products, in terms of public health impact, resource use and additional costs.

Considerations for successful implementation of dual treponemal/non-treponemal RDTs include:

- **Affordable and quality assured products**. Currently there are no WHO prequalified dual treponemal/non-treponemal RDTs available for procurement.[3] It is important that these products meet WHO performance standards and are affordable and priced to ensure impact.
- **Integration into quality management systems.** The adoption of new diagnostic tests should be considered in the context of each country's national quality management system, irrespective of where or how testing takes place. Quality management comprises quality assurance, quality control and quality improvement. It encompasses the quality of the processes required for effective testing rather than just the quality of the product used for testing *(16)*.
- **Clear, supportive and strategic policies and regulations, standard training and supervision, and operating procedures need to be in place**. Current testing guidelines and policies may need updating to align with the latest WHO recommendations. This includes developing new testing strategies and algorithms for syphilis testing; enabling lay providers to perform RDTs; updating training packages and standard operating procedures for providers; and updating quality assurance and quality control materials and guidance.
- **Linkage and engagement in STI prevention and treatment is critical**. A key reason dual treponemal/non-treponemal RDTs are being implemented is to provide the opportunity for same-day diagnosis and treatment for syphilis. It is critical that programmes design simple pathways to facilitate linkage to treatment, such as making penicillin available in all facilities that can provide testing, using task-sharing and providing clear, evidence-based guidance to health workers on the very low risk of severe adverse effects when using penicillin *(81)*.
- **Consider opportunities for the integration of services.** Programmes should consider how best to integrate the use of these RDTs within a variety of services and settings based on the epidemiological context and available resources, to optimize outcomes.
- **Partner services:** When an individual is diagnosed with syphilis, options for partner services should be offered in order that the patient's sexual partner(s) can be notified, tested and treated if needed. When the patient is pregnant, partner notification is particularly critical to avoid reinfection (see Chapter 5 for more details).

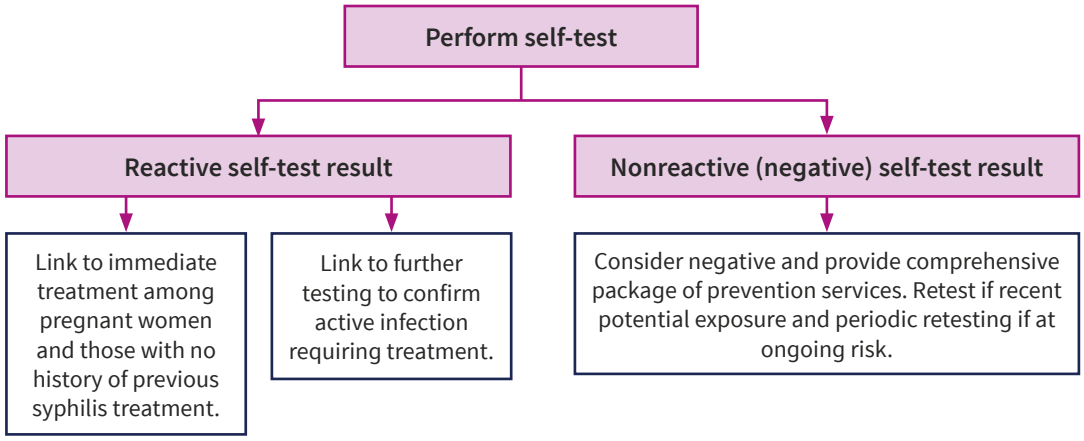
4.4.2 Implementation considerations for syphilis self-testing

As with other self-tests, syphilis self-testing does not provide a definitive diagnosis as most syphilis self-tests only detect treponemal antibodies such that it is recommended to perform a confirmatory test to support the diagnosis of active infection. When there is no history of prior syphilis treatment or, in some settings, where there are no non-treponemal tests available for confirmatory diagnosis, or the time to return results is long, treatment should be initiated immediately for pregnant women due to the high risk of severe adverse birth outcomes. Individuals with a non-reactive self-test result can be considered negative and do not require further testing. Instead, these individuals should receive information based on their individual risk and in accordance with national guidance to link to or engage in STI prevention (and HIV prevention if not on PrEP) and other sexual health services (see Fig. 4.1). Syphilis self-testing may be undertaken using a single treponemal, dual treponemal/non-treponemal or dual HIV/syphilis test. When available in the market, the use of quality assured self-test products is essential.[4] Where dual syphilis tests, including dual self-tests, are to be used, programmes need to adapt their training, communications, support and monitoring tools and approaches to ensure linkage and person-centred service delivery across testing, partner services and treatment.

3 For an up-to-date list of WHO prequalified diagnostics, please see the WHO Prequalification of Medical Products website (section on in vitro diagnostics): https://extranet.who.int/prequal/vitro-diagnostics.

4 Currently there are no WHO prequalified syphilis self-test products. For an up-to-date list of WHO prequalified diagnostics, please see the WHO Prequalification of Medical Products website (section on in vitro diagnostics): https://extranet.who.int/prequal/vitro-diagnostics.

Fig. 4.1 Syphilis treponemal self-testing strategy[a]



[a] Syphilis self-testing strategy can be adapted to include quality assured products such as dual HIV/syphilis self-tests and dual treponemal/non-treponemal syphilis self-tests.

When syphilis self-tests become available, to maximize the benefits, it will be important to not only consider the use of a quality-assured product with clear instructions for use, but also the other components of a successful programme, including service-delivery approaches, ways to facilitate linkage to confirmatory testing (when treponemal tests are used) and treatment if needed, and monitoring and reporting systems. Programmes that have all these components will be more successful when developed by or in close collaboration with the national ministry of health and other relevant governmental departments and nongovernmental institutions, such as community-based and community-led organizations, communities and people at higher risk of infection, such as key populations and people who use HIV PrEP, as well as researchers and implementers.

A wide range of different service-delivery approaches for syphilis self-testing can be considered, depending on the context, setting and population that the programme is trying to reach (Fig. 4.2). Different options can be considered along with varying levels of support and assistance, including more direct assistance, such as in-person demonstration and support from a health worker, or minimal to no direct support, such as manufacturer instructions for use and links to hotlines and instructional videos. When planning to introduce syphilis self-testing, it is important to first analyse and evaluate existing HIV and STI services to determine how best to address any gaps in current syphilis testing coverage, and where and how to implement syphilis self-testing. Implementation will likely vary across settings and depend on whether there are already any self-care and self-testing programmes and policies in place.

In settings where self-testing for other disease areas and conditions is already well implemented and scaled up, it may be beneficial to start the implementation of syphilis self-testing by integrating it within these existing programmes. For instance, this could be done within HIV self-testing programmes that are distributing kits through community outreach or HIV social network testing approaches reaching members of key populations and their partners, as part of PrEP programmes using HIV self-testing to support initiation and continuation, or as part of secondary distribution of self-test kits to male partners of pregnant women at antenatal care clinics. Currently, many countries already have policies to support self-testing, primarily for HIV *(47)*, and they should consider updating their guidelines and strategic plans to include syphilis self-testing.

Regardless of the service-delivery approach used, when implementing syphilis self-testing, it is important that the following key messages are also delivered consistently.

Fig. 4.2 Syphilis self-test service-delivery models

Facility-based
Can be used as first-test in general health facilities as well as other public and private clinics. Examples include primary care, antenatal care clinics, STI clinics, community or key population clinics or drop-in centres, and PrEP programmes.

Community-based
Distribution in the community during periodic campaigns, including at workplaces, places of faith or worship, events, by mobile outreach or to homes (door-to-door). Can be implemented as part of community-based PrEP delivery. Community health and care workers, lay providers or peers can distribute syphilis self-test kits and support self-testers in the community. Integration with existing programmes can improve efficiency and optimize resources. Community-led models can be considered.

Secondary distribution
Includes distribution to partners, social contacts or peers. It may involve distribution through social or sexual contacts, households, drug-injecting partners and networks. In high syphilis-burden settings, distributing kits through antenatal care clinics or other health services to partners of women clients can be considered as part of dual elimination efforts.

Virtual distribution
This involves online ordering through websites or other platforms and home delivery or in-person collection. A range of online platforms can be used, such as websites, social media, dating apps and other digital media.

Retail locations
Through these models, kits are typically provided at a cost to service users, but the price can be reduced or subsidized through public–private partnership, special promotions and bundling, and distribution of coupons or vouchers.

Dual HIV/syphilis self-testing should not be used by people with HIV who are on antiretroviral treatment, as false-negative HIV results can occur. People with HIV who require syphilis testing should be encouraged to access syphilis self-testing products that do not detect HIV-1/2 antibodies or to choose standard laboratory-based syphilis testing services. Anyone with HIV who is uncertain of their diagnosis should be encouraged to seek further support from a health worker to talk about their concerns.

- **Linkage and engagement in prevention and treatment, when appropriate, is critical**. It is important that programmes offering syphilis self-testing are in settings with reliable access to syphilis confirmatory testing (non-treponemal tests), and effective provision of adequate treatment (on-site or by referral to another local service), and monitoring of cure (i.e. they should be able to perform quantitative non-treponemal tests to observe decrease in titres over time). Care pathways could be adapted to ensure they benefit priority populations in need of immediate treatment, such as pregnant women and their sexual partners. Additionally, in some settings, syphilis treatment with benzathine penicillin G (the recommended first-line medicine) may not be available at the clinic level due to unfounded concerns about serious side-effects or other concerns. Not providing timely treatment at the point of care adds an unnecessary barrier to achieving cure and stopping further transmission.
- **Partner services:** Individuals diagnosed with syphilis should be offered a range of options for notifying their sexual partners and offering testing and treatment, if needed. In the context of pregnancy, partner notification is particularly critical to avoid reinfection (please see Chapter 5 for more details).
- **Syphilis self-testing means testing yourself**. Self-testing is for individuals who want to test themselves and learn whether they may have syphilis. Health workers should be available to provide support if requested.

Offering syphilis self-testing to a sexual partner, friend, peer or adult family member, and encouraging them to use the self-test, can also be a good way to help that person start engaging with and prioritizing their sexual health. However, a person should never be coerced or forced to self-test. Coercive or mandatory use of a syphilis self-testing kit should never be supported or encouraged and is not considered self-testing.

- **Any person uncertain about the result of their syphilis self-test should be supported to seek testing from a trained health worker, ideally at a health-care facility.** Those with invalid syphilis self-test results need to repeat the test using another syphilis self-testing kit or seek testing from a trained health worker in a facility or community-based setting.

Additional considerations for successful syphilis self-testing implementation include:

- **Clear and supportive policies, regulations and standard training and operating procedures need to be in place**. These should ensure syphilis self-testing is offered appropriately with clear messages and information for those who may test in a facility, in the community/at home or who receive kits from a partner or peer. Importantly, health workers and health facilities should ensure that they are using quality-assured products, as well as using quality management and post-market surveillance systems to address and report any quality issues that occur.
- **The support needs of populations should be considered.** While many people will be able to self-test with minimal or no support from health workers, some users may need assistance. Programmes should consider developing brief on-site demonstrations and support resources that can be shared with self-testers in person, as well as through videos or messaging platforms. Settings with limited resources and staff may want to prioritize instructional videos and other forms of virtual intervention, or consider group demonstrations, which may be easier to provide for larger numbers of people, and require less supervision and time.
- **Syphilis self-testing should be accessible and available to sexually active adolescents**. To enable adolescents to access the benefits of self-testing, countries need to review and revise national age of consent policies. This can be coordinated across related disease areas including STIs, HIV and sexual and reproductive health services more broadly, and prevention and treatment services can be appropriately tailored to different age groups. Health workers should provide messages about syphilis self-testing that are adapted and appropriate to adolescents, such as messages promoting autonomy and self-care.
- **Opportunities for integration should be considered.** People that may benefit from syphilis self-testing may also have high ongoing risks related to other STIs, including HIV or viral hepatitis. Programmes should consider how best to integrate services based on the epidemiological context and available resources. For example, a programme could leverage dual HIV/syphilis self-testing and develop fully integrated messaging, mobilization/demand generation, service delivery and onward linkage and referrals to treatment and care.
- **Careful ongoing monitoring and evaluation is required.** Implementation of syphilis self-testing should be routinely monitored and reported on, as part of the national response. Currently, WHO advises countries to use pragmatic approaches and triangulate available data – for example, using both standard HIV testing and treatment data and HIV self-test distribution data *(82).* Monitoring and evaluation approaches for syphilis self-testing can be adapted from the available self-care and self-testing measurement tool *(83)*. Ultimately, it is important for programmes to regularly review these data and apply lessons learned to optimize programming.

4.5 Research needs

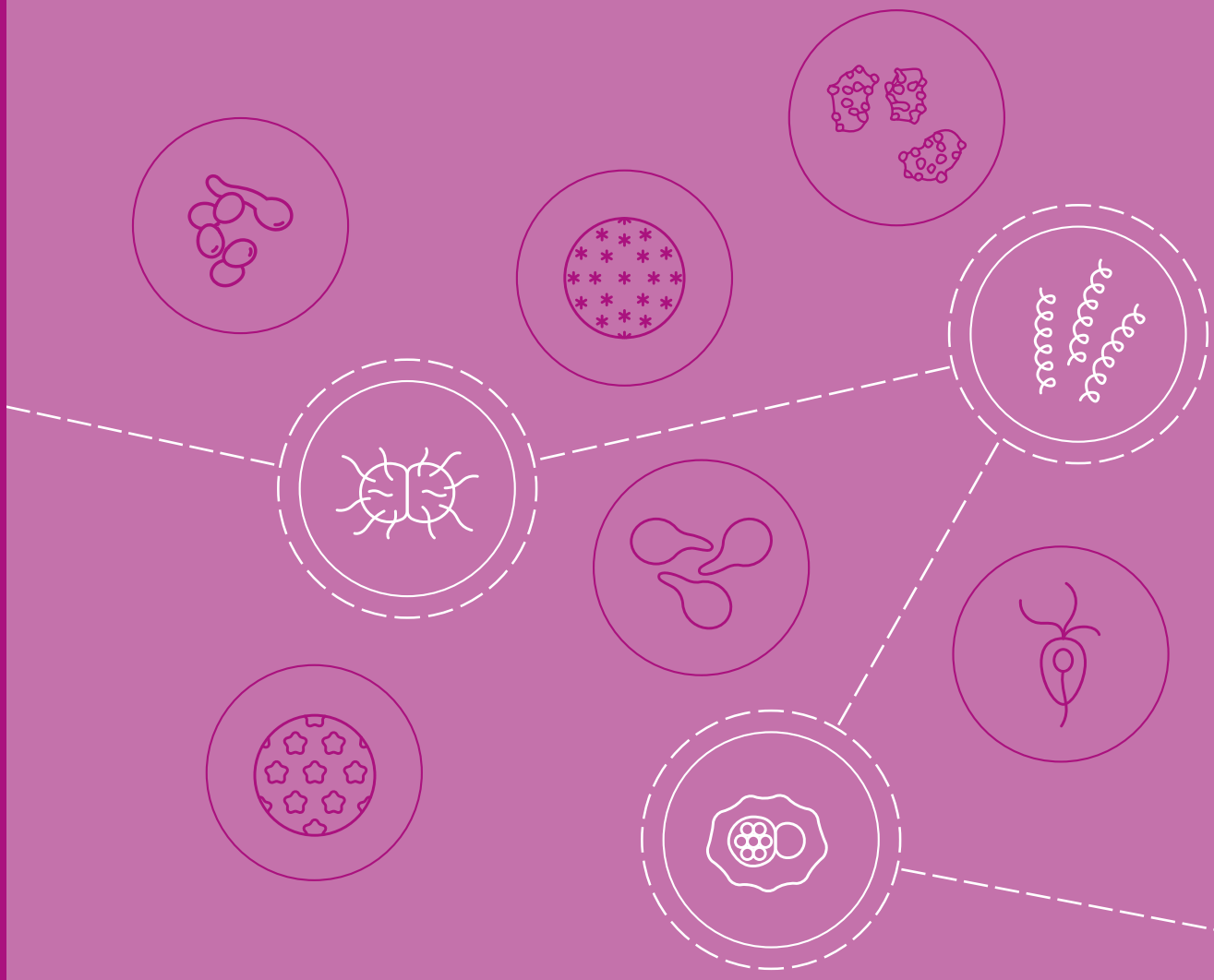
The GDG identified several areas for future research to inform decisions relating to implementation and scale-up of syphilis testing (Table 4.1). Notably, it is important to partner with a range of stakeholders, including communities and networks of key populations who are disproportionally affected by syphilis and other STIs, to identify priorities and to inform the design, implementation and monitoring of research efforts and outcomes.

Table 4.1 Key research priorities and questions related to syphilis testing

Topic	Research priorities	Research questions
Dual treponemal/non-treponemal syphilis rapid diagnostic tests (dual T/NT RDTs)	• Conduct more geographically representative studies and more studies across different populations, particularly in high-prevalence populations. • Assess different algorithms and testing strategies, as well as linkage pathways for treatment and care after testing and diagnosis. • Conduct implementation research in resource-limited settings with lay providers using community-based delivery. • Adapt and trial the use of dual T/NT RDTs for self-testing. • Undertake budget impact analysis to understand the affordability of using dual T/NT RDTs in different populations and settings considering the available resources in programme budgets. • Better understand provider-side and user-side barriers and facilitators to design optimal services. • Better understand social harm using existing monitoring systems in real-world settings. • Develop tests that perform better with low titre levels.	• What is the performance of dual T/NT RDTs at different stages of syphilis infection, clinical and treatment history and what are the implications for different settings and populations? • What is the best algorithm and testing strategy when using dual T/NT RDTs? How can diagnostic algorithms be optimized for different populations and contexts? • How can dual T/NT RDTs be adapted and used for self-testing? • In which contexts and populations are dual T/NT RDTs affordable, cost-saving and/or cost-effective? • What is the impact of the use of these dual T/NT RDTs on time to treatment initiation and on loss to follow-up? • What are the barriers and facilitators for adoption and scale-up? • Are there significant social harms when dual T/NT RDTs are used, in different populations and contexts? • What is the impact of the use of dual T/NT RDTs on partner services (e.g. time to elicit, test and treat partners)?
Syphilis self-testing	• Conduct more geographically representative studies and more studies across different populations, including pregnant women and male partners, adolescents, people taking pre-exposure prophylaxis (PrEP) for HIV and people with symptomatic STIs. • Conduct implementation research to understand optimal service-delivery approaches and ways to facilitate linkage to prevention and care services, and on the usability of dual treponemal/non-treponemal RDTs for self-testing. • Develop tools and approaches for monitoring implementation at local and programme levels. • Leverage and contribute to indirect evidence for self-care and self-testing more broadly. • Better understand provider-side and user-side barriers and facilitators to design optimal services. • Better understand social harm using existing monitoring systems in real-world settings.	• In which contexts should reactive self-tests be used without further confirmatory testing to initiate immediate treatment? • What strategies can be used to optimize linkage to prevention and care for different populations and settings? • What are the optimal syphilis self-testing service-delivery strategies (that are effective, affordable, acceptable) using different tests (single, dual HIV/syphilis, and dual treponemal/non-treponemal syphilis RDTs) by population and settings? • Can syphilis self-testing increase testing and linkage to care for partners of pregnant women? If so, does it also contribute to decreasing reinfection rates and congenital syphilis cases? • What are the benefits and limitations of syphilis self-testing implementation on partner services initiation and referral? • What is the impact of the use of syphilis self-testing on "time to referral" for treatment?

*RDT: ra*pid diagnostic test; STI: sexually transmitted infections; T/NT: treponemal/non-treponemal.

5. Recommendation on STI partner services



5. Recommendation on STI partner services

5.1 STI partner services

5.1.1 Background on partner services

There is a range of existing WHO recommendations for partner services strategies and contact-tracing approaches, including for HIV, viral hepatitis, mpox, tuberculosis (TB) and other communicable diseases *(16, 17, 24-28)* (Box 5.1). Across these disease areas, evidence has shown how effective partner services are if they are applied strategically – not only for identifying new cases to enable individuals and their partners to access treatment and care *(84, 85)*, but also for stopping onward transmission *(86)*, helping to end outbreaks *(87)* and supporting the achievement of elimination goals *(88)*.

Box 5.1 Examples of existing WHO recommendations and guidance on partner services across HIV, viral hepatitis, mpox and tuberculosis

HIV *(16)*

- *Recommendation*: Provider-assisted referral should be offered to all people with HIV as part of a voluntary comprehensive package of testing, care and prevention *(strong recommendation, moderate-quality evidence).*
- *Recommendation*: Social network-based approaches can be offered as part of a comprehensive package of testing and care *(conditional recommendation, very low-quality evidence).*
- *Recommendation*: Provider-assisted referral should be offered to all people with HIV-associated tuberculosis (TB) as part of a voluntary comprehensive package of HIV testing, care and prevention services *(strong recommendation, moderate-quality evidence)*.
- *Good practice statement*: Extending provider-assisted referral to the biological children of people with HIV may also be considered as part of a voluntary provider referral package.

Viral hepatitis *(24)*

- *Implementation guidance*: Encourage and offer hepatitis B virus and hepatitis C virus testing for family members (including children) and sexual partners. This can be done individually, through couples testing and partner services (e.g. provider-assisted referral).

Mpox *(25)*

- *Interim guidance*: Cases should be promptly interviewed as soon as possible to elicit the names and contact information of all potential contacts and identify places visited where contact with other people may have occurred. Contacts of cases should be notified within 24 hours of identification and advised to monitor their health status and seek medical care if they develop symptoms. In the current context, as soon as a suspected case is identified, contact identification and contact tracing should be initiated, while further investigation of the source case is ongoing to determine if the case can be classified as probable or confirmed; if the case is discarded, contact tracing may be stopped.

Tuberculosis (TB)

- *Recommendation*: In conjunction with health workers' representatives, develop and implement programmes for regular, free, voluntary and confidential counselling and testing for HIV and TB, including addressing sexual and reproductive health issues, as well as intensified case finding in the families of health workers with TB *(strong recommendation, moderate-quality evidence) (26).*
- *Recommendation*: Household contacts and other close contacts of individuals with TB should be systematically screened for TB *(strong recommendation, moderate-quality evidence) (27).*

Notifying an STI-exposed sexual partner is an integral part of quality STI case management. Many STIs, such as gonorrhoea, chlamydial infections and syphilis, can be asymptomatic, and people may not be aware that they are infected. Thus, partner services can also be one way to detect and treat asymptomatic individuals with STIs. Among the various types of partner services, using "simple patient referral" (also known as passive referral or partner referral) is a common practice whereby patients diagnosed with STIs are advised by a health worker to inform their sexual partners of their infection and to encourage them to attend a clinic for testing and treatment (see Glossary and Box 5.2).

Within WHO recommended approaches for partner services, there is a range of supported options, including both patient-led and provider-led approaches. In these guidelines, WHO adds to existing guidance (listed in Box 5.1) which recommends partner services approaches across different infectious disease areas to provide further guidance to STI programmes and services on efficient and effective approaches to consider for their setting. The use of different STI partner services strategies and approaches with some level of support from a health worker may be a way to prioritize and optimize the use of existing resources to reach those at greatest risk of acquiring and transmitting STIs.

STI partner services are defined here as a range of voluntary processes, or provision of services, whereby a trained health worker asks for information about sexual partners and offers individuals with an STI effective options for notifying their sexual partners about possible exposure and the benefits of seeking STI services, and ensures that sexual partners are appropriately managed or linked to care and other preventive services. STI partner services may also include offering STI assessment and/or testing to the social contacts of consenting individuals with ongoing STI risks, where this is feasible and acceptable (see Box 5.2).

Section 5.1.2 presents the new recommendation related to STI partner services and summarizes the findings of the systematic review (see Web Annex F for more details).

5.1.2 STI partner services offered within a comprehensive package

Recommendation on STI partner services (new 2023)

WHO recommends that STI partner services should be offered to people with STIs as part of a range of options based on their needs and preferences and within a comprehensive package of voluntary STI testing, care and prevention.

Strong recommendation, low certainty in evidence of effects

Remarks:

- **Human rights:** STI partner services must always be voluntary and never mandatory. Coercive or forced testing is never warranted. All consenting patients should have their privacy protected and personal information should be kept confidential.

- **Important to offer options:** There are a range of STI partner services that should be offered based on patient preferences, feasibility and resources available. Partner services include several options, such as simple patient referral, enhanced patient referral, delayed provider referral, provider–patient referral, provider-assisted referral and social network approaches. Approaches with provider (health worker) support are particularly effective and can be prioritized or encouraged where feasible. Expedited partner therapy (EPT) could also be considered as part of partner services for some curable STIs, such as chlamydia or gonorrhoea.
- **Linkage:** Linkage to STI management services for sexual partners is an essential component of STI services.
- **Integration:** STI partner services should be based within a broader programme and package of services. It is important to build on existing services (e.g. sexual and reproductive health services and family planning services), and integrated delivery across disease areas (e.g. HIV and viral hepatitis).

Rationale for making the recommendation

The Guideline Development Group (GDG) determined that the overall benefits of routinely offering STI partner services, as a package of options, outweighed the potential harms and made a strong recommendation. Consideration was also given to the presence of some moderate-certainty evidence for critical outcomes. STI partner services that had greatest impact included those with some provider support, such as delayed provider referral or provider-assisted referral, and should be prioritized where acceptable, feasible to implement and when resources are available. Overall, the GDG noted that there are substantial gaps in the implementation of STI partner services and it remains important to offer a range of different options to achieve the global goals and address the million new STIs reported every day.

Summary of the evidence

Effects

Evidence on the effectiveness of STI partner services was derived from a systematic review that compared different approaches (including enhanced patient referral, provider-assisted referral and delayed provider referral – see Box 5.2 for the definitions, which are also in the Glossary) with simple patient referral (see Web Annex F). The review also compared expedited partner therapy (EPT) with simple patient referral. EPT could be implemented as part of the above-mentioned partner services approaches. Additionally, the review summarized values and preferences and resource use needs.

In total, the review identified 37 RCTs in Australia, the USA and 12 other countries in Asia, Europe, South America and sub-Saharan Africa. The trials included individuals with bacterial STIs or trichomoniasis *(89-103)*, STI syndromes *(102, 104, 105)*, multiple STIs *(106-108)* and HIV *(109-112)*. Across the trials, 17 directly compared enhanced patient referral with simple patient referral, four compared provider-assisted referral with simple patient referral, and six compared delayed provider referral with simple patient referral. Eleven studies compared EPT versus simple patient referral among patients with chlamydial infection *(99, 113)*, trichomoniasis *(89, 90)*, gonorrhoea or chlamydia *(94, 95, 114-116)*, HIV, herpes simplex virus-2, syphilis, chlamydial infection, gonorrhoea (pharyngeal and anal) *(117)*, or any STI syndrome *(108)*. No studies addressed provider–patient referral or social network testing approaches for STIs.

Enhanced patient referral

The evidence identified showed that enhanced patient referral probably makes little to no difference when compared with simple patient referral. Overall, there appeared to be no difference between these approaches in terms of reinfection of patients, partners elicited and notified, partners presenting for testing, partners testing positive, and partners treated. One study that compared additional counselling versus simple patient referral suggested a positive effect of counselling on reinfection of patients *(96)*. An analysis of five studies indicated that the number of harmful events was low overall and harmful events may be similarly rare following the offer of partner services, but the certainty of the evidence was low (see Web Annex F).

Box 5.2 Definitions of types of STI partner services

Delayed provider referral (also known as contract referral, provider-assisted delayed referral or delayed assisted partner services): A patient with possible or confirmed STIs enters into an agreement with a trained health worker to disclose their diagnosis or the potential exposure to their sexual partner(s) by themselves and to suggest that the partner(s) seek STI testing within an agreed period. If a partner does not access STI testing services or contact the health worker within that period, the health worker will contact the partner directly and offer STI testing.

Enhanced patient referral (also known as enhanced partner referral): A trained provider uses various support tools to facilitate disclosure and the offer of testing by patients with possible or confirmed STIs to their sexual partners. These tools may include providing written information, leaflets and a referral slip or card for a partner, use of web-based messaging platforms to inform a partner anonymously. STI self-collection kits could also be provided to patients to give to partners to collect a sample for testing.

Expedited partner therapy (EPT): The clinical practice of treating the sex partners of patients diagnosed with one or more STIs by providing prescriptions or medication to these patients to give to their partners without the health worker first examining the partners.

Patient referral (also known as simple patient referral, passive referral or partner referral): A trained health worker encourages a patient with possible or confirmed STIs to disclose their diagnosis or the potential exposure to their sexual partner(s) by themselves and to suggest that the partner(s) seek testing. Patient referral involves advice from the trained health worker regarding the need for partner(s) to get tested, strategies for safely disclosing one's diagnosis and information about where and how the partner(s) can access STI testing services.

Provider-assisted referral (also known as assisted partner notification or provider-assisted partner services): A trained provider (health worker) asks people with possible or confirmed STIs about their sexual partners and then, with the consent of the patient, informs the partners of their potential STI exposure. The provider then offers STI testing to partners.

Provider–patient referral: A process whereby a trained health worker accompanies and provides support to a patient with possible or confirmed STIs when they disclose their diagnosis and the potential exposure to an STI to the patient's partner(s). The health worker then offers STI testing to the partner(s). This can be useful when the patient prefers to disclose their diagnosis or potential exposure to a partner but needs support from a provider.

Social network approaches (also known as social network testing services): A trained health worker asks people who are identified as having a high ongoing risk of acquiring STIs (including HIV), independently of STI diagnosis, to encourage and invite individuals in their sexual or social networks to seek STI testing services.

Provider-assisted referral

The evidence identified showed that provider-assisted referral probably achieves greater impact than simple patient referral, but the magnitude of the effect was uncertain. Overall, provider-assisted referral probably led to an increase in positive diagnoses among referred partners. The effects on number of partners elicited and linkage to care was uncertain. Provider-assisted referral may make little to no difference to the number of partners treated, although a sub-group analysis suggested that provider-assisted referral may increase the number of partners treated with non-gonococcal urethritis *(104)*. Social harm also appeared to be rare overall, and no difference was found between the two approaches. Outcomes relating to reinfection of patients and numbers of partners contacted were not found.

Delayed provider referral

The evidence identified suggested that delayed provider referral probably achieves greater impact than simple patient referral – but the magnitude of the effect on clinical outcomes was somewhat uncertain. Overall, results of the meta-analysis suggest that delayed provider referral may have led to an increase in the number of partners presenting to care and positive diagnoses among the partners when compared with simple patient referral (see Web Annex F). The effects on reinfection in patients and on the number of partners elicited or notified were uncertain. Delayed provider referral may increase the number of partners treated, although it may also make little to no difference, compared with simple partner referral. Two studies reported no difference in harmful events between the two approaches *(109, 111)*.

Expedited partner therapy (EPT) for curable STIs

When compared with simple patient referral, EPT probably reduced reinfection in patients and increased the number of partners treated, with four of the five trials showing a moderate difference favouring EPT *(90, 95, 103, 108)*, while a fifth trial indicated no difference between groups, although the evidence was of low certainty *(99)*. When stratified according to type of STI, there was low-certainty evidence for patients' reinfection with chlamydia and trichomoniasis, and moderate-certainty evidence for reinfection with gonorrhoea. The certainty of the evidence regarding the number of partners treated for the three STIs was low. As with other approaches, social harm linked to the intervention appeared to be rare.

Values and preferences

Patients and health workers mentioned that their preferred STI partner services approach would depend on the type of relationship between patients and their sexual partners, and that having options was important. Some patients desired the ability to notify certain partners themselves (simple patient referral) and wanted the option of support from a health worker to inform other partners (provider-assisted referral). Overall, patients noted that they would prefer simple patient referral and EPT for regular partners and provider-assisted strategies for tracing partners whom they did not know well *(102, 118-126)*.

Some health workers prefer simple patient referral for the reason that they feel it is the patient's responsibility to inform their partners *(127)* and because it assures the patient's privacy *(120, 128-130)*. Other health workers preferred provider-assisted referral as they could give details about the treatment to the partner and provide help/support to the patient, including to mitigate violent responses from sexual partners *(123, 131, 132)*. Health workers also indicated that to deliver services effectively they would need support, including training, data management tools, funding, more staff time allocated to complete certain tasks, and supportive policies *(124, 127, 132-139)*.

Similar to health workers, patients' main reason for preferring simple patient referral was to maintain privacy *(124, 128, 129)*. Some patients preferred provider-led interventions to decrease the burden of having to notify the partner themselves *(140)*, and they also felt that providers could better deliver correct information, and provide support to them on how to communicate with partners as well as give psychological support *(108, 120, 123, 125, 132, 136, 141-145)*.

Patients and health workers reported that they preferred EPT, including self-test kits and/or treatment offered to the partner by the patient, because it is convenient for the sexual partner, as there is no need to go for consultation. In addition, health workers said they prefer EPT as it allows the partner to start treatment as soon as possible, but they shared their concerns about incomplete treatment, making medication too accessible to patients, not trusting that partners would receive the medication intended for them and not having the opportunity to discuss the importance of prevention. Legal implications of EPT were also raised by health workers in certain contexts. Patients found EPT preferable for partners facing transportation barriers, and it was also seen as a way to maintain their partner's privacy. Some sexual partners expressed a preference for receiving medication directly from the patient, appreciating their honesty, and expressed they would do the same. Conversely, some partners expressed reservations about the reliability of the test or treatment provided by the patient, especially in the case of casual partners, and would prefer formal testing prior to taking any medication.

Key barriers and facilitators for the implementation of STI partner services were also mentioned by health workers and patients. Overall, the most commonly mentioned barrier was individuals' concerns about potential harm or other negative consequences (e.g. fear of relationship break-up, violence, loss of social and financial support) *(108, 124, 128-130, 136, 140-144, 146-164)*, even despite very little evidence of actual harm. Additionally, patients in many studies mentioned stigma due to being exposed as having been unfaithful, as well as blame and embarrassment, as motives not to want to notify sexual partners *(119, 124, 126, 136, 138, 141, 143, 149, 159, 160, 162, 165, 166)*. Another common issue was the difficulty of retrieving and/or having the correct contact information for all sexual partners, in addition to notifications being ignored *(123, 124, 127, 132, 137, 138, 140, 144, 149, 151, 152, 155, 158, 167-170)*. Absence of STI symptoms or signs were also noted as a reason not to notify partners *(142, 149, 151, 167)*.

Key facilitators mentioned by both patients and health workers were (a) that they felt there was a duty and moral responsibility to notify sexual partners, as "they have the right to know" *(118, 123, 137, 141, 155, 156, 158, 159, 165)*, and (b) to protect others from infection and to avoid reinfection *(119, 146, 158-160, 168)*, particularly in the case of pregnancy, to prevent vertical transmission *(127, 128, 159)*. Patients noted that they were more likely to notify current partners *(127, 134, 135, 141, 142, 147, 149-151, 159, 161, 165, 167)*.

Resource use

Across 22 studies *(95, 101, 116, 171-189)*, STI partner services were generally found to be affordable and cost-effective in both high-income countries (HICs) and low- and middle-income countries (LMICs). A previous systematic review also reported that scale-up of STI partner services was more cost-effective than only expanding testing coverage for chlamydia *(190)*. Even though cost-effectiveness improved over time, the initial investment costs were substantial. STI partner services using EPT were more costly than other approaches. A summary of findings from this systematic review is presented in Box 5.3.

Equity and human rights

In light of the evidence reviewed, the GDG noted that routinely offering a range of options for STI partner services may increase equity by enabling more people to access STI testing, particularly those at higher risk and those who may not otherwise receive testing and treatment. However, equity could also vary based on the cost of different service-delivery approaches, local epidemiology in different settings, the availability of resources, as well as gender, culture, populations and enabling environment factors. Some programmes may need to prioritize implementation for specific population groups and certain STIs, which could affect how equitable services are in practice.

5.2 Implementation considerations

When implementing partner services, it is important to consider the components that are necessary for a successful programme, including: training of health workers; context-appropriate service-delivery models; methods to facilitate linkage to onward services and support; ethical aspects; the surrounding legal and policy environment; the available resources; and patient preferences, which may vary for different sexual partners.

To maximize impact, it is important to offer a range of options or approaches for STI partner services. Current evidence suggests that approaches involving support from a health worker, including lay providers, such as provider-assisted referral and delayed provider referral, may be more effective than simple patient referral. Programmes should consider ways to encourage and prioritize these approaches where acceptable and feasible, and where resources permit. EPT may also be beneficial and could be considered as part of partner services for some STIs (e.g. chlamydia and gonorrhoea), but implementation challenges need to be addressed, such as resource needs, legal aspects, acceptability based on context and populations, and concerns about drug resistance and overtreatment.

The selection of different service-delivery approaches, however, should always be patient-centred, voluntary, focused on providing individual choices, and tailored to align with the epidemiological context and resources available. Some patients may not be ready or willing to disclose their infection status or the identity of their

Box 5.3 Key findings from a systematic review on STI partner services

- **Enhanced patient referral probably makes little to no difference** when compared to simple patient referral *(very low- to moderate-certainty evidence).*
- **Provider-assisted referral probably achieves greater impact** on partners' positive diagnoses and could increase the number of partners receiving treatment compared with simple patient referral; however, the magnitude of the effect on clinical outcomes is somewhat uncertain *(low-certainty evidence)*.
- **Delayed provider referral probably achieves greater impact** than simple patient referral on the number of positive diagnoses and the number of partners presenting for testing and care; however, the magnitude of the effect on clinical outcomes is somewhat uncertain *(moderate-certainty evidence)*.
- **Expedited partner therapy (EPT) probably achieves greater impact** than simple patient referral on patient reinfection and number of partners treated *(low- to moderate-certainty evidence).*
- **Social harm appears rare** in all approaches based on the systematic review. Overall, there was no increase in social harm or adverse events following partner services, but patients and health workers still highlighted this as the main barrier for partner services *(low-certainty evidence)*.
- **Values and preferences expressed by health workers, patients and partners indicated that they generally find all STI partner services options acceptable**, although preferences varied for both patient-led and provider-led options based on context, relationships and time/resources available. Having options is important *(qualitative/narrative evidence)*.
- **Feasibility is probably good for both patient-led and provider-led options**, but support was noted to be needed for: training, monitoring, ensuring adequate health worker time and resources, as well as a need for updated laws and policies (improving the enabling environment), using flexible and decentralized service-delivery options, building on existing services and systems from HIV, and investing in virtual service-delivery options *(qualitative/narrative evidence)*.
- **STI partner services (particularly provider-led options) are affordable and can be cost-effective but do require substantial investment.** Costs will vary based on setting, population and context, including whether there are existing programmes to build on or if new programmes need to be started. Options including EPT are generally more costly *(qualitative/narrative evidence)*.

Source: See Web Annex F.

partner(s), so services need to be offered with care and patience and follow-up may be needed. Concerns about whom to contact (e.g. primary and/or other partners) should be discussed with each patient, and action should be undertaken only after the different options, benefits and risks have been explained and jointly assessed. Partner services should always be voluntary and never involve mandatory or coercive interventions in any setting or context.

When implementing STI partner services, it is important to note that some reproductive tract infections are not sexually transmitted, such as bacterial vaginosis, which may be diagnosed and treated in women with vaginal discharge. Although *Candida albicans* can be transmitted by sexual contact, it is not classified as an STI. The sexual partners of a patient with candidiasis do not need treatment unless they exhibit symptoms. Offering partner services, therefore, needs to be carefully considered for women with vaginal discharge, since they may not have a sexually transmitted pathogen. This is one reason that affordable, rapid diagnostic tests (RDTs) for STIs are urgently needed in such situations as they can guide appropriate partner services and treatment.

Box 5.4 WHO recommendations on intimate partner violence care

- *Recommendation*: Health-care providers should ask about exposure to intimate partner violence when assessing conditions that may be caused or complicated by intimate partner violence, in order to improve diagnosis/identification and subsequent care *(strong recommendation, indirect evidence).*
- *Recommendation*: Women who disclose any form of violence by an intimate partner (or other family member) or sexual assault by any perpetrator should be offered immediate support. Health-care providers should, as a minimum, offer first-line support when women disclose violence. If health-care providers are unable to provide first-line support, they should ensure that someone else (within their health-care setting or another that is easily accessible) is immediately available to do so *(strong recommendation, indirect evidence)*.

Source: WHO, 2013 *(192)*.

Additionally, when offering partner services, it is critical for the health worker to consider the risk of intimate partner violence *(191)* and to refer the patient for available services as needed in line with WHO guidance, as described in Box 5.4. In cases where violence is a risk, partner services may not be an option.

Settings which offer partner services and contact tracing for other disease areas should also assess where they can incorporate STI partner services and further integrate services. For instance, programmes already offering HIV partner services should seek to incorporate testing and other services for STIs more broadly, particularly for priority groups such as pregnant women and key populations. Strategies could also be implemented with a combination of self-testing and self-collection of samples for testing, as well as with innovative diagnostic tools, such as dual HIV/syphilis RDTs. It is important to note that, reversely, STI services should always offer HIV testing for those at risk or diagnosed with an STI.

Additional considerations for successfully implementing STI partner services include the following.

- **Services should always be voluntary**, they should never involve mandatory or coercive testing, and they must respect and protect the privacy and confidentiality of individuals and their partners. This is particularly important when partners express concerns or are from groups that may feel more vulnerable, such as key populations and adolescents. Health workers must be aware of the potential for sexual violence and abuse by partners, and must support patients in making decisions that ensure their safety.
- **Prioritize and provide options.** STI partner services will be most effective when offered as part of a package that promotes different options based on the situation, context and an individual's needs. Programme managers need to review and select the options that will be most feasible and effective to implement in their setting, and may need to focus on specific entry points, geographies or populations to optimize their use of limited resources. Because it may not be feasible to offer partner services for all STIs, programmes will also need to use available epidemiological data to determine which STIs to prioritize in their setting, in addition to considering the morbidity and mortality associated with different STIs. For example, partner services could be prioritized for sexual partners of pregnant women who tested positive for syphilis due to the severe adverse birth outcomes; sexual partners of adolescent girls and young women diagnosed with chlamydial infections or vaginal discharge due to the risk of infertility; and gay men who have sex with men and have multiple sexual partners when they present with urethral discharge or are diagnosed with gonorrhoea due to ongoing selective pressure for antimicrobial resistance. Offering innovative options, such as multiplex testing (e.g. dual HIV/syphilis RDTs), self-testing, self-collection of samples or virtual services, may be desirable and feasible.
- **Health worker support and training.** Health workers delivering STI partner services will need training, resources and support to enable them to effectively trace and locate partners, deliver support and clinical services in a non-judgemental way, facilitate disclosure, respect the privacy and confidentiality of the patients, and recognize and support those with concerns and risks of intimate partner violence. Special training on the needs of adolescents, key populations, pregnant women and their sexual partners may be

needed. It is also important that health workers are trained on how to avoid harm that may be directed at them personally, especially when referrals are carried out in homes or other community-based locations. Health workers who have already been trained to offer a range of effective HIV partner services will require only basic training on STIs.

- **Ongoing monitoring and evaluation** of STI partner services are needed to improve service delivery while optimizing the use of limited resources and the impact of the intervention. Depending on the approaches used, different monitoring and reporting systems may be needed and should be factored into national programme planning. This may require defining and collecting data on relevant indicators and developing a monitoring and evaluation plan. It is also important to monitor for social harms and, if unintended adverse outcomes are identified, to review and adjust programmes promptly. If a system is already in place to monitor partner services of people diagnosed with HIV, this system could be adapted to include selected STIs, depending on the context.

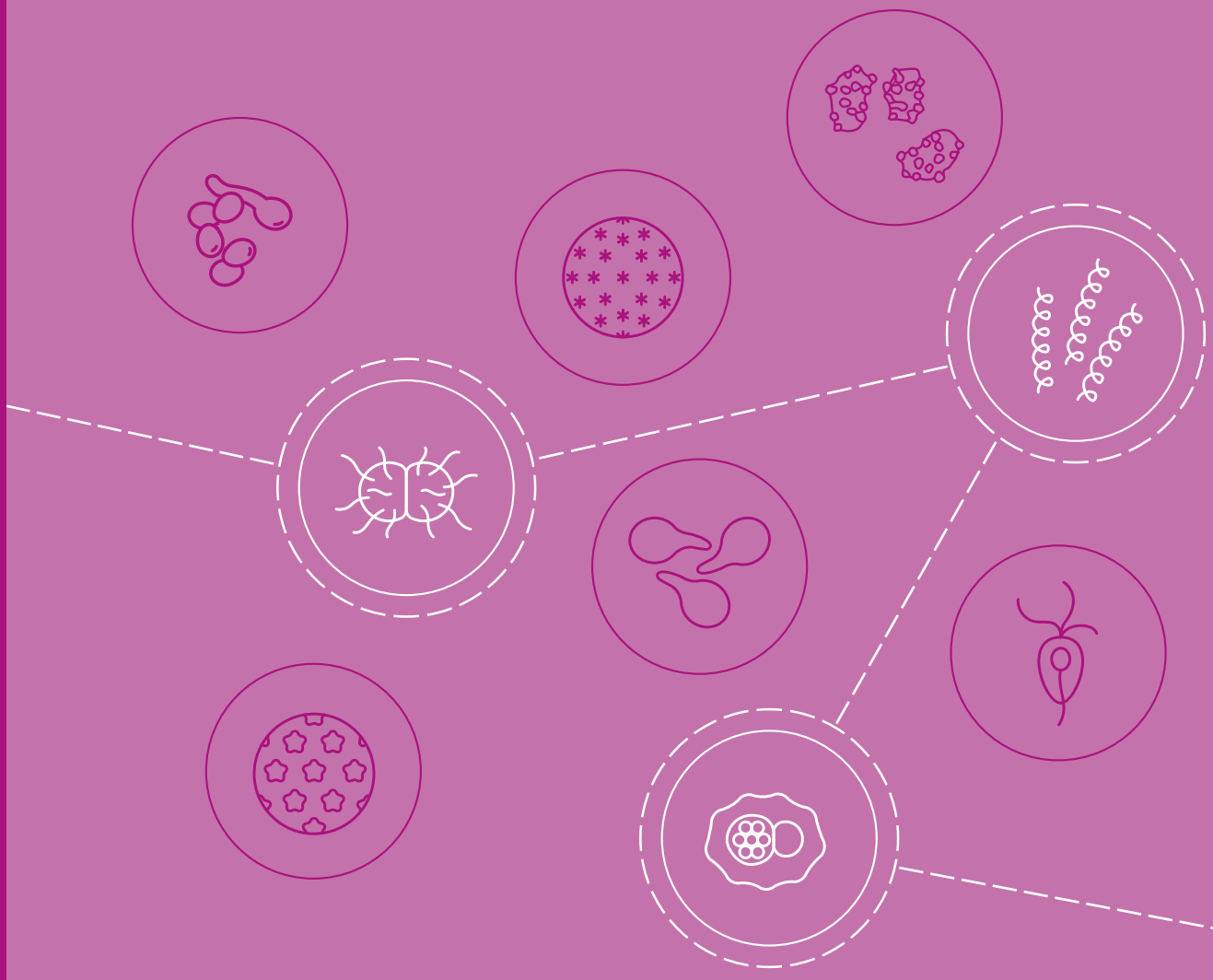
5.3 Research needs

The GDG identified several areas of need for future research to inform decisions about implementation and scale-up of STI partner services (Table 5.1). Notably, it is important to partner with a range of stakeholders, including communities and networks of key populations who are disproportionally affected by STIs, to identify priorities and to inform the design, implementation and monitoring of research efforts and outcomes.

Table 5.1 Key research priorities and questions related to STI partner services

Research priorities	Research questions
• Conduct more geographically representative studies and more studies across different populations, including pregnant women and their sexual partners, adolescents, people using pre-exposure prophylaxis (PrEP) for HIV, key populations, and people with symptomatic STIs. • Identify effective approaches to integration across disease areas and within different services (e.g. antenatal care [ANC], HIV services, STI clinics, PrEP programmes). • Use comparative study designs that assess the best combination of STI partner service options (including social network approaches, provider-led approaches), and which include innovations such as self-tests and virtual tools. • Develop tools and approaches for monitoring implementation at local and programme levels. • Explore user values and preferences for alternative options through discrete choice experiments and qualitative research.	• How and for whom should STI partner services be prioritized in resource-limited settings? • How can integrated partner services be best delivered across HIV, STIs and viral hepatitis? • What is the best combination of STI partner services strategies, considering the index patient demographics, sexual orientation, relationship type and/or other factors that might inform optimization of partner services for specific subgroups? • How should social network approaches be further expanded and included as part of routine partner services? • What innovations can improve feasibility, effectiveness and affordability of STI partner services (e.g. self-testing and virtual interventions)? • Which partner services approaches are most appropriate during STI outbreaks or epidemics? • What is the impact of expedited partner therapy (EPT) using doxycycline for treatment of syphilis in sexual partners of pregnant women on reinfection of the patient and congenital syphilis?

6. Disseminating and updating the guidelines



6. Disseminating and updating the guidelines

6.1 Dissemination

These guidelines will be made available on the WHO website at https://www.who.int/health-topics/sexually-transmitted-infections – click on "Guidelines" (there will also be links to other supporting documents).

WHO headquarters will work with WHO regional offices and country offices to ensure that countries receive support in adapting and implementing these guidelines, and monitoring their utility.

Every level of WHO (headquarters, regional offices and country offices) will work with regional and national partners – including UNFPA, UNICEF, UNAIDS, international and national nongovernmental organizations and other agencies implementing HIV, STI and sexual and reproductive health services – to ensure an integrated approach to preventing and controlling STIs. WHO will advocate that these external partners support the dissemination and implementation of these guidelines.

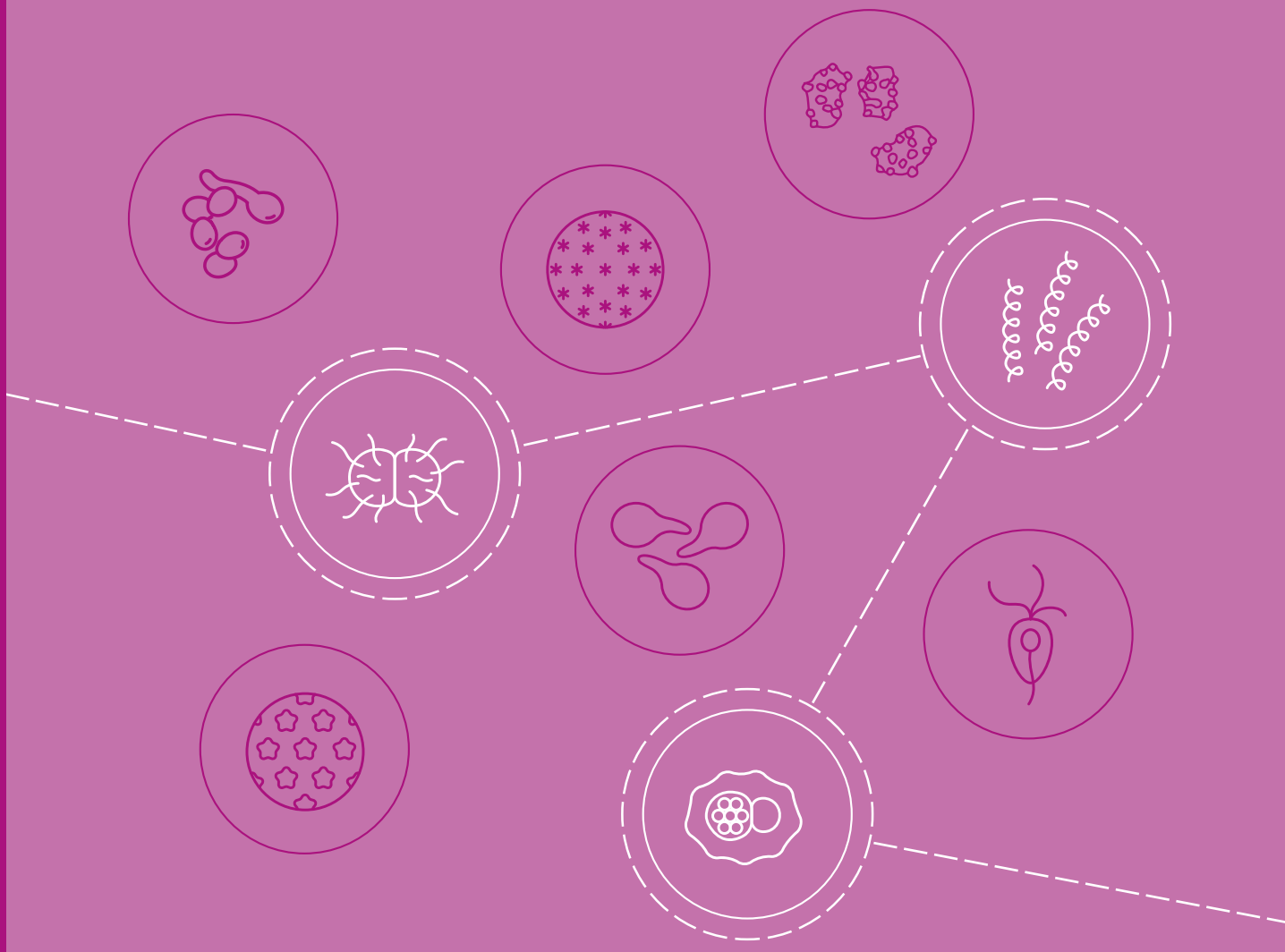
These guidelines will also be disseminated at conferences related to HIV, STIs and sexual and reproductive health, and through electronic media. These recommendations will also be included in WHO's forthcoming consolidated guidelines for the prevention, diagnosis, treatment and care of STIs.

The WHO AWaRe list will need to be revised to align with the treatment recommendations in these guidelines. Revisions will ensure that the recommendations are consistent across WHO products.

6.2 Updating the STI guidelines and user feedback

A system of monitoring relevant new evidence and updating the recommendations in these guidelines will be established and mechanisms for disseminating the new information put into operation. These mechanisms will include electronic communications. An electronic follow-up survey of key end-users of these guidelines will be conducted a year after they have been disseminated. The results of the survey will be used to identify challenges and barriers to the uptake of the guidelines, to evaluate their usefulness for improving the delivery of STI services, and to identify new topics or gaps in treatment that need to be addressed in future editions.

References



References[5]

1. Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021: accountability for the global health sector strategies 2016–2021: actions for impact. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/341412). Licence: CC BY-NC-SA 3.0 IGO.

2. Adachi K, Nielsen-Saines K, Klausner JD. *Chlamydia trachomatis* infection in pregnancy: the global challenge of preventing adverse pregnancy and infant outcomes in sub-Saharan Africa and Asia. Biomed Res Int. 2016;2016:9315757 (https://doi.org/10.1155/2016/9315757).

3. Hoenderboom BM, van Benthem BHB, van Bergen J, Dukers-Muijrers N, Gotz HM, Hoebe C et al. Relation between *Chlamydia trachomatis* infection and pelvic inflammatory disease, ectopic pregnancy and tubal factor infertility in a Dutch cohort of women previously tested for chlamydia in a chlamydia screening trial. Sex Transm Infect. 2019;95(4):300-6 (https://doi.org/10.1136/sextrans-2018-053778).

4. Wi T, Lahra MM, Ndowa F, Bala M, Dillon JR, Ramon-Pardo P et al. Antimicrobial resistance in *Neisseria gonorrhoeae*: global surveillance and a call for international collaborative action. PLoS Med. 2017;14(7):e1002344 (https://doi.org/10.1371/journal.pmed.1002344).

5. Unemo M, Seifert HS, Hook EW, 3rd, Hawkes S, Ndowa F, Dillon JR. Gonorrhoea. Nat Rev Dis Primers. 2019;5(1):79 (https://doi.org/10.1038/s41572-019-0128-6).

6. Unemo M, Lahra MM, Cole M, Galarza P, Ndowa F, Martin I et al. World Health Organization Global Gonococcal Antimicrobial Surveillance Program (WHO GASP): review of new data and evidence to inform international collaborative actions and research efforts. Sex Health. 2019;16(5):412-25 (https://doi.org/10.1071/SH19023).

7. Korenromp EL, Rowley J, Alonso M, Mello MB, Wijesooriya NS, Mahiane SG et al. Global burden of maternal and congenital syphilis and associated adverse birth outcomes: estimates for 2016 and progress since 2012. PLoS One. 2019;14(2):e0211720 (https://doi.org/10.1371/journal.pone.0211720).

8. Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022–2030. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/360348). Licence: CC BY-NC-SA 3.0 IGO.

9. Unemo M, Lahra MM, Escher M, Eremin S, Cole MJ, Galarza P et al. WHO global antimicrobial resistance surveillance for *Neisseria gonorrhoeae* 2017–18: a retrospective observational study. Lancet Microbe. 2021;2(11):e627-e36 (https://doi.org/10.1016/S2666-5247(21)00171-3).

10. Lahra MM, Martin I, Demczuk W, Jennison AV, Lee KI, Nakayama SI et al. Cooperative recognition of internationally disseminated ceftriaxone-resistant *Neisseria gonorrhoeae* strain. Emerg Infect Dis. 2018;24(4):735-40 (https://doi.org/10.3201/eid2404.171873).

11. Jennison AV, Whiley D, Lahra MM, Graham RM, Cole MJ, Hughes G et al. Genetic relatedness of ceftriaxone-resistant and high-level azithromycin resistant *Neisseria gonorrhoeae* cases, United Kingdom and Australia, February to April 2018. Euro Surveill. 2019;24(8):1900118 (https://doi.org/10.2807/1560-7917.ES.2019.24.8.1900118).

12. van der Veen S. Global transmission of the penA allele 60.001–containing high-level ceftriaxone-resistant gonococcal fc428 clone and antimicrobial therapy of associated cases: a review. Infect Microb Dis. 2023;5(1):13-20 (https://doi.org/10.1097/im9.0000000000000113).

13. Ouk V, Pham CD, Wi T, Van Hal SJ, Lahra MM. The Enhanced Gonococcal Surveillance Programme, Cambodia. Lancet Infect Dis. 2023;23(9):e332-e3 (https://doi.org/10.1016/s1473-3099(23)00479-6).

5 All links for references available online were accessed on 20 June 2024, unless another date is specified.

14. Guidelines for the management of sexually transmitted infections. Geneva: World Health Organization; 2003 (https://iris.who.int/handle/10665/42782).

15. WHO guideline on syphilis screening and treatment for pregnant women. Geneva: World Health Organization; 2017 (https://iris.who.int/handle/10665/259003). Licence: CC BY-NC-SA 3.0 IGO.

16. Consolidated guidelines on HIV testing services, 2019. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/336323). Licence: CC BY-NC-SA 3.0 IGO.

17. Consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment and care for key populations. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/360601). Licence: CC BY-NC-SA 3.0 IGO.

18. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/342523). Licence: CC BY-NC-SA 3.0 IGO.

19. The WHO AWaRe (access, watch, reserve) antibiotic book. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/365237). Licence: CC BY-NC-SA 3.0 IGO.

20. AWaRe Antibiotic Categorization [website]. World Health Organization; undated (https://aware.essentialmeds.org/groups).

21. WHO guidelines for the treatment of *Neisseria gonorrhoeae*. Geneva: World Health Organization; 2016 (https://iris.who.int/handle/10665/246114).

22. WHO guidelines for the treatment of *Chlamydia trachomatis*. Geneva: World Health Organization; 2016 (https://iris.who.int/handle/10665/246165).

23. WHO guidelines for the treatment of *Treponema pallidum* (syphilis). Geneva: World Health Organization; 2016 (https://iris.who.int/handle/10665/249572).

24. WHO guidelines on hepatitis B and C testing. Geneva: World Health Organization; 2017 (https://apps.who.int/iris/handle/10665/254621). Licence: CC BY-NC-SA 3.0 IGO.

25. Surveillance, case investigation and contact tracing for mpox (monkeypox): interim guidance, 22 December 2022. Geneva: World Health Organization; 2022 (WHO/MPX/Surveillance/2022.4; https://apps.who.int/iris/handle/10665/365398). Licence: CC BY-NC-SA 3.0 IGO.

26. World Health Organization (WHO), International Labour Organization (ILO). Joint WHO/ILO policy guidelines on improving health worker access to prevention, treatment and care services for HIV and TB. Geneva: World Health Organization; 2010 (https://apps.who.int/iris/handle/10665/44467).

27. WHO consolidated guidelines on tuberculosis: module 2: screening: systematic screening for tuberculosis disease. Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/340255). Licence: CC BY-NC-SA 3.0 IGO.

28. Global Outbreak Alert and Response Network [website]. GOARN; 2023 (https://goarn.who.int/).

29. WHO handbook for guideline development, second edition. Geneva: World Health Organization; 2014 (https://iris.who.int/handle/10665/145714).

30. GRADEpro Guideline Development Tool (GDT) [Software]. McMaster University and Evidence Prime; 2024 (https://www.gradepro.org/).

31. Enhanced gonococcal antimicrobial surveillance programme (EGASP): general protocol. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/341333). Licence: CC BY-NC-SA 3.0 IGO.

32. Cole MJ, Day M, Jacobsson S, Amato-Gauci AJ, Spiteri G, Unemo M. The European response to control and manage multi- and extensively drug-resistant *Neisseria gonorrhoeae*. Euro Surveill. 2022;27(18):2100611 (https://doi.org/10.2807/1560-7917.es.2022.27.18.2100611).

33. Paez-Canro C, Alzate JP, Gonzalez LM, Rubio-Romero JA, Lethaby A, Gaitan HG. Antibiotics for treating urogenital *Chlamydia trachomatis* infection in men and non-pregnant women. Cochrane Database Syst Rev. 2019;(1):CD010871 (https://doi.org/10.1002/14651858.CD010871.pub2).

34. Machalek DA, Tao Y, Shilling H, Jensen JS, Unemo M, Murray G et al. Prevalence of mutations associated with resistance to macrolides and fluoroquinolones in *Mycoplasma genitalium*: a systematic review and meta-analysis. Lancet Infect Dis. 2020;20(11):1302-14 (https://doi.org/10.1016/S1473-3099(20)30154-7).

35. Read TRH, Fairley CK, Murray GL, Jensen JS, Danielewski J, Worthington K et al. Outcomes of resistance-guided sequential treatment of *Mycoplasma genitalium* infections: a prospective evaluation. Clin Infect Dis. 2019;68(4):554-60 (https://doi.org/10.1093/cid/ciy477).

36. Ryan R, Santesso N, Lowe D, Hill S, Grimshaw J, Prictor M et al. Interventions to improve safe and effective medicines use by consumers: an overview of systematic reviews. Cochrane Database Syst Rev. 2014;(4):CD007768 (https://doi.org/10.1002/14651858.CD007768.pub3).

37. Mabilat C, Gros MF, Van Belkum A, Trubiano JA, Blumenthal KG, Romano A et al. Improving antimicrobial stewardship with penicillin allergy testing: a review of current practices and unmet needs. JAC Antimicrob Resist. 2022;4(6):dlac116 (https://doi.org/10.1093/jacamr/dlac116).

38. UNICEF Supply Catalogue [website]. United Nations Children's Fund; 2018 (https://supply.unicef.org, accessed 1 June 2023).

39. World Health Organization, United Nations Population Fund, Joint United Nations Programme on HIV/AIDS, World Bank, Global Network of Sex Work Projects. Implementing comprehensive HIV/STI programmes with sex workers: practical approaches from collaborative interventions. Geneva: World Health Organization; 2013 (https://iris.who.int/handle/10665/90000).

40. United Nations Population Fund, Global Forum on MSM and HIV, United Nations Development Programme, Joint United Nations Programme on HIV/AIDS, World Health Organization, United States Agency for International Development et al. Implementing comprehensive HIV and STI programmes with men who have sex with men: practical guidance for collaborative interventions. New York: United Nations Population Fund; 2015 (https://www.unfpa.org/publications/implementing-comprehensive-hiv-and-sti-programmes-men-who-have-sex-men).

41. United Nations Development Programme, IRGT: A Global Network of Trans Women and HIV, United Nations Population Fund, UCSF Center of Excellence for Transgender Health, Johns Hopkins Bloomberg School of Public Health, World Health Organization et al. Implementing comprehensive HIV and STI programmes with transgender people: practical guidance for collaborative interventions. New York: United Nations Development Programme; 2016 (https://www.undp.org/publications/implementing-comprehensive-hiv-and-sti-programmes-transgender-people).

42. United Nations Office on Drugs and Crime, International Network of People Who Use Drugs, Joint United Nations Programme on HIV/AIDS, United Nations Development Programme, United Nations Population Fund, World Health Organization et al. Implementing comprehensive HIV and HCV programmes with people who inject drugs: practical guidance for collaborative interventions. Vienna: United Nations Office on Drugs and Crime; 2017 (https://www.undp.org/publications/implementing-comprehensive-hiv-and-hcv-programmes-people-who-inject-drugs).

43. Wu MY, Gong HZ, Hu KR, Zheng HY, Wan X, Li J. Effect of syphilis infection on HIV acquisition: a systematic review and meta-analysis. Sex Transm Infect. 2021;97(7):525-33 (https://doi.org/10.1136/sextrans-2020-054706).

44. Sena AC, Wolff M, Martin DH, Behets F, Van Damme K, Leone P et al. Predictors of serological cure and serofast state after treatment in HIV-negative persons with early syphilis. Clin Infect Dis. 2011;53(11):1092-9 (https://doi.org/10.1093/cid/cir671).

45. Zhang RL, Wang QQ, Zhang JP, Yang LJ. Molecular subtyping of *Treponema pallidum* and associated factors of serofast status in early syphilis patients: identified novel genotype and cytokine marker. PLoS One. 2017;12(4):e0175477 (https://doi.org/10.1371/journal.pone.0175477).

46. Laboratory and point-of-care diagnostic testing for sexually transmitted infections, including HIV. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/374252). Licence: CC BY-NC-SA 3.0 IGO.

47. Laws and Policies Analytics [website]. Joint United Nations Programme on HIV/AIDS; 2018 (https://lawsandpolicies.unaids.org/).

48. Global Sexually Transmitted Infections Programme: Strategic information [website]. World Health Organization; 2024 (https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/stis/strategic-information).

49. Abdulai M, Ayisi Addo S, Danso K, Senya K, Owusu K, Adu-Gyamfi R et al. Increasing syphilis testing coverage in antenatal care by 70% in Ghana: lessons from the rollout of dual HIV/syphilis rapid diagnostic tests [poster]. Montreal: 24th International AIDS Conference; 2022 (programme.aids2022.org/Abstract/Abstract/?abstractid=11780).

50. Guidance on syphilis testing in Latin America and the Caribbean: improving uptake, interpretation, and quality of testing in different clinical settings. Washington, DC: Pan American Health Organization; 2015 (https://iris.paho.org/handle/10665.2/7706).

51. Prevention and treatment of HIV and other sexually transmitted infections among men who have sex with men and transgender people: recommendations for a public health approach. Geneva: World Health Organization; 2011 (https://iris.who.int/handle/10665/44619).

52. Zhang Y, Goh SM, Mello MB, Baggaley RC, Wi T, Johnson CC et al. Improved rapid diagnostic tests to detect syphilis and yaws: a systematic review and meta-analysis. Sex Transm Infect. 2022;98(8):608-16 (https://doi.org/10.1136/sextrans-2022-055546).

53. Eradication of yaws: a guide for programme managers. Geneva: World Health Organization; 2018 (https://iris.who.int/handle/10665/259902). Licence: CC BY-NC-SA 3.0 IGO.

54. Eradication of yaws: surveillance, monitoring and evaluation: a manual for yaws eradication programme managers. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/351333). Licence: CC BY-NC-SA 3.0 IGO.

55. Owusu-Edusei K, Jr., Gift TL, Ballard RC. Cost-effectiveness of a dual non-treponemal/treponemal syphilis point-of-care test to prevent adverse pregnancy outcomes in sub-Saharan Africa. Sex Transm Dis. 2011;38(11):997-1003 (https://doi.org/10.1097/OLQ.0b013e3182260987).

56. Terris-Prestholt F, Vickerman P, Torres-Rueda S, Santesso N, Sweeney S, Mallma P et al. The cost-effectiveness of 10 antenatal syphilis screening and treatment approaches in Peru, Tanzania, and Zambia. Int J Gynaecol Obstet. 2015;130(Suppl 1):S73-80 (https://doi.org/10.1016/j.ijgo.2015.04.007).

57. Recommendations and guidance on hepatitis C virus self-testing. Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/342803). Licence: CC BY-NC-SA 3.0 IGO.

58. WHO guideline on self-care interventions for health and well-being, 2022 revision. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/357828). Licence: CC BY-NC-SA 3.0 IGO.

59. Use of SARS-CoV-2 antigen-detection rapid diagnostic tests for COVID-19 self-testing: interim guidance, 9 March 2022. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/352350). Licence: CC BY-NC-SA 3.0 IGO.

60. Towns JM, Tieosapjaroen W, Mello MB, Baggaley RC, Johnson CC, Jamil MS et al. The role of syphilis self-testing as an additional syphilis testing approach in key populations: a systematic review and meta-analysis. Lancet Public Health. 2023;8(9):e726-e34 (https://doi.org/10.1016/S2468-2667(23)00128-7).

61. Balan IC, Lopez-Rios J, Nayak S, Lentz C, Arumugam S, Kutner B et al. SMARTtest: a smartphone app to facilitate HIV and syphilis self- and partner-testing, interpretation of results, and linkage to care. AIDS Behav. 2020;24(5):1560-73 (https://doi.org/10.1007/s10461-019-02718-y).

62. Balán IC, Rios JL, Lentz C, Arumugam S, Dolezal C, Kutner B et al. Acceptability and use of a dual HIV/syphilis rapid test and accompanying smartphone app to facilitate self- and partner-testing among cisgender men and transgender women who have sex with men. AIDS and Behavior. 2021;26(1):35-46 (https://doi.org/10.1007/s10461-021-03322-9).

63. Lentz C, Lopez-Rios J, Dolezal C, Kutner BA, Rael CT, Balan IC. Negotiating use of a blood-based, dual HIV and syphilis test with potential sexual partners among a sample of cisgender men and transgender women who have sex with men in New York City. Arch Sex Behav. 2022;51(4):2015-25 (https://doi.org/10.1007/s10508-021-02275-3).

64. Nhamo D, Mangenah C, Chapwanya G, Mamvuto T, Mahaka I, Sri-Pathmanathan C et al. Feasibility and economic costs of syphilis self-testing to expand test uptake among gay, bisexual and transgender men: results from a randomised controlled trial in Zimbabwe. Sex Health. 2023;20(6):514-22 (https://doi.org/10.1071/SH23038).

65. Rael CT, Kutner BA, Lopez-Rios J, Lentz C, Dolezal C, Balan IC. Experiences of transgender women who used a dual HIV/syphilis rapid self-test to screen themselves and potential sexual partners (the SMARTtest Study). AIDS Behav. 2022;26(4):1229-37 (https://doi.org/10.1007/s10461-021-03478-4).

66. Wang C, Ong JJ, Zhao P, Weideman AM, Tang W, Smith MK et al. Expanding syphilis test uptake using rapid dual self-testing for syphilis and HIV among men who have sex with men in China: a multiarm randomized controlled trial. PLoS Med. 2022;19(3):e1003930 (https://doi.org/10.1371/journal.pmed.1003930).

67. Sri-Pathmanathan C, Nhamo D, Mamvuto T, Chapwanya G, Terris-Prestholt F, Mahaka I et al. Syphilis self-testing to expand test uptake among men who have sex with men: a theoretically informed mixed methods study in Zimbabwe. Sex Transm Infect. 2022;98(3):197-202 (https://doi.org/10.1136/sextrans-2020-054911).

68. Wang C, Cheng W, Li C, Tang W, Ong JJ, Smith MK et al. Syphilis self-testing: a nationwide pragmatic study among men who have sex with men in China. Clin Infect Dis. 2020;70(10):2178-86 (https://doi.org/10.1093/cid/ciz603).

69. Wang C, Li X, Wang Y, Yang B. Syphilis self-testing among female sex workers in China: implications for expanding syphilis screening. Front Public Health. 2022;10 (https://doi.org/10.3389/fpubh.2022.744240).

70. Wu D, Zhou Y, Yang N, Huang S, He X, Tucker J et al. Social media-based secondary distribution of human immunodeficiency virus/syphilis self-testing among Chinese men who have sex with men. Clin Infect Dis. 2021;73(7):e2251-e7 (https://doi.org/10.1093/cid/ciaa825).

71. Yang N, Wu D, Zhou Y, Huang S, He X, Tucker J et al. Sexual health influencer distribution of HIV/syphilis self-tests among men who have sex with men in China: secondary analysis to inform community-based interventions. J Med Internet Res. 2021;23(6):e24303 (https://doi.org/10.2196/24303).

72. Zhong F, Tang W, Cheng W, Lin P, Wu Q, Cai Y et al. Acceptability and feasibility of a social entrepreneurship testing model to promote HIV self-testing and linkage to care among men who have sex with men. HIV Med. 2017;18(5):376-82 (https://doi.org/10.1111/hiv.12437).

73. Figueroa C, Johnson C, Ford N, Sands A, Dalal S, Meurant R et al. Reliability of HIV rapid diagnostic tests for self-testing compared with testing by health-care workers: a systematic review and meta-analysis. Lancet HIV. 2018;5(6):e277-e90 (https://doi.org/10.1016/S2352-3018(18)30044-4).

74. Reipold E, Van Nguyen T, Shiha G, Stvilia K, Monroe-Wise A, Wang C. Self-testing for HCV: multicountry evidence on usability and acceptability. Abstract. Boston: Conference on Retroviruses and Opportunistic Infections; 2021 (https://www.natap.org/2021/CROI/croi_129.htm).

75. Rael CT, Giguere R, Lopez-Rios J, Lentz C, Balan IC, Sheinfil A et al. Transgender women's experiences using a home HIV-testing kit for partner-testing. AIDS Behav. 2020;24(9):2732-41 (https://doi.org/10.1007/s10461-020-02829-x).

76. Eshun-Wilson I, Jamil MS, Witzel TC, Glidded DV, Johnson C, Le Trouneau N et al. A systematic review and network meta-analyses to assess the effectiveness of human immunodeficiency virus (HIV) self-testing distribution strategies. Clin Infect Dis. 2021;73(4):e1018-e28 (https://doi.org/10.1093/cid/ciab029).

77. Jamil MS, Eshun-Wilson I, Witzel TC, Siegfried N, Figueroa C, Chitembo L et al. Examining the effects of HIV self-testing compared to standard HIV testing services in the general population: a systematic review and meta-analysis. EClinicalMedicine. 2021;38:100991 (https://doi.org/10.1016/j.eclinm.2021.100991).

78. Witzel TC, Eshun-Wilson I, Jamil MS, Tilouche N, Figueroa C, Johnson CC et al. Comparing the effects of HIV self-testing to standard HIV testing for key populations: a systematic review and meta-analysis. BMC Med. 2020;18(1):381 (https://doi.org/10.1186/s12916-020-01835-z).

79. Nichols BE, Offorjebe OA, Cele R, Shaba F, Balakasi K, Chivwara M et al. Economic evaluation of facility-based HIV self-testing among adult outpatients in Malawi. J Int AIDS Soc. 2020;23(9):e25612 (https://doi.org/10.1002/jia2.25612).

80. Nichols BE, de Nooy A, Benade M, Balakasi K, Mphande M, Rao G et al. Facility-based HIV self-testing strategies may substantially and cost-effectively increase the number of men and youth tested for HIV in Malawi: results from an individual-based mathematical model. J Int AIDS Soc. 2022;25(10):e26020 (https://doi.org/10.1002/jia2.26020).

81. Galvao TF, Silva MT, Serruya SJ, Newman LM, Klausner JD, Pereira MG et al. Safety of benzathine penicillin for preventing congenital syphilis: a systematic review. PLoS One. 2013;8(2):e56463 (https://doi.org/10.1371/journal.pone.0056463).

82. Simo Fotso A, Johnson C, Vautier A, Kouame KB, Diop PM, Silhol R et al. Routine programmatic data show a positive population-level impact of HIV self-testing: the case of Côte d'Ivoire and implications for implementation. AIDS. 2022;36(13):1871-9 (https://doi.org/10.1097/QAD.0000000000003328).

83. Rothschild C, Sedgh G, Cover J, Gerdts C, Hatzold K, Holt K et al. Sexual and Reproductive Health Self-Care Measurement Tool. Washington, DC: Self-Care Trailblazer Group; 2023 (https://doi.org/10.6084/m9.figshare.21954377).

84. Dalal S, Johnson C, Fonner V, Kennedy CE, Siegfried N, Figueroa C et al. Improving HIV test uptake and case finding with assisted partner notification services. AIDS. 2017;31(13):1867-76 (https://doi.org/10.1097/QAD.0000000000001555).

85. Begun M, Newall AT, Marks GB, Wood JG. Contact tracing of tuberculosis: a systematic review of transmission modelling studies. PLoS One. 2013;8(9):e72470 (https://doi.org/10.1371/journal.pone.0072470).

86. Juneau CE, Briand AS, Collazzo P, Siebert U, Pueyo T. Effective contact tracing for COVID-19: a systematic review. Glob Epidemiol. 2023;5:100103 (https://doi.org/10.1016/j.gloepi.2023.100103).

87. Saurabh S, Prateek S. Role of contact tracing in containing the 2014 Ebola outbreak: a review. Afr Health Sci. 2017;17(1):225-36 (https://doi.org/10.4314/ahs.v17i1.28).

88. Katzman C, Mateu-Gelabert P, Kapadia SN, Eckhardt BJ. Contact tracing for hepatitis C: The case for novel screening strategies as we strive for viral elimination. Int J Drug Policy. 2019;72:33-9 (https://doi.org/10.1016/j.drugpo.2019.04.003).

89. Kissinger P, Schmidt N, Mohammed H, Leichliter JS, Gift TL, Meadors B et al. Patient-delivered partner treatment for *Trichomonas vaginalis* infection: a randomized controlled trial. Sex Transm Dis. 2006;33(7):445-50 (https://doi.org/10.1097/01.olq.0000204511.84485.4c).

90. Schwebke JR, Desmond RA. A randomized controlled trial of partner notification methods for prevention of trichomoniasis in women. Sex Transm Dis. 2010;37(6):392-6 (https://doi.org/10.1097/OLQ.0b013e3181dd1691).

91. Cleveland J. A cost-effective study of alternate methods for gonorrhea contact referral and rescreening. Dade County: Dade County Department of Public Health; 1994.

92. Potterat JJ, Rothenberg R. The case-finding effectiveness of self-referral system for gonorrhea: a preliminary report. Am J Public Health. 1977;67(2):174-6 (https://doi.org/10.2105/ajph.67.2.174).

93. Solomon MZ, DeJong W. The impact of a clinic-based educational videotape on knowledge and treatment behavior of men with gonorrhea. Sex Transm Dis. 1988;15(3):127-32 (https://doi.org/10.1097/00007435-198807000-00001).

94. Kerani RP, Fleming M, DeYoung B, Golden MR. A randomized, controlled trial of inSPOT and patient-delivered partner therapy for gonorrhea and chlamydial infection among men who have sex with men. Sex Transm Dis. 2011;38(10):941-6 (https://doi.org/10.1097/OLQ.0b013e318223fcbc).

95. Kissinger P, Mohammed H, Richardson-Alston G, Leichliter JS, Taylor SN, Martin DH et al. Patient-delivered partner treatment for male urethritis: a randomized, controlled trial. Clin Infect Dis. 2005;41(5):623-9 (https://doi.org/10.1086/432476).

96. Wilson TE, Hogben M, Malka ES, Liddon N, McCormack WM, Rubin SR et al. A randomized controlled trial for reducing risks for sexually transmitted infections through enhanced patient-based partner notification. Am J Public Health. 2009;99(Suppl 1):S104-10 (https://doi.org/10.2105/AJPH.2007.112128).

97. Andersen B, Ostergaard L, Moller JK, Olesen F. Home sampling versus conventional contact tracing for detecting *Chlamydia trachomatis* infection in male partners of infected women: randomised study. BMJ. 1998;316(7128):350-1 (https://doi.org/10.1136/bmj.316.7128.350).

98. Apoola A, Beardsley J. Does the addition of a urine testing kit to use of contact slips increase the partner notification rates for genital chlamydial infection? Int J STD AIDS. 2009;20(11):775-7 (https://doi.org/10.1258/ijsa.2009.009196).

99. Cameron ST, Glasier A, Scott G, Young H, Melvin L, Johnstone A et al. Novel interventions to reduce re-infection in women with chlamydia: a randomized controlled trial. Hum Reprod. 2009;24(4):888-95 (https://doi.org/10.1093/humrep/den475).

100. Falk L, Hegic S, Wilson D, Wirehn AB. Home-sampling as a tool in the context of *Chlamydia trachomatis* partner notification: a randomized controlled trial. Acta Derm Venereol. 2014;94(1):72-4 (https://doi.org/10.2340/00015555-1624).

101. Low N, McCarthy A, Roberts TE, Huengsberg M, Sanford E, Sterne JA et al. Partner notification of chlamydia infection in primary care: randomised controlled trial and analysis of resource use. BMJ. 2006;332(7532):14-9 (https://doi.org/10.1136/bmj.38678.405370.7C).

102. Tomnay JE, Pitts MK, Kuo TC, Fairley CK. Does the Internet assist clients to carry out contact tracing? A randomized controlled trial using web-based information. Int J STD AIDS. 2006;17(6):391-4 (https://doi.org/10.1258/095646206777323391).

103. Clark JL, Segura ER, Oldenburg CE, Salvatierra HJ, Rios J, Perez-Brumer AG et al. Traditional and web-based technologies to improve partner notification following syphilis diagnosis among men who have sex with men in Lima, Peru: pilot randomized controlled trial. J Med Internet Res. 2018;20(7):e232 (https://doi.org/10.2196/jmir.9821).

104. Katz BP, Danos CS, Quinn TS, Caine V, Jones RB. Efficiency and cost-effectiveness of field follow-up for patients with *Chlamydia trachomatis* infection in a sexually transmitted diseases clinic. Sex Transm Dis. 1988;15(1):11-6 (https://doi.org/10.1097/00007435-198801000-00003).

105. Trent M, Chung SE, Burke M, Walker A, Ellen JM. Results of a randomized controlled trial of a brief behavioral intervention for pelvic inflammatory disease in adolescents. J Pediatr Adolesc Gynecol. 2010;23(2):96-101 (https://doi.org/10.1016/j.jpag.2009.06.005).

106. Moyo W, Chirenje ZM, Mandel J, Schwarcz SK, Klausner J, Rutherford G et al. Impact of a single session of counseling on partner referral for sexually transmitted disease treatment, Harare, Zimbabwe. AIDS Behav. 2002;6(3):237-43 (https://doi.org/10.1023/a:1019891808383).

107. Faxelid E, Tembo G, Ndulo J, Krantz I. Individual counseling of patients with sexually transmitted diseases. A way to improve partner notification in a Zambian setting? Sex Transm Dis. 1996;23(4):289-92 (https://www.ncbi.nlm.nih.gov/pubmed/8836022).

108. Nuwaha F, Kambugu F, Nsubuga PS, Hojer B, Faxelid E. Efficacy of patient-delivered partner medication in the treatment of sexual partners in Uganda. Sex Transm Dis. 2001;28(2):105-10 (https://doi.org/10.1097/00007435-200102000-00008).

109. Brown LB, Miller WC, Kamanga G, Nyirenda N, Mmodzi P, Pettifor A et al. HIV partner notification is effective and feasible in sub-Saharan Africa: opportunities for HIV treatment and prevention. J Acquir Immune Defic Syndr. 2011;56(5):437-42 (https://doi.org/10.1097/qai.0b013e318202bf7d).

110. Landis SE, Schoenbach VJ, Weber DJ, Mittal M, Krishan B, Lewis K et al. Results of a randomized trial of partner notification in cases of HIV infection in North Carolina. N Engl J Med. 1992;326(2):101-6 (https://doi.org/10.1056/NEJM199201093260205).

111. Rosenberg NE, Mtande TK, Saidi F, Stanley C, Jere E, Paile L et al. Recruiting male partners for couple HIV testing and counselling in Malawi's option B+ programme: an unblinded randomised controlled trial. Lancet HIV. 2015;2(11):e483-91 (https://doi.org/10.1016/S2352-3018(15)00182-4).

112. Cherutich P, Golden MR, Wamuti B, Richardson BA, Asbjornsdottir KH, Otieno FA et al. Assisted partner services for HIV in Kenya: a cluster randomised controlled trial. Lancet HIV. 2017;4(2):e74-e82 (https://doi.org/10.1016/S2352-3018(16)30214-4).

113. Schillinger JA, Kissinger P, Calvet H, Whittington WL, Ransom RL, Sternberg MR et al. Patient-delivered partner treatment with azithromycin to prevent repeated *Chlamydia trachomatis* infection among women: a randomized, controlled trial. Sex Transm Dis. 2003;30(1):49-56 (https://doi.org/10.1097/00007435-200301000-00011).

114. Golden MR, Kerani RP, Stenger M, Hughes JP, Aubin M, Malinski C et al. Uptake and population-level impact of expedited partner therapy (EPT) on *Chlamydia trachomatis* and *Neisseria gonorrhoeae*: the Washington State community-level randomized trial of EPT. PLoS Med. 2015;12(1):e1001777 (https://doi.org/10.1371/journal.pmed.1001777).

115. Golden MR, Whittington WL, Handsfield HH, Hughes JP, Stamm WE, Hogben M et al. Effect of expedited treatment of sex partners on recurrent or persistent gonorrhea or chlamydial infection. N Engl J Med. 2005;352(7):676-85 (https://doi.org/10.1056/NEJMoa041681).

116. Gift TL, Kissinger P, Mohammed H, Leichliter JS, Hogben M, Golden MR. The cost and cost-effectiveness of expedited partner therapy compared with standard partner referral for the treatment of chlamydia or gonorrhea. Sex Transm Dis. 2011;38(11):1067-73 (https://doi.org/10.1097/OLQ.0b013e31822e9192).

117. Silva-Santisteban A, Konda KA, Leon S, Salazar X, Sandoval C, Clark J et al. P4.122 Effectiveness of communidades positivas: a randomised community-level combination HIV prevention intervention for men who have sex with men in Peru. Sex Transm Infect. 2013;89(Suppl 1):A325.3-A6 (https://doi.org/10.1136/sextrans-2013-051184.1019).

118. Balfe M, Brugha R, O'Donovan D, O'Connell E, Vaughan D. Young women's decisions to accept chlamydia screening: influences of stigma and doctor–patient interactions. BMC Public Health. 2010;10:425 (https://doi.org/10.1186/1471-2458-10-425).

119. McBride KR, Goldsworthy RC, Fortenberry JD. Patient and partner perspectives on patient-delivered partner screening: acceptability, benefits, and barriers. AIDS Patient Care STDS. 2010;24(10):631-7 (https://doi.org/10.1089/apc.2010.0109).

120. Sutcliffe L, Brook MG, Chapman JL, Cassell JM, Estcourt CS. Is accelerated partner therapy a feasible and acceptable strategy for rapid partner notification in the UK?: a qualitative study of genitourinary medicine clinic attenders. Int J STD AIDS. 2009;20(9):603-6 (https://doi.org/10.1258/ijsa.2009.009036).

121. van den Broek IVF, Donker GA, Hek K, van Bergen J, van Benthem BHB, Gotz HM. Partner notification and partner treatment for chlamydia: attitude and practice of general practitioners in the Netherlands; a landscape analysis. BMC Fam Pract. 2017;18(1):103 (https://doi.org/10.1186/s12875-017-0676-3).

122. Wayal S, Cassell JA, Edwards S, Hart G. O19 Sexual partnership patterns and sexually transmitted infections in HIV positive men who have sex with men: implications for partner notification. Sex Transm Infect. 2012;88(Suppl 1):A7.3-A8 (https://doi.org/10.1136/sextrans-2012-050601a.19).

123. Contesse MG, Fredericksen RJ, Wohlfeiler D, Hecht J, Kachur R, Strona FV et al. Attitudes about the use of geosocial networking applications for HIV/STD partner notification: a qualitative study. AIDS Educ Prev. 2019;31(3):273-85 (https://doi.org/10.1521/aeap.2019.31.3.273).

124. Quinn C, Nakyanjo N, Ddaaki W, Burke VM, Hutchinson N, Kagaayi J et al. HIV Partner notification values and preferences among sex workers, fishermen, and mainland community members in Rakai, Uganda: a qualitative study. AIDS Behav. 2018;22(10):3407-16 (https://doi.org/10.1007/s10461-018-2035-3).

125. Wynn A, Moucheraud C, Moshashane N, Offorjebe OA, Ramogola-Masire D, Klausner JD et al. Using partner notification to address curable sexually transmitted infections in a high HIV prevalence context: a qualitative study about partner notification in Botswana. BMC Public Health. 2019;19(Suppl 1):606 (https://doi.org/10.1186/s12889-019-6813-2).

126. Reed JL, Huppert JS, Gillespie GL, Taylor RG, Holland CK, Alessandrini EA et al. Adolescent patient preferences surrounding partner notification and treatment for sexually transmitted infections. Acad Emerg Med. 2015;22(1):61-6 (https://doi.org/10.1111/acem.12557).

127. Theunissen KA, Schipper P, Hoebe CJ, Crutzen R, Kok G, Dukers-Muijrers NH. Barriers to and facilitators of partner notification for *Chlamydia trachomatis* among health care professionals. BMC Health Serv Res. 2014;14(1):647 (https://doi.org/10.1186/s12913-014-0647-5).

128. Klisch SA, Mamary E, Diaz Olavarrieta C, Garcia SG. Patient-led partner notification for syphilis: strategies used by women accessing antenatal care in urban Bolivia. Soc Sci Med. 2007;65(6):1124-35 (https://doi.org/10.1016/j.socscimed.2007.04.025).

129. Njozing BN, Edin KE, Sebastian MS, Hurtig AK. "If the patients decide not to tell what can we do?" – TB/HIV counsellors' dilemma on partner notification for HIV. BMC Int Health Hum Rights. 2011;11:6 (https://doi.org/10.1186/1472-698X-11-6).

130. Adams OP, Carter AO, Redwood-Campbell L. Understanding attitudes, barriers and challenges in a small island nation to disease and partner notification for HIV and other sexually transmitted infections: a qualitative study. BMC Public Health. 2015;15:455 (https://doi.org/10.1186/s12889-015-1794-2).

131. Rosenfeld EA, Marx J, Terry MA, Stall R, Pallatino C, Miller E. Healthcare providers' perspectives on expedited partner therapy for chlamydia: a qualitative study. Sex Transm Infect. 2015;91(6):407-11 (https://doi.org/10.1136/sextrans-2014-051873).

132. Wood H, Hall C, Ioppolo E, Ioppolo R, Scacchia E, Clifford R et al. Barriers and facilitators of partner treatment of chlamydia: a qualitative investigation with prescribers and community pharmacists. Pharmacy. 2018;6(1):17 (https://doi.org/10.3390/pharmacy6010017).

133. Shackleton T, Sutcliffe L, Estcourt C. Is Accelerated Partner Therapy partner notification for sexually transmissible infections acceptable and feasible in general practice? Sex Health. 2011;8(1):17-22 (https://doi.org/10.1071/SH10031).

134. Gamarel KE, Mouzoon R, Rivas A, Stephenson R, Mmeje O. Healthcare providers and community perspectives on expedited partner therapy (EPT) for use with gay, bisexual and other men who have sex with men. Sex Transm Infect. 2020;96(2):101-5 (https://doi.org/10.1136/sextrans-2019-054156).

135. Pavlin NL, Parker RM, Piggin AK, Hopkins CA, Temple-Smith MJ, Fairley CK et al. Better than nothing? Patient-delivered partner therapy and partner notification for chlamydia: the views of Australian general practitioners. BMC Infect Dis. 2010;10(1):274 (https://doi.org/10.1186/1471-2334-10-274).

136. Monroe-Wise A, Maingi Mutiti P, Kimani H, Moraa H, Bukusi DE, Farquhar C. Assisted partner notification services for patients receiving HIV care and treatment in an HIV clinic in Nairobi, Kenya: a qualitative assessment of barriers and opportunities for scale-up. J Int AIDS Soc. 2019;22(Suppl 3):e25315 (https://doi.org/10.1002/jia2.25315).

137. Rose SB, Garrett SM, Pullon SRH. Overcoming challenges associated with partner notification following chlamydia and gonorrhoea diagnosis in primary care: a postal survey of doctors and nurses. J Prim Health Care. 2017;9(2):136-44 (https://doi.org/10.1071/HC17006).

138. Cavalcante EGF, de Lima ICV, Pinheiro AKB, Miranda MCC, Galvão MTG. Difficulties and facilities for notification of sexual partners with sexually transmitted infections. Rev Rene. 2017;18(2) (https://doi.org/10.15253/2175-6783.2017000200015).

139. Lorch R, Hocking J, Guy R, Vaisey A, Wood A, Donovan B et al. Do Australian general practitioners believe practice nurses can take a role in chlamydia testing? A qualitative study of attitudes and opinions. BMC Infect Dis. 2015;15:31 (https://doi.org/10.1186/s12879-015-0757-7).

140. Klitzman R, Kirshenbaum S, Kittel L, Morin S, Daya S, Mastrogiacomo M et al. Naming names: perceptions of name-based HIV reporting, partner notification, and criminalization of non-disclosure among persons living with HIV. Sex Res Social Policy. 2004;1(3):38-57 (https://doi.org/10.1525/srsp.2004.1.3.38).

141. Goyette M, Wamuti BM, Owuor M, Bukusi D, Maingi PM, Otieno FA et al. Understanding barriers to scaling up HIV-assisted partner services in Kenya. AIDS Patient Care STDS. 2016;30(11):506-11 (https://doi.org/10.1089/apc.2016.0151).

142. Zhang K, Zhao J, Li X, Chen X, Wang H, Williams AB et al. Perceived facilitators and barriers regarding partner notification in people living with HIV in Hunan, China: a qualitative study from the patient perspective. J Assoc Nurses AIDS Care. 2019;30(6):658-67 (https://doi.org/10.1097/JNC.0000000000000093).

143. Garcia PJ, Williams E, Carcamo CP, Chiappe M, Holmes KK, Peeling RW et al. Partner notification among Peruvian pregnant women with syphilis. Sex Transm Dis. 2015;42(8):457-62 (https://doi.org/10.1097/OLQ.0000000000000314).

144. Nakku-Joloba E, Kiguli J, Kayemba CN, Twimukye A, Mbazira JK, Parkes-Ratanshi R et al. Perspectives on male partner notification and treatment for syphilis among antenatal women and their partners in Kampala and Wakiso districts, Uganda. BMC Infect Dis. 2019;19(1):124 (https://doi.org/10.1186/s12879-019-3695-y).

145. Rocha AFB, Araujo MAL, Miranda AE, de Leon RGP, da Silva Junior GB, Vasconcelos L. Management of sexual partners of pregnant women with syphilis in northeastern Brazil: a qualitative study. BMC Health Serv Res. 2019;19(1):65 (https://doi.org/10.1186/s12913-019-3910-y).

146. Netsanet F, Dessie A. Acceptance of referral for partners by clients testing positive for human immunodeficiency virus. HIV AIDS. 2013;5:19-28 (https://doi.org/10.2147/HIV.S39250).

147. Kamanga G, Brown L, Jawati P, Chiwanda D, Nyirenda N. Maximizing HIV partner notification opportunities for index patients and their sexual partners in Malawi. Malawi Med J. 2015;27(4):140-4.

148. Lichtenstein B, Schwebke JR. Partner notification methods for African American men being treated for trichomoniasis: a consideration of main men, second hitters, and third players. Med Anthropol Q. 2005;19(4):383-401 (https://doi.org/10.1525/maq.2005.19.4.383).

149. Clark JL, Perez-Brumer A, Salazar X. "Manejar la Situacion": partner notification, partner management, and conceptual frameworks for HIV/STI control among MSM in Peru. AIDS Behav. 2015;19(12):2245-54 (https://doi.org/10.1007/s10461-015-1049-3).

150. Hino S, Grodensky C, Rutstein SE, Golin C, Smith MK, Christmas L et al. HIV status disclosure during acute HIV infection in Malawi. PLoS One. 2018;13(7):e0201265 (https://doi.org/10.1371/journal.pone.0201265).

151. Plotkin M, Kahabuka C, Christensen A, Ochola D, Betron M, Njozi M et al. Outcomes and experiences of men and women with partner notification for HIV testing in Tanzania: results from a mixed method study. AIDS Behav. 2018;22(1):102-16 (https://doi.org/10.1007/s10461-017-1936-x).

152. Gorbach PM, Aral SO, Celum C, Stoner BP, Whittington WL, Galea J et al. To notify or not to notify: STD patients' perspectives of partner notification in Seattle. Sex Transm Dis. 2000;27(4):193-200 (https://doi.org/10.1097/00007435-200004000-00003).

153. Cavalcante EG, Miranda MC, Carvalho AZ, Lima IC, Galvao MT. Partner notification for sexually transmitted infections and perception of notified partners. Rev Esc Enferm USP. 2016;50(3):450-7 (https://doi.org/10.1590/S0080-623420160000400011).

154. Maman S, Mbwambo J, Hogan NM, Kilonzo GP, Sweat M. Women's barriers to HIV-1 testing and disclosure: challenges for HIV-1 voluntary counselling and testing. AIDS Care. 2001;13(5):595-603 (https://doi.org/10.1080/09540120120063223).

155. Tomnay JE, Hulme-Chambers A, Bilardi J, Fairley CK, Huffam S, Chen MY. A qualitative study of means to improve partner notification after an HIV diagnosis among men who have sex with men in Australia. AIDS Patient Care STDS. 2017;31(6):269-74 (https://doi.org/10.1089/apc.2017.0080).

156. Temple-Smith M, Hopkins C, Fairley C, Tomnay J, Pavlin N, Parker R et al. The right thing to do: patients' views and experiences of telling partners about chlamydia. Fam Pract. 2010;27(4):418-23 (https://doi.org/10.1093/fampra/cmq028).

157. Temkin E, Klassen AC, Mmari K, Gillespie DG. A qualitative study of patients' use of expedited partner therapy. Sex Transm Dis. 2011;38(7):651-6 (https://doi.org/10.1097/OLQ.0b013e31820cb206).

158. Mimiaga MJ, Reisner SL, Tetu AM, Bonafide KE, Cranston K, Bertrand T et al. Partner notification after STD and HIV exposures and infections: knowledge, attitudes, and experiences of Massachusetts men who have sex with men. Public Health Rep. 2009;124(1):111-9 (https://doi.org/10.1177/003335490912400114).

159. Nuwaha F, Faxelid E, Neema S, Eriksson C, Hojer B. Psychosocial determinants for sexual partner referral in Uganda: qualitative results. Int J STD AIDS. 2000;11(3):156-61 (https://doi.org/10.1258/0956462001915598).

160. Cunningham SD, Meyers T, Kerrigan D, Ellen JM. Psychosocial factors influencing the disclosure of sexually transmissible infection diagnoses among female adolescents. Sex Health. 2007;4(1):45-50 (https://doi.org/10.1071/sh06032).

161. Clark JL, Perez-Brumer AG, Segura ER, Salvatierra HJ, Sanchez J, Lama JR. Anticipated notification of sexual partners following STD diagnosis among men who have sex with men and transgender women in Lima, Peru: a mixed methods analysis. PLoS One. 2016;11(9):e0163905 (https://doi.org/10.1371/journal.pone.0163905).

162. John SA, Walsh JL, Cho YI, Weinhardt LS. Perceived risk of intimate partner violence among STI clinic patients: implications for partner notification and patient-delivered partner therapy. Arch Sex Behav. 2018;47(2):481-92 (https://doi.org/10.1007/s10508-017-1051-0).

163. Rosenfeld EA, Marx J, Terry MA, Stall R, Pallatino C, Borrero S et al. Intimate partner violence, partner notification, and expedited partner therapy: a qualitative study. Int J STD AIDS. 2016;27(8):656-61 (https://doi.org/10.1177/0956462415591938).

164. Hopkins CA, Temple-Smith MJ, Fairley CK, Pavlin NL, Tomnay JE, Parker RM et al. Telling partners about chlamydia: how acceptable are the new technologies? BMC Infect Dis. 2010;10(1):58 (https://doi.org/10.1186/1471-2334-10-58).

165. Wood JM, Harries J, Kalichman M, Kalichman S, Nkoko K, Mathews C. Exploring motivation to notify and barriers to partner notification of sexually transmitted infections in South Africa: a qualitative study. BMC Public Health. 2018;18(1):980 (https://doi.org/10.1186/s12889-018-5909-4).

166. McBride K, Goldsworthy RC, Fortenberry JD. Formative design and evaluation of patient-delivered partner therapy informational materials and packaging. Sex Transm Infect. 2009;85(2):150-5 (https://doi.org/10.1136/sti.2008.033746).

167. Nanhoe AC, Watzeels A, Gotz HM. Patient initiated partner treatment for *Chlamydia trachomatis* infection in the Netherlands: views of patients with and partners notified for Chlamydia. Int J STD AIDS. 2019;30(11):1071-9 (https://doi.org/10.1177/0956462419851906).

168. Nanhoe AC, Visser M, Omlo JJ, Watzeels A, van den Broek IV, Gotz HM. A pill for the partner via the chlamydia patient? Results from a mixed method study among sexual health care providers in the Netherlands. BMC Infect Dis. 2018;18(1):243 (https://doi.org/10.1186/s12879-018-3139-0).

169. Iturrieta-Guaita NG, Temple-Smith MJ, Tomnay J. Using electronic communication technologies for improving syphilis partner notification in Chile: healthcare providers' perspectives – a qualitative case study. Sex Health. 2019;16(4):377-82 (https://doi.org/10.1071/SH19007).

170. Iturrieta N, Temple-Smith M, Tomnay J. P4.76 How do I notify partners? Challenges faced by healthcare providers managing syphilis in Chile. Sex Transm Dis. 2017;93:A219 (https://doi.org/10.1136/sextrans-2017-053264.571).

171. Armbruster B, Helleringer S, Kalilani-Phiri L, Mkandawire J, Kohler HP. Exploring the relative costs of contact tracing for increasing HIV case finding in sub-Saharan countries. J Acquir Immune Defic Syndr. 2011;58(2):e29-36 (https://doi.org/10.1097/QAI.0b013e31822a9fa8).

172. Cherutich P, Farquhar C, Wamuti B, Otieno FA, Ng'ang'a A, Mutiti PM et al. HIV partner services in Kenya: a cost and budget impact analysis study. BMC Health Serv Res. 2018;18(1):721 (https://doi.org/10.1186/s12913-018-3530-y).

173. Clarke J, White KA, Turner K. Exploring short-term responses to changes in the control strategy for *Chlamydia trachomatis*. Comput Math Methods Med. 2012;2012:803097 (https://doi.org/10.1155/2012/803097).

174. Gift TL, Gaydos CA, Kent CK, Marrazzo JM, Rietmeijer CA, Schillinger JA et al. The program cost and cost-effectiveness of screening men for Chlamydia to prevent pelvic inflammatory disease in women. Sex Transm Dis. 2008;35(11 Suppl):S66-75 (https://doi.org/10.1097/OLQ.0b013e31818b64ac).

175. Gift TL, Lincoln T, Tuthill R, Whelan M, Briggs LP, Conklin T et al. A cost-effectiveness evaluation of a jail-based chlamydia screening program for men and its impact on their partners in the community. Sex Transm Dis. 2006;33(10 Suppl):S103-10 (https://doi.org/10.1097/01.olq.0000235169.45680.7c).

176. Gunn RA, Weinberg MS, Borntrager D, Murray PJ. Partner notification for persons with chronic hepatitis B virus infection: use of a syphilis model service. Sex Transm Dis. 2006;33(7):437-40 (https://doi.org/10.1097/01.olq.0000200495.96528.40).

177. Johnson BL, Tesoriero J, Feng W, Qian F, Martin EG. Cost analysis and performance assessment of partner services for human immunodeficiency virus and sexually transmitted diseases, New York State, 2014. Health Serv Res. 2017;52(Suppl 2):2331-42 (https://doi.org/10.1111/1475-6773.12748).

178. Li XC, Kusi L, Marak T, Bertrand T, Chan PA, Galarraga O. The cost and cost-utility of three public health HIV case-finding strategies: evidence from Rhode Island, 2012–2014. AIDS Behav. 2018;22(11):3726-33 (https://doi.org/10.1007/s10461-017-1940-1).

179. Macke BA, Hennessy MH, McFarlane M. Predictors of time spent on partner notification in four US sites. Sex Transm Infect. 2000;76(5):371-4 (https://doi.org/10.1136/sti.76.5.371).

180. Nichols BE, Gotz HM, van Gorp EC, Verbon A, Rokx C, Boucher CA et al. Partner notification for reduction of HIV-1 transmission and related costs among men who have sex with men: a mathematical modeling study. PLoS One. 2015;10(11):e0142576 (https://doi.org/10.1371/journal.pone.0142576).

181. Rahman MM, Khan M, Gruber D. A low-cost partner notification strategy for the control of sexually transmitted diseases: a case study from Louisiana. Am J Public Health. 2015;105(8):1675-80 (https://doi.org/10.2105/AJPH.2014.302434).

182. Reynolds SL, Kapadia AS, Leonard L, Ross MW. Examining the direct costs and effectiveness of syphilis detection by selective screening and partner notification. J Public Health Med. 2001;23(4):339-45 (https://doi.org/10.1093/pubmed/23.4.339).

183. Roberts TE, Tsourapas A, Sutcliffe L, Cassell J, Estcourt C. Is Accelerated Partner Therapy (APT) a cost-effective alternative to routine patient referral partner notification in the UK? Preliminary cost-consequence analysis of an exploratory trial. Sex Transm Infect. 2012;88(1):16-20 (https://doi.org/10.1136/sextrans-2011-050176).

184. Rutstein SE, Brown LB, Biddle AK, Wheeler SB, Kamanga G, Mmodzi P et al. Cost-effectiveness of provider-based HIV partner notification in urban Malawi. Health Policy Plan. 2014;29(1):115-26 (https://doi.org/10.1093/heapol/czs140).

185. Sharma M, Smith JA, Farquhar C, Ying R, Cherutich P, Golden M et al. Assisted partner notification services are cost-effective for decreasing HIV burden in western Kenya. AIDS. 2018;32(2):233-41 (https://doi.org/10.1097/QAD.0000000000001697).

186. Shrestha RK, Sansom SL, Kimbrough L, Hutchinson AB, Daltry D, Maldonado W et al. Cost-effectiveness of using social networks to identify undiagnosed HIV infection among minority populations. J Public Health Manag Pract. 2010;16(5):457-64 (https://doi.org/10.1097/PHH.0b013e3181cb433b).

187. Silverman RA, Katz DA, Levin C, Bell TR, Spellman D, St John L et al. Sexually transmitted disease partner services costs, other resources, and strategies across jurisdictions to address unique epidemic characteristics and increased incidence. Sex Transm Dis. 2019;46(8):493-501 (https://doi.org/10.1097/OLQ.0000000000001010).

188. Turner K, Adams E, Grant A, Macleod J, Bell G, Clarke J et al. Costs and cost effectiveness of different strategies for chlamydia screening and partner notification: an economic and mathematical modelling study. BMJ. 2011;342(jan04 1):c7250 (https://doi.org/10.1136/bmj.c7250).

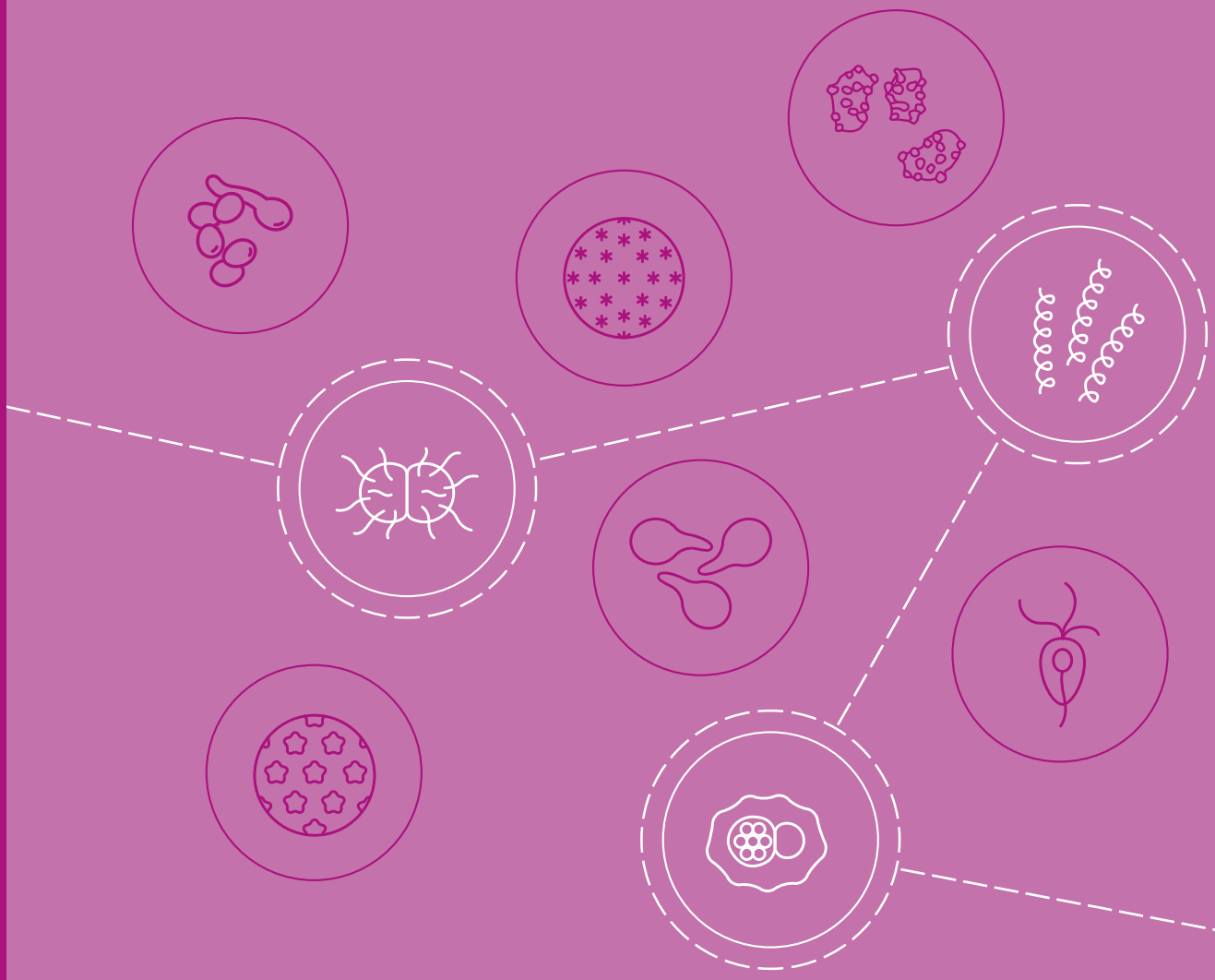
189. Welte R, Kretzschmar M, Leidl R, van den Hoek A, Jager JC, Postma MJ. Cost-effectiveness of screening programs for *Chlamydia trachomatis*: a population-based dynamic approach. Sex Transm Dis. 2000;27(9):518-29 (https://doi.org/10.1097/00007435-200010000-00005).

190. Althaus CL, Turner KM, Mercer CH, Auguste P, Roberts TE, Bell G et al. Effectiveness and cost-effectiveness of traditional and new partner notification technologies for curable sexually transmitted infections: observational study, systematic reviews and mathematical modelling. Health Technol Assess. 2014;18(2):1-100, vii-viii (https://doi.org/10.3310/hta18020).

191. Caring for women subjected to violence: a WHO training curriculum for health care providers. Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/349539). Licence: CC BY-NC-SA 3.0 IGO.

192. Responding to intimate partner violence and sexual violence against women: WHO clinical and policy guidelines. Geneva: World Health Organization; 2013 (https://apps.who.int/iris/handle/10665/85240).

Annex 1.
Contributors to the guidelines



Annex 1.
Contributors to the guidelines

STI Guideline Development Group

Laith Abu Raddad
Director
WHO Collaborating Centre for Disease Epidemiology Analytics on HIV/AIDS, STIs, and Viral Hepatitis
Weill Cornell Medical College
Doha, Qatar

Yaw Adu-Sarkodie
Professor of Clinical Microbiology
Kwame Nkrumah University of Science and Technology
Kumasi, Ghana

Mircea Betiu
Associate Professor
Nicolae Testimitanu State University of Medicine and Pharmacy
Chisinau, Republic of Moldova

Catriona Bradshaw
Professor of Sexual Health
Melbourne Sexual Health Centre
School of Translational Medicine
Monash University and Alfred Hospital
Melbourne, Australia

Xiang-Sheng Chen
Deputy Director
National Center for AIDS/STD Control and Prevention
Nanjing, China

Chido Dziva Chikwari
Assistant Professor of Epidemiology
London School of Hygiene & Tropical Medicine and The Health Research Unit Zimbabwe
Biomedical Research and Training Institute
Harare, Zimbabwe

Amina El Kettani
Medical Officer
Direction de l'Epidémiologie et de Lutte Contre les Maladies
Ministry of Health
Rabat, Morocco

Patricia Garcia
Professor
Universidad Peruana Cayetano Heredia
Lima, Peru

William M. Geisler
Clinical Associate Director and Medical Scientist
University of Alabama at Birmingham
Birmingham, United States of America (USA)

Kristina Grabbe
Jhipiego
USA

Kimberly Green
Global Program Director, Primary Health Care
PATH
Hanoi, Viet Nam

Somesh Gupta
Dermatologist
All India Institute of Medical Sciences
New Delhi, India

Edward W. Hook III
Director
Division of Infectious Diseases
University of Alabama at Birmingham
Birmingham, USA

Rena Janamnuaysook
Program Manager, Implementation Science
Institute of HIV Research and Innovation
Bangkok, Thailand

Nathalie Kapp
Chief Medical Adviser
International Planned Parenthood Federation
London, United Kingdom of Great Britain and Northern Ireland

Hamida Khattabi
Independent consultant
Rabat, Morocco

Rossaphorn Kittyaowamarn
Chief of Bangrak STIs Center
Bureau of AIDS, TB and STIs
Department of Diseases Control
Ministry of Public Health
Nonthaburi, Thailand

Jeffrey D. Klausner
Professor of Medicine and Public Health
David Geffen School of Medicine
University of California, Los Angeles (UCLA)
Los Angeles, USA

Ranmini Kularatne
Clinical Microbiologist
Labtests
Auckland, New Zealand

Peter Kyambadde
Executive Director
Most at Risk Populations Initiative (MARPI)
National Coordinator, Key Populations/STI Program,
Ministry of Health
Kampala, Uganda

David Lewis
Director
Western Sydney Sexual Health Centre
Sydney, Australia

Philippe Mayaud
Professor of Infectious Diseases and
Reproductive Health
London School of Hygiene & Tropical Medicine
London, United Kingdom

Saiqa Mullick
Director, Implementation Science
Wits Reproductive Health and HIV Institute
Johannesburg, South Africa

Francis Ndowa
Physician
Skin and Genito-Urinary Medicine Clinic
Harare, Zimbabwe

Lilani Rajapaksa
Consultant Venereologist
Ministry of Health
Colombo, Sri Lanka

Kees Rietmeijer
Medical Director
Denver STD Prevention Training Center
Denver Public Health Department
Denver, USA

Danvic Rosadiño
Program and Innovations Director
LoveYourself Inc.
Manila, Philippines

Jonathan Ross
Consultant Physician
University Hospitals Birmingham NHS
Foundation Trust
Birmingham, United Kingdom

Anna Shapiro
Policy Officer
Global Network of Sex Work Projects
Edinburgh, United Kingdom

Daniel Simões
Strategic Information Manager
Coalition Plus
Lisbon, Portugal

Jane Thiomi
GBV and HIV Prevention Manager
LVCT Health
Nairobi, Kenya

Jane Tomnay
Director
Centre for Excellence in Rural Sexual Health
University of Melbourne
Melbourne, Australia

Magnus Unemo
Associate Professor in Medical Microbiology and
Molecular Biology
Örebro University Hospital
Örebro, Sweden

Bea Vuylsteke
Institute of Tropical Medicine
Antwerp, Belgium

Judith Wasserheit
Professor of Global Health and Medicine
University of Washington
Seattle, USA

Observers

Laura Bachman
Chief Medical Officer
Division of STD Prevention
Centers for Disease Control and Prevention
Atlanta, USA

Azadeh Baghaki
Strategy Manager
Unitaid
Geneva, Switzerland

Lindley Barbee
Clinical Team Lead
Division of STD Prevention
Centers for Disease Control and Prevention
Atlanta, USA

Francis Kakooza
Head, Global Health Security Department
Infectious Diseases Institute
Makerere University
Kampala, Uganda

Fernando Pascal Martinez
Research and Development Access
Development Lead
Global Antibiotic Research and
Development Partnership
Barcelona, Spain

Tim Sladden
Senior Advisor, Sexual and Reproductive Health
United Nations Population Fund
New York, USA

External Review Group

Henry J.C. de Vries
Amsterdam Sexual Health Clinic
Amsterdam, Kingdom of the Netherlands

Hans Benjamin Hampel
University of Zurich
Zurich, Switzerland

Kausar Jabeen
Professor and Consultant Microbiologist, Pathology and Laboratory Medicine
The Aga Khan University
Karachi, Pakistan

Monica Lahra
WHO Collaborating Centre for STIs and Antimicrobial Resistance
Prince of Wales Hospital
Sydney, Australia

Pham Thi Lan
National Hospital of Dermatology and Venereology
Hanoi Medical University
Hanoi, Viet Nam

Ahmed Latif
Public health consultant
Brisbane, Australia

Ioannis Mameletzis
Consultant
Kyiv, Ukraine

Angelica Espinosa Miranda
Coordinator of Surveillance of STIs
Ministry of Health
Brasília, Brazil

Koleka Mlisana
Executive Manager, Academic Affairs, Research and Quality Assurance
National Health Laboratory Service
Johannesburg, South Africa

Lori Newman
Medical Officer
National Institutes of Health
Washington, DC, USA

Catherine Ngugui
Head, National AIDS and STI Control
Ministry of Health
Nairobi, Kenya

Remco Peters
University of Pretoria
Pretoria, South Africa

Reshmie Ramautarsing
Physician
Institute of HIV Research and Innovation
Bangkok, Thailand

Pachara Sirivongrangson
Ministry of Public Health
Bangkok, Thailand

Melanie Taylor
Centers for Disease Control and Prevention
Atlanta, USA

Janet Wilson
Consultant in Genito-Urinary Medicine
Leeds Teaching Hospitals NHS Trust
Leeds, United Kingdom

Valerie Wilson
Caribbean Med Labs Foundation
Port of Spain, Trinidad and Tobago

Methodologist and evidence review team

Methodologist

Maria Ximena Rojas Reyes
Institut d'Recerca Hospital de la Santa Creu i Sant Pau
Barcelona, Spain

Systematic review team

For treatment recommendations:
Nancy Santesso (lead), Angela Barbara and **Meha Bhatt**
Michael G. DeGroote Cochrane Canada Centre
McMaster University
Hamilton, Canada

For syphilis testing:
Jason Ong (lead), Eric Chow, Christopher Fairley, Su Mei Goh, Janet Towns, Warittha Tieosapjareon and **Ying Zhang**
Monash University and Melbourne Sexual Health Centre
Melbourne, Australia

For partner services:
Nicholas Henschke
Cochrane Response
Heidelberg, Germany

Michael Marks
London School of Hygiene & Tropical Medicine
London, United Kingdom

Oriol Mitjà
Fight AIDS and Infectious Disease Foundation
Barcelona, Spain

Minh Duc Pham
Burnet Institute
Melbourne, Australia

Gemma Villanueva
Cochrane Response
London, United Kingdom

WHO Secretariat and Steering Committee

Members based at WHO headquarters (Geneva, Switzerland)

Avni Amin
Technical Officer
Department of Sexual and Reproductive Health and Research (SRH)

Kingsley Asiedu
Medical Officer
Department of Neglected Tropical Diseases

Rachel Baggaley
Unit Head, Testing, Prevention and Populations
Department of Global HIV, Hepatitis and Sexually Transmitted Infection Programmes (HHS)

Magdalena Barr-DiChiara
Technical Officer
Department of HHS

Maeve Brito de Mello
Technical Officer
Department of HHS

Peter Cherutich
Consultant
Department of HHS

Meg Doherty
Director
Department of HHS

Sami Gottlieb
Medical Officer
Department of SRH

Benedikt Huttner
Team Lead
Department of Access to Medicines and Health Products

Cheryl Johnson
Technical Officer
Department of HHS

James Kiarie
Unit Head
Department of SRH

Mark Lanigan
Technical Officer
Regulation and Prequalification

Celine Lastrucci
Technical Officer
Department of HHS

Niklas Luhmann
Technical Officer
Department of HHS

Ismail Maatouk
Technical Officer
Department of HHS

Gitau Mburu
Scientist
Department of SRH

Daniel McCartney
Consultant
Department of HHS

Antons Mozalevskis
Technical Officer
Department of HHS

Yamuna Mundade
Programme Manager
Department of HHS

Morkor Newman Owiredu
Medical Officer
Department of HHS

Anne-Laure Page
Scientist
Regulation and Prequalification

Carmen Pessoa da Silva
Unit Head
Department of Surveillance, Prevention and Control

Jane Rowley
Technical Officer
Department of HHS

Özge Tunçalp
Medical Officer
Department of Maternal, Newborn, Child and Adolescent Health and Ageing

Igor Toskin
Scientist
Department of SRH

Annette Verster
Technical Officer
Department of HHS

Marco Vitoria
Medical Officer
Department of HHS

Lara Vojnov
Technical Officer
Department of HHS

Teodora Wi[a]
Lead, Sexually Transmitted Infections
Department of HHS

[a] Overall coordinator of the STI guidelines.

Members based at WHO regional offices

Stela Bivol
Unit Lead, Joint Infectious Diseases
WHO Regional Office for Europe

Joumana Hermez
Regional Adviser
WHO Regional Office for the Eastern Mediterranean

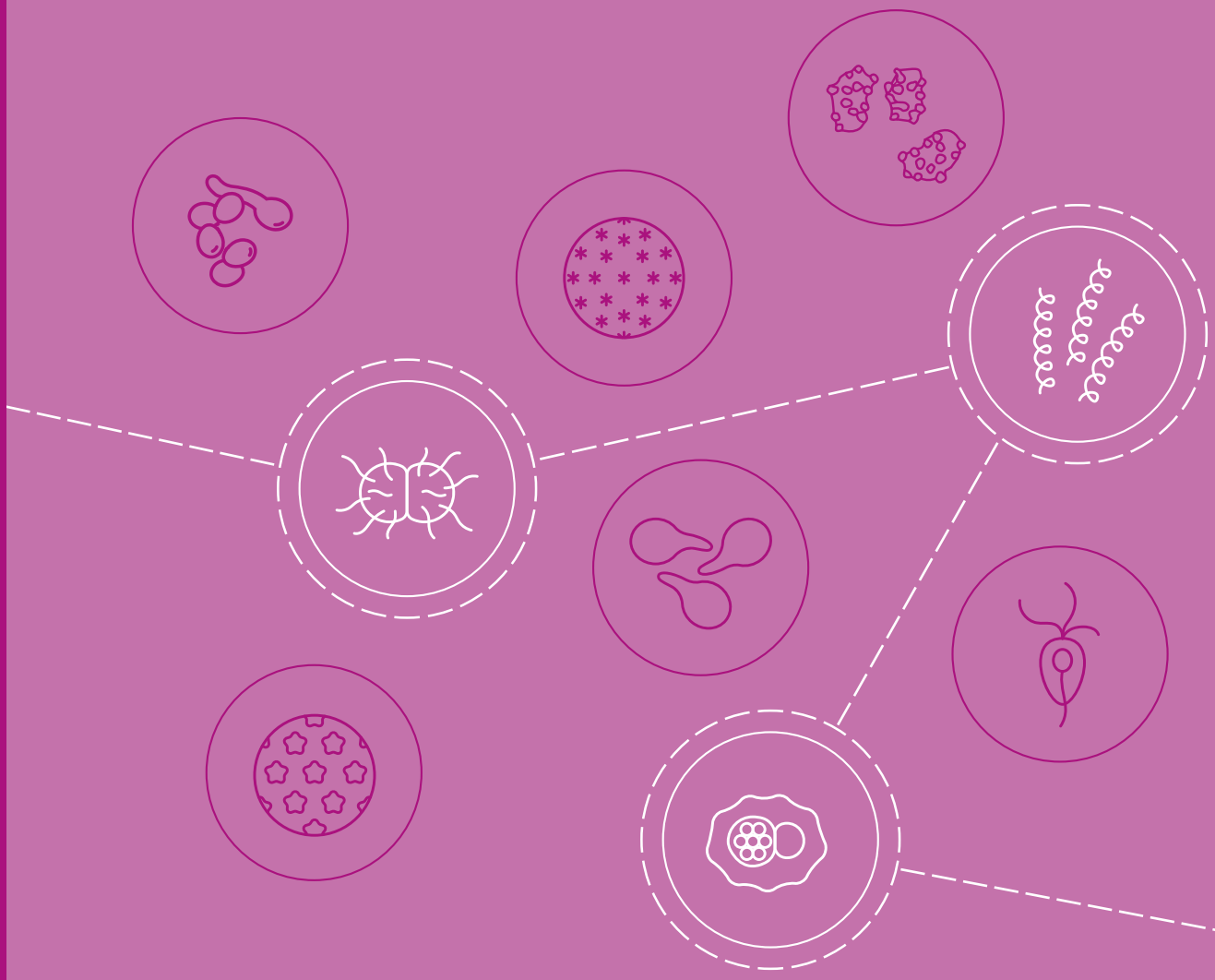
Kiyohika Izumi
Medical Officer
WHO Regional Office for the Western Pacific

Frank Lule
Medical Officer, HIV/AIDS Treatment and Care
WHO Regional Office for Africa

Ruben Mayorga Sagastume
Unit Chief, HIV, Hepatitis, Tuberculosis and STIs
WHO Regional Office for the Americas

Bharat Rewari
Regional Advisor, Hepatitis, HIV and STIs
WHO Regional Office for South-East Asia

Annex 2.
Declarations of interests and management of conflicts of interest



STI Guideline Development Group members

Name	1. Employment and consulting	2. Research support	3. Investment interests	4. Intellectual property	5. Public statements and positions	6. Tobacco products	Conflicts and management plan*
Laith Abu Raddad (Weill Cornell Medical College, Qatar)	–	–	–	–	–	–	Full participation
Yaw Adu-Sarkodie (Kwame Nkrumah University of Science and Technology, Ghana)	–	–	–	–	–	–	Full participation
Mircea Betiu (Nicolae Testimitanu State University of Medicine and Pharmacy, Republic of Moldova)	–	–	–	–	–	–	Full participation
Catriona Bradshaw (Monash University and Alfred Hospital, Australia)	Funding from Abbott to support development of STI testing recommendations in countries across the Asia-Pacific region (A$ 3800).	Australian Research Council Grant to Monash University that contains contributions from the Government, two diagnostic companies (SpeeDx and Cepheid) and nongovernmental organizations including the Global Antibiotic Research and Development Partnership (GARDP) to support work on the development of resistance diagnostics and antimicrobial resistance (AMR) (A$ 1.5 million). Diagnostic kits and GeneXpert platform donated for use in specific investigator-initiated research.	–	–	–	–	Full participation – not related to gonorrhoea, chlamydia or syphilis treatment
Xiang-Sheng Chen (National Center for AIDS/STD Control and Prevention, China)	–	–	–	–	–	–	Full participation

Name	1. Employment and consulting	2. Research support	3. Investment interests	4. Intellectual property	5. Public statements and positions	6. Tobacco products	Conflicts and management plan*
Chido Dziva Chikwari (Biomedical Research and Training Institute, Zimbabwe)	–	–	–	–	–	–	Full participation
Amina El Kettani (Ministry of Health, Morocco)	–	–	–	–	–	–	Full participation
Patricia Garcia (Cayetano Heredia University, Peru)	–	–	–	–	–	–	Full participation
William M. Geisler (University of Alabama at Birmingham, United States of America [USA])	–	Research support from Hologic for study of *M. genitalium* prevalence and resistance in the USA (US$ 240 920).	–	–	–	–	Full participation – not related to gonorrhoea, chlamydia or syphilis treatment
Kimberly Green (PATH, Viet Nam)	–	Funding from the United States Agency for International Development (USAID) for STI screening among key populations as part of provision of pre-exposure prophylaxis (PrEP). Funding from the Hepatitis Fund for triple elimination, including syphilis screening (US$ 50 000).	–	–	–	–	Full participation – not related to gonorrhoea, chlamydia or syphilis treatment
Somesh Gupta (All India Institute of Medical Sciences, India)	–	–	–	–	–	–	Full participation
Edward W. Hook III (University of Alabama at Birmingham, USA)	Member of advisory board for Visby Diagnostics (US$ 10 000) and Talsis Diagnostics.	–	–	–	–	–	Full participation – not related to gonorrhoea, chlamydia or syphilis treatment

Name	1. Employment and consulting	2. Research support	3. Investment interests	4. Intellectual property	5. Public statements and positions	6. Tobacco products	Conflicts and management plan*
Rena Janamnuaysook (Institute of HIV Research and Innovation, Thailand)	–	–	–	–	–	–	Full participation
Nathalie Kapp (International Planned Parenthood Federation, United Kingdom of Great Britain and Northern Ireland)	–	–	–	–	–	–	Full participation
Hamida Khattabi (Independent consultant, Morocco)	–	–	–	–	–	–	Full participation
Rossaphorn Kittyaowamarn (Ministry of Public Health, Thailand)	–	Multicentre randomized, open-label, non-inferiority trial to evaluate the efficacy and safety of single-dose oral Zoliflodacin for treatment of patients with uncomplicated gonorrhoea (GARDP).	–	–	–	–	Partial participation – no participation in any gonorrhoea treatment recommendations
Jeffrey D. Klausner (University of California, Los Angeles, USA)	Consulting with Diagnostics Direct (< US$ 5000) and Visby (< US$ 5000).	Research support from Cepheid for donated research supplies and loaned research equipment (US$ 10 000).	–	–	–	–	Full participation – not related to gonorrhoea, chlamydia or syphilis treatment
Ranmini Kularatne (Labtests, New Zealand)	–	–	–	–	–	–	Full participation
Peter Kyambadde (Ministry of Health, Uganda)	–	–	–	–	–	–	Full participation
David Lewis (Western Sydney Sexual Health Centre, Australia)	–	–	–	–	–	–	Full participation

Name	1. Employment and consulting	2. Research support	3. Investment interests	4. Intellectual property	5. Public statements and positions	6. Tobacco products	Conflicts and management plan*
Philippe Mayaud (London School of Hygiene & Tropical Medicine, United Kingdom)	–	Research support from Abbott Diagnostics for sample collection for development of diagnostic tests for *N. gonorrhoeae* and *C. trachomatis* (US$ 350 000).	–	–	–	–	Full participation – not related to gonorrhoea, chlamydia or syphilis treatment
Saiqa Mullick (Wits Reproductive Health and HIV Institute [RHI], South Africa)	–	Wits RHI is awaiting a potential donation of long-acting injectable cabotegravir (CAB-LA) from the drug developer for a planned implementation science study. Wits RHI has also been involved in the clinical trials of CAB-LA; however, funding was not received directly from the product developer. Wits RHI runs various clinical trials (where Saiqa Mullick is not a principal investigator) with multiple donors but no profit is made from any of these trials/projects.	–	–	–	–	Full participation – not related to gonorrhoea, chlamydia or syphilis treatment
Francis Ndowa (Skin and Genito-Urinary Medicine Clinic, Zimbabwe)	–	–	–	–	–	–	Full participation
Lilani Rajapaksa (Ministry of Health, Sri Lanka)	–	–	–	–	–	–	Full participation
Kees Rietmeijer (Denver Public Health Department, USA)	Past consulting with Sentient (ceased 2023), and WHO (ceased 2022).	–	–	–	–	–	Declared. None are active. Full participation.

Name	1. Employment and consulting	2. Research support	3. Investment interests	4. Intellectual property	5. Public statements and positions	6. Tobacco products	Conflicts and management plan*
Danvic Rosadiño (LoveYourself Inc., Philippines)	–	–	–	–	–	–	Full participation
Jonathan Ross (University Hospitals Birmingham NHS Foundation Trust, United Kingdom)	Consultancy advice in relation to clinical trials (GSK plc.).	Research payments to his employer for his role as principal investigator for clinical trial.	Investments (participant and his wife) in GSK and AstraZeneca.	–	–	–	Declared. Finance not significant. Full participation.
Anna Shapiro (Global Network of Sex Work Projects, United Kingdom)	–	–	–	–	–	–	Full participation
Daniel Simões (Coalition Plus, Portugal)	Consultant with European AIDS Treatment Group.	Member of Country Support core team (trainer) with the Center of Excellence for Health Immunity and Infections.	–	–	–	–	Full participation
Jane Thiomi (LVCT Health, Kenya)	–	–	–	–	–	–	Full participation
Jane Tomnay (University of Melbourne, Australia)	–	–	–	–	–	–	Full participation
Magnus Unemo (Örebro University Hospital, Sweden)	–	–	–	–	–	–	Full participation
Bea Vuylsteke (Institute of Tropical Medicine, Belgium)	–	–	–	–	–	–	Full participation
Judith Wasserheit (University of Washington, USA)	–	–	–	–	–	–	Full participation
Observers							

Name	1. Employment and consulting	2. Research support	3. Investment interests	4. Intellectual property	5. Public statements and positions	6. Tobacco products	Conflicts and management plan*
Laura Bachman (Centers for Disease Control and Prevention, USA)	–	–	–	–	–	–	NA
Azadeh Baghaki (Unitaid, Switzerland)	–	–	–	–	–	–	NA
Lindley Barbee (Centers for Disease Control and Prevention, USA)	–	Previous research support from Hologic, Nabriva, SpeeDx (ended 30 June 2022).	–	–	–	–	NA
Francis Kakooza (Makerere University, Uganda)	–	–	–	–	–	–	NA
Fernando Pascal Martinez (Global Antibiotic Research and Development Partnership, Spain)	–	–	–	–	–	–	NA
Tim Sladden (United Nations Population Fund, USA)	–	–	–	–	–	–	NA

External Review Group members

Name	1. Employment and consulting	2. Research support	3. Investment interests	4. Intellectual property	5. Public statements and positions	6. Tobacco products	Conflicts and management plan
Henry J.C. de Vries (Amsterdam Sexual Health Clinic, Kingdom of the Netherlands)	–	–	–	–	–	–	Full participation
Hans Benjamin Hampel (University of Zurich, Switzerland)	–	–	–	–	–	–	Full participation
Kausar Jabeen (The Aga Khan University, Pakistan)	–	–	–	–	–	–	Full participation
Monica Lahra (Prince of Wales Hospital, Australia)	–	–	–	–	–	–	Full participation
Pham Thi Lan (Hanoi Medical University, Viet Nam)	–	–	–	–	–	–	Full participation
Ahmed Latif (public health consultant, Australia)	–	–	–	–	–	–	Full participation
Ioannis Mameletzis (consultant, Ukraine)	–	–	–	–	–	–	Full participation
Angelica Espinosa Miranda (Ministry of Health, Brazil)	–	–	–	–	–	–	Full participation
Koleka Mlisana (National Health Laboratory Service, South Africa)	–	–	–	–	–	–	Full participation
Lori Newman (National Institutes of Health, USA)	–	–	–	–	–	–	Full participation

Name	1. Employment and consulting	2. Research support	3. Investment interests	4. Intellectual property	5. Public statements and positions	6. Tobacco products	Conflicts and management plan
Catherine Ngugui (Ministry of Health, Kenya)	–	Research support from GARDP, Drugs for Neglected Diseases Initiative (DNDI) and the Ministry of Health for a study on prevalence of *C. trachomatis* and *N. gonorrhoeae* infections among pregnant women and key populations in Kenya (US$ 40 000; ceased 2022).	–	–	Former Director of National AIDS and STI Control in Kenya.	–	None are active. Full participation.
Remco Peters (University of Pretoria, South Africa)	–	Research support from the Foundation for Innovative New Diagnostics (FIND) for evaluation of lateral flow assay for point-of-care detection of *N. gonorrhoeae* (US$ 645 000). Support from the South African Medical Research Council for a project on AMR and molecular typing of *N. gonorrhoeae* isolates in the Eastern Cape province, South Africa (US$ 50 000, ceased March 2023).	–	–	–	–	Full participation – not related to gonorrhoea, chlamydia or syphilis treatment
Reshmie Ramautarsing (Institute of HIV Research and Innovation, Thailand)	–	–	–	–	–	–	Full participation
Pachara Sirivongrangson (Ministry of Public Health, Thailand)	Consulting work for GARDP (US$ 10 000).	–	–	–	–	–	Full participation
Melanie Taylor (Center for Disease Control and Prevention, USA)	–	–	–	–	–	–	Full participation

Name	1. Employment and consulting	2. Research support	3. Investment interests	4. Intellectual property	5. Public statements and positions	6. Tobacco products	Conflicts and management plan
Janet Wilson (Leeds Teaching Hospitals NHS Trust, United Kingdom)	–	–	–	–	–	–	Full participation
Valerie Wilson (Caribbean Med Labs Foundation, Trinidad and Tobago)	–	–	–	–	–	–	Full participation

For more information, please contact:

World Health Organization
Global HIV, Hepatitis and Sexually Transmitted Infections Programmes
20 Avenue Appia
1211 Geneva 27
Switzerland

Email: hiv-aids@who.int
Website: https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/
www.who.int

978-92-4-009076-7