

Guidelines for the management of asymptomatic sexually transmitted infections



World Health
Organization

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Executive summary

The global burden of sexually transmitted infections (STIs) is high, with more than 30 pathogens, including bacteria, viruses and parasites, known to be transmitted through sexual contact. WHO estimates for 2020 indicate that there were 374 million new cases of curable STIs (gonorrhoea, chlamydia, syphilis and trichomoniasis) among people 15–49 years old. This includes 156 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, amounting to about 1 million new curable STIs every day. In 2022, the number of new syphilis cases increased to 8.0 million.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. In addition, 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 in the recent global health sector strategies for HIV, viral hepatitis and STIs. To achieve these targets, such as a 90% reduction in both gonorrhoea and syphilis infections by 2030, the strategy emphasizes the importance of improving access to prevention, diagnostic and treatment services for people with STIs. These guidelines support the management of asymptomatic STIs.

One challenge to responding to the burden of STIs is that these infections can be asymptomatic to a large and variable extent. In some individuals, such as biological women, gonococcal and chlamydial infections of the cervix can be asymptomatic in about 50–97% of cases. In anatomical sites other than the urethra and cervix, such as the anorectal and oropharyngeal sites, symptoms are usually minimal to absent in up to about 85% of cases.

Further, the treatment of people with STIs is complicated by the rapidly changing antimicrobial susceptibility patterns of various sexually transmitted pathogens, such as *N. gonorrhoeae* and *Mycoplasma genitalium*, to available antibiotics, with concerns about the eventual development of untreatable infections with serious sexual and reproductive health consequences. Asymptomatic STIs, especially in the pharynx or rectum, may be a reservoir for the selection of antimicrobial resistance when antimicrobial agents are given for other conditions but are below the minimal inhibitory concentration of the pre-existing STI pathogens.

Antimicrobial resistance in *N. gonorrhoeae* has emerged for every drug available for empirical first-line treatment, with the extended-spectrum cephalosporin, ceftriaxone, currently being the last option in most countries. Certain antibiotics, including azithromycin, are at relatively high risk of selection of bacterial resistance, and use needs to be reserved for certain pathogens, including *M. genitalium*.

These guidelines focus on the management of people with asymptomatic STIs by providing evidence-informed recommendations to screen for *N. gonorrhoeae* and *C. trachomatis*. These recommendations complement the WHO guidelines on syphilis screening among pregnant women, sex workers and men who have sex with men, syphilis self-testing and treponemal and non-treponemal testing; guidelines on STI partner services; guidelines on treatment of people with specific STIs (*N. gonorrhoeae*, *C. trachomatis*, *M. genitalium*, *T. pallidum*, *Trichomonas vaginalis*, bacterial vaginosis, *Candida albicans*, herpes simplex virus, human papillomavirus [genital warts]) and guidelines for the management of symptomatic STIs. All these guidelines will be included in the forthcoming WHO consolidated guidelines on STI prevention and care.

The objectives of these guidelines are:

- to provide evidence-informed recommendations on the screening of people with asymptomatic STIs; and
- to support countries and national programmes in developing national guidelines for the management of STIs towards reaching the 2030 global sector strategy targets on STIs.

These guidelines are intended for policy-makers, programme managers, health-care 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,

¹ The most up-to-date STI estimates are always 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>.

international, nongovernmental, civil society and community-based organizations as well as 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. Systematic reviews and modelling were conducted to address the guideline objectives. The 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 before they were submitted to the WHO Guidelines Review Committee.

Summary of recommendations

These guidelines provide recommendations for the asymptomatic screening of *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. The recommendations apply to pregnant women, sexually active adolescents and young people, sex workers and men who have sex with men (Table 1).

The recommendations are based on the combined prevalence of *N. gonorrhoeae* and *C. trachomatis* at a population level. For sexually active adolescents and young people, a high prevalence in a setting is suggested to be about 15–20% combined for both infections. For pregnant women, due to the adverse health effects on infants, a combined prevalence of 10% in a setting may be considered high. Decision-makers may have access to prevalence data from countries, programmes or clinics, which can be used to determine whether screening should be implemented for the population addressed in the recommendation. Note that the recommendations are intended to be applied based on population-level prevalence and do not involve an assessment of an individual’s risk of infection.

The frequency of screening should depend on sexual exposure, rates of partner exchange and transmission and the cost of the test. It should be balanced against the cost, the number of cases detected and the consequences of not screening. For sex workers and men who have sex with men, screening is advised at least annually or every six months.

Table 1. Summary of the new and updated recommendations on screening asymptomatic sexually transmitted infections (see further detail in Chapter 3)

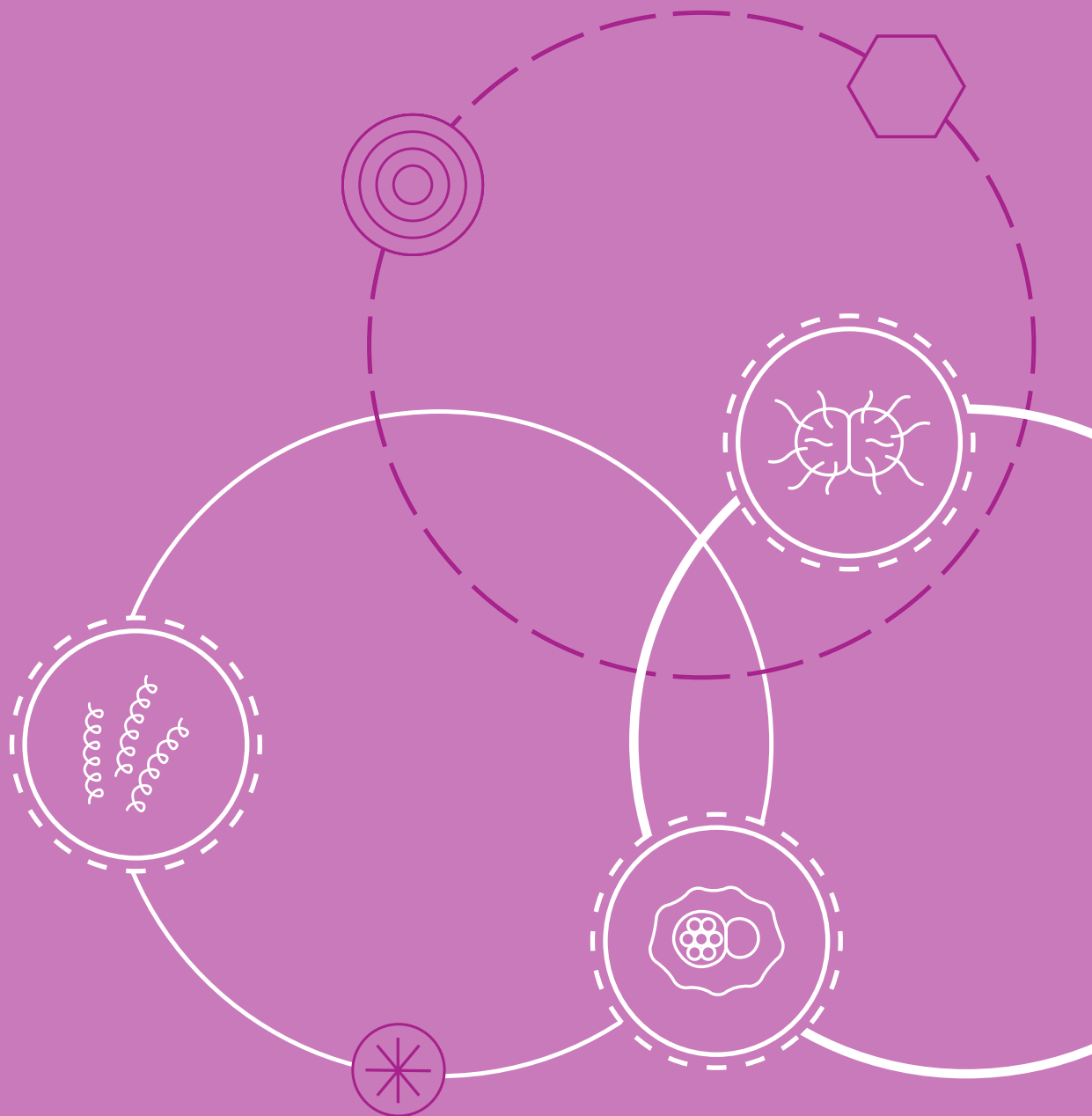
Recommendations	Strength of recommendation and certainty of evidence
Pregnant women	
WHO suggests that pregnant women who have no symptoms of a sexually transmitted infection and are accessing health-care services for antenatal visits be screened for <i>N. gonorrhoeae</i> and/or <i>C. trachomatis</i> in settings where prevalence is high and resources and capacity are available. Recommendations for the management of symptomatic sexually transmitted infections should continue to be followed. ^a	Conditional recommendation, low certainty in evidence of effects (new 2024)
<i>Remarks:</i>	
<ul style="list-style-type: none">This recommendation applies to population-level prevalence rather than individual risk assessments, which have been shown to lack accuracy. This recommendation also applies to screening with either a quality-assured molecular assay, such as nucleic-acid amplification testing or a rapid test with a minimum sensitivity of 80% and specificity of 90%, where treatment is available.Screening should be voluntary with informed consent. Treat for <i>N. gonorrhoeae</i> and/or <i>C. trachomatis</i> based on the results of the quality-assured test using the national treatment guidelines. Sexual partners of people testing positive should also be tested and treated, if positive.	

Recommendations	Strength of recommendation and certainty of evidence
Adolescents and young people	
<p>WHO suggests that sexually active adolescents and young people (10–24 years old) who have no symptoms of a sexually transmitted infection and are accessing health-care services be screened for <i>N. gonorrhoeae</i> and/or <i>C. trachomatis</i> in settings where prevalence is high and resources and capacity are available. Recommendations for the management of symptomatic sexually transmitted infections should continue to be followed.^a</p> <p><i>Remarks:</i></p> <ul style="list-style-type: none"> When balancing resources and benefits of screening, adolescent girls and young women may be prioritized. This recommendation applies to population-level prevalence rather than individual risk assessments, which have been shown to lack accuracy. However, exploring sexual activity in the past 12 months prior to screening is essential. This recommendation also applies to screening with either a quality-assured molecular assay, such as nucleic-acid amplification testing, or a rapid test with a minimum sensitivity of 80% and specificity of 90%, where treatment is available. Screening should be voluntary with informed consent. Treat for <i>N. gonorrhoeae</i> and/or <i>C. trachomatis</i> based on the results of the quality-assured test using the national treatment guidelines. Sexual partners of people testing positive should also be tested and treated, if positive. 	<p>Conditional recommendation, low certainty in evidence of effects (new 2024)</p>
Sex workers	
<p>WHO suggests that sex workers accessing health-care services who have no symptoms of a sexually transmitted infection be screened for <i>N. gonorrhoeae</i> and/or <i>C. trachomatis</i>. Recommendations for the management of symptomatic sexually transmitted infections should continue to be followed.^a</p> <p><i>Remarks:</i></p> <ul style="list-style-type: none"> This recommendation applies to screening with either a quality-assured molecular assay, such as nucleic-acid amplification testing, or a rapid test with a minimum sensitivity of 80% and specificity of 90%, where treatment is available. The anatomical site depends on sexual behaviour, and pooling samples can reduce cost and increase yield, depending on the resources available. Screening should be voluntary with informed consent. Treat for <i>N. gonorrhoeae</i> and/or <i>C. trachomatis</i> based on the results of the quality-assured test using the national treatment guidelines. Sexual partners of people testing positive should also be tested and treated, if positive. 	<p>Conditional recommendation, low certainty in evidence of effects (updated 2024)</p>

Recommendations	Strength of recommendation and certainty of evidence
Men who have sex with men	
<p>WHO suggests that men who have sex with men accessing health-care services who have no symptoms of a sexually transmitted infection be screened for <i>N. gonorrhoeae</i> and/or <i>C. trachomatis</i>. Recommendations for the management of symptomatic sexually transmitted infections should continue to be followed.^a</p> <p><i>Remarks:</i></p> <ul style="list-style-type: none"> • This recommendation applies to screening with either a quality-assured molecular assay, such as nucleic-acid amplification testing, or a rapid test with a minimum sensitivity of 80% and specificity of 90%, where treatment is available. The anatomical site depends on sexual behaviour, and pooling samples can reduce cost and increase yield, depending on the resources available. • Screening should be voluntary with informed consent. Treat for <i>N. gonorrhoeae</i> and/or <i>C. trachomatis</i> based on the results of the quality-assured test using the national treatment guidelines. Sexual partners of people testing positive should also be tested and treated, if positive. 	<p>Conditional recommendation, low certainty in evidence of effects (<i>updated 2024</i>)</p>

^a 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.

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, cancer and pregnancy complications, and they further indirectly facilitate the sexual transmission of HIV; therefore, in addition to affecting 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. WHO estimates that, in 2020, 128.5 million (90.0 million–173.8 million) new cases of chlamydia and 82.4 million (47.7 million–130.4 million) new cases of gonorrhoea occurred among people 15–49 years old worldwide (1). The burden of chlamydia falls primarily on women, who have higher rates of this disease than men and among 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). Men have higher rates of gonococcal infection, but the complications disproportionately 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 leads to significant morbidity and mortality. WHO estimates that in 2022, 8.0 million (5.6 million–10.4 million) new cases occurred among adolescents and adults aged 15–49 years worldwide (7). Syphilis is transmitted through sexual contact with infectious lesions of the mucous membranes or abraded skin, blood transfusion or across the placenta during pregnancy. Without treatment, syphilis can cause serious health complications, including neurological problems. Congenital syphilis results in a wide range of adverse birth outcomes. Global estimates from 2022 indicate 150 000 early fetal deaths and stillbirths, 70 000 neonatal deaths and 55 000 preterm or low-birthweight births (8). However, syphilis can be easily cured with treatment, and the risk of adverse outcomes 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, men who have sex with men, trans and gender-diverse 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 *Global health sector strategies on HIV, viral hepatitis and sexual transmitted infections 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 (9). To achieve these targets, the strategy on STIs highlights the importance of enabling people with STIs or at risk of STIs to more easily access prevention, diagnostics, treatment and care.

1.2 Rationale for new and updated recommendations

To reduce STIs and prevent complications, high-quality STI prevention and care services are essential. Many STIs are transmitted from people who are unaware of their infections, either from lack of knowledge or awareness of the symptoms and signs of STIs or from lack of any symptoms. This requires developing evidence-informed guidelines on STI treatment and comprehensive case management, including screening, diagnosis, treatment and care. Correct and effective treatment of people with STIs, ideally given and taken on the same day at the first contact between patients and health-care providers, is an important public health measure in controlling STIs since it endeavours to break the chain of transmission of the infection without delay.

Since the publication of the WHO *Guidelines for the management of sexually transmitted infections* in 2003 (10), changes in the epidemiology of STIs and progress in prevention, diagnosis and treatment of STIs and HIV have necessitated changes in approaches to STI prevention and management.

In 2021, WHO published *Guidelines for the management of symptomatic sexually transmitted infections* with evidence-informed recommendations to improve the quality of STI case management of people with symptomatic STIs, including aetiological diagnosis and syndromic management (11).

Syndromic management is widely used to manage symptomatic people with STIs. In most resource-limited settings, the syndromic management flowcharts are still the standard of care, where laboratory diagnosis is not available or where available but results are not available on the same day. Although there are some shortcomings related to the STI syndromic approach, it remains an essential component of the management of symptomatic STIs. These guidelines aim to raise the quality of STI case management of symptomatic people with STIs by providing evidence-informed recommendations to address symptomatic STIs.

Many STIs, such as gonococcal infection, chlamydial infection, syphilis and HIV may be asymptomatic for many infected people, who therefore may not be aware that they are infected. The accurate identification of asymptomatic and symptomatic STIs depends on the availability of diagnostic tests and a screening strategy. Although high-quality diagnostic tests for STIs are available, they are often expensive, frequently labour intensive and, at this stage, often not suitable for use as rapid point-of-care tests.

Traditionally, diagnostic tests for STIs have been used to address STI prevention and control in the following areas:

- to provide a definitive diagnosis for aetiology-guided treatment;
- to provide screening services for asymptomatic individuals at risk of infection;
- to provide statistical information on the prevalence of various infections;
- to determine the antimicrobial susceptibility of causative organisms; and
- to assist with the management of sexual partners.

These areas remain important in supporting national programmes to know the burden of infections in their settings, to set evidence-informed targets for control of infections in their communities and to determine trends over time. To this end, WHO updated the manual on *Laboratory and point-of-care diagnostic testing for sexually transmitted infections, including HIV* (12).

1.3 Objectives

The objectives of these guidelines are:

- to provide evidence-informed recommendations on the screening of people with asymptomatic STIs, specifically *N. gonorrhoeae* and *C. trachomatis*; and
- to support countries and national programmes in developing national guidelines for the management of STIs towards reaching the 2030 global health sector strategy targets on STIs.

1.4 Target audience

These guidelines are intended for STI prevention and control programme managers at the national level and for frontline health-care providers in primary, secondary and tertiary health-care facilities involved in treating and managing people with STIs. The recommendations and guidance are also important for health-care workers, including lay providers and community health workers, responsible for offering and performing STI services. These guidelines will be relevant for implementers of STI services, including HIV, sexual and reproductive health services and maternal and child health 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, and service providers and users of pre-exposure prophylaxis (PrEP) for HIV. The guidelines will be able to support the planning, implementation and monitoring and evaluation of such services, and be used as an advocacy tool in seeking the financial and human resources required to deliver adequate, acceptable and equitable STI care for everyone who needs STI services.

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

1.5 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 the 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 follow the guideline principles of the WHO Model List of Essential Medicines, including to prevent the emergence and spread of antibiotic resistance, parsimony, feasibility and alignment with the WHO List of Critically Important Antimicrobials for Human Medicine, including the WHO AWaRe (access, watch, reserve) categorization of antibiotics (13,14).

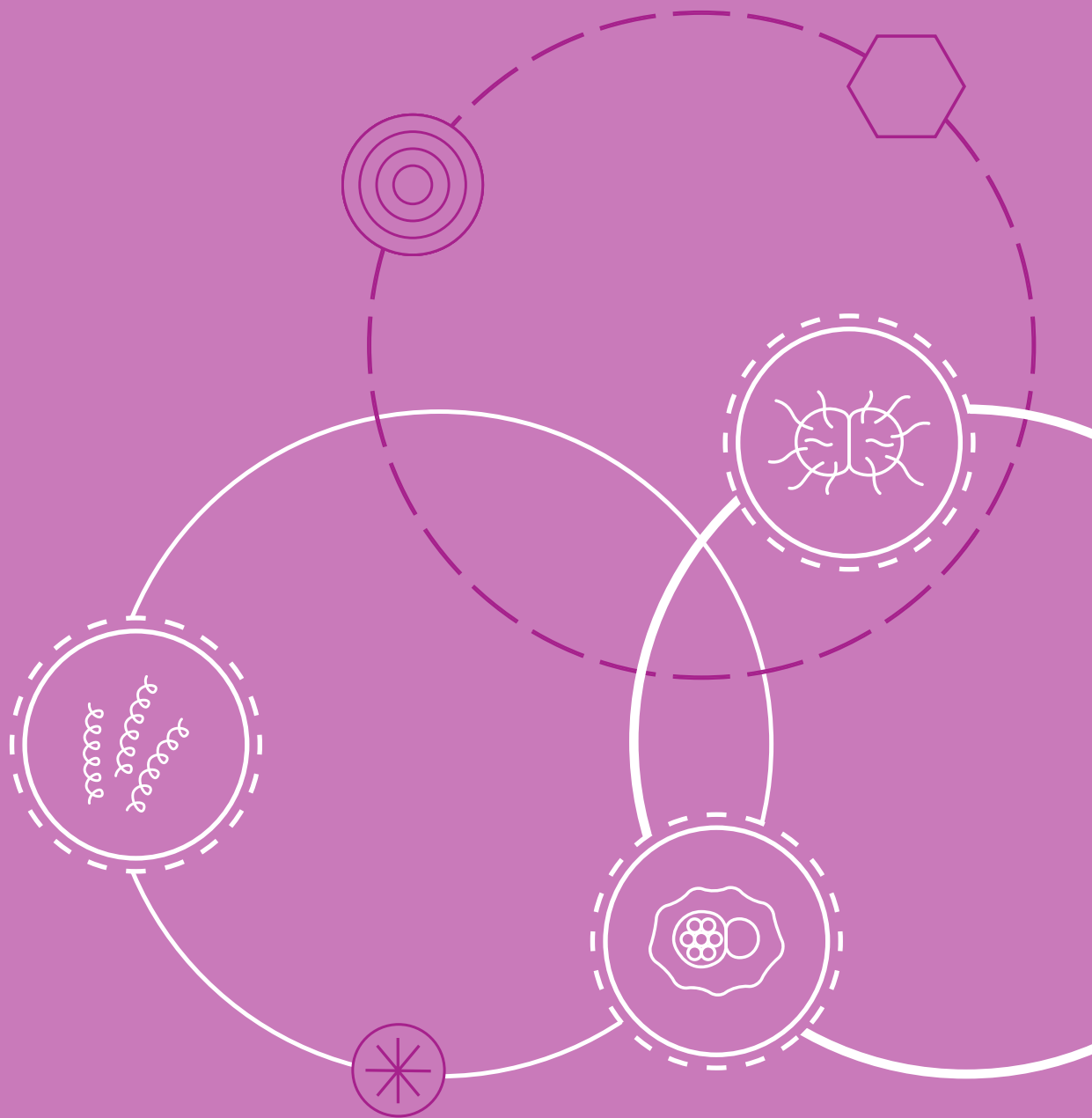
1.6 Structure of the guidelines

These guidelines provide evidence-informed recommendations for screening for asymptomatic STIs and are intended to become subsections of the forthcoming consolidated guidelines for the prevention, diagnosis, treatment and care of STIs.

Chapter 3 presents the new and updated recommendations for the screening of asymptomatic *N. gonorrhoeae* and *C. trachomatis* among pregnant women, sexually active adolescents and young people, sex workers and men who have sex with men. The recommendations are based on the most recent evidence. These guidelines provide direction for countries as they develop national recommendations; however, national guidelines should also consider the local prevalence and health service capacity and resources.

Chapter 4 presents other existing recommendations related to the asymptomatic screening of *T. pallidum* (syphilis) along with implementation considerations for the management of asymptomatic STIs in Chapter 5.

2. Methods



2. Methods

2.1 Overview

These guidelines were developed in accordance with procedures in the *WHO handbook for guideline development* (15).

The Guideline Development Group identified key questions about screening for asymptomatic STIs in 2020. A systematic review was conducted and modelling work completed. Evidence summaries were developed for each question and evidence assessed according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

The Guideline Development Group developed the recommendations by 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 electronically via the GRADEpro application with the Guideline Development Group for their feedback and used in meetings to support the judgements of the Guideline Development Group to make recommendations. Consistent with previous WHO guidelines, these guidelines are based on a public health approach.

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 WHO. Each group played a specific role, as described below. Annex 1 lists the members of these groups and other contributors and their affiliations.

- 1. 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. Participants included other units and WHO staff members from the Department of Global HIV, Hepatitis and Sexually Transmitted Infections Programmes, 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 WHO Steering Committee also included WHO technical staff members from every WHO region.
- 2. Guideline Development Group.** This group comprised non-United Nation and non-WHO experts, health professionals and representatives of groups most affected by the recommendations in the guidelines. The 37 Guideline Development Group 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 Guideline Development Group 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 members were selected in coordination with the WHO Steering Committee and WHO country and regional offices. The WHO Steering Committee reviewed curricula vitae, declaration-of-interest forms and confidentiality agreements. The proposed membership list was posted for public review and comment and then finalized.
- 3. External Review Group.** 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.

4. **External evidence reviewers and modellers, led by a methodologist.** 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.
5. **External observers.** Representatives of the European Centre for Disease Prevention and Control (ECDC), the Global Antibiotic Research and Development Partnership (GARDP), and the United Nations Population Fund (UNFPA) attended the Guideline Development Group meeting as observers. These organizations have a long history of collaboration with the WHO Department of Global HIV, Hepatitis and Sexually Transmitted Infections Programmes.

All members of the Guideline Development Group, External Review Group 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. WHO reviewed all declarations, and no conflicts of interest sufficient to preclude any Guideline Development Group 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 questions

In December 2013, the first Guideline Development Group meeting was held to agree on the scope of the STI guidelines and to identify the different phases for developing the various components of the guidelines. In December 2020, Guideline Development Group met to determine the population, intervention, comparison, outcome (PICO) questions for the management of asymptomatic STIs. The populations identified included adults and other special populations: adolescents, pregnant women, people living with HIV and populations disproportionately affected by STIs, such as men who have sex with men and sex workers.

Specific questions were developed using the PICO elements outlined in Table 2.1, in the following format:

- Should screening [using strategy] versus no screening for *N. gonorrhoeae* and *C. trachomatis* infections be used for [population] with no symptoms of an STI who are accessing health-care services?

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

Population	Intervention and comparator		Outcomes (in order of importance)
	Screening	Treatment based on diagnosis	
Women and men without STI symptoms and high risk of infection <ul style="list-style-type: none"> Sexually active People living with HIV Sex workers Men who have sex with men Adolescents and young people Pregnant women Family planning attendees Settings: <ul style="list-style-type: none"> Low prevalence High prevalence Primary health care or health-care facility Community centre 	STIs: chlamydial infection and gonorrhoea With laboratory test <ul style="list-style-type: none"> Nucleic acid amplification test for gonorrhoea, chlamydia and trichomoniasis Culture and sensitivity (gonorrhoea) Rapid syphilis test Microscopy Risk assessment, genital examination No screening Frequency of screening	Diagnosis and treatment based on specific aetiology <ul style="list-style-type: none"> Gonorrhoea Chlamydial infection 	<ul style="list-style-type: none"> STI incidence and prevalence Adverse birth outcomes for pregnant women (miscarriage, stillborn, preterm, low birthweight) Pelvic inflammatory disease, chronic pelvic pain or infertility Antimicrobial resistance Adverse drug or treatment effect Stigma Treatment of infected partner Microbiological cure HIV transmission or acquisition

2.4 Reviews of the evidence and modelling to inform guidelines

2.4.1. Reviews of the evidence

A systematic review of screening approaches for the management of asymptomatic STIs was conducted in PubMed up to July 2022 for studies published in English (Web Annex E). Studies of any study design reporting on outcomes (including acceptability, feasibility, resources and equity indicators) when screening people with no symptoms or unknown symptom status for an STI in low- and middle-income countries were included. The search for primary studies was updated in April 2024 in Ovid Medline and Embase for low- and middle-income countries and high-income countries in any language. Targeted searches for key guidelines published in high-income countries were also conducted to determine the evidence supporting the recommendations.

Very few studies were found measuring important outcomes, and data were not pooled statistically across studies. Individual studies were summarized narratively, and if more than one study contributed data to an outcome the results were pooled as a range. Studies that reported the prevalence of an STI (not measured at follow-up) were used as input for a decision-tree model.

2.4.2. Modelling

A decision-tree model was used to explore the health-care outcomes and costs of screening asymptomatic individuals for *N. gonorrhoeae* and *C. trachomatis*. The model provided a framework for considering the clinical and economic impact of alternative screening approaches for asymptomatic individuals in different populations. This is based on a model commissioned by WHO to inform the WHO symptomatic STI case management guidelines (see Web Annex F).

The model was used to explore different scenarios that included combinations of approaches for managing asymptomatic infections. This included no screening or treatment, screening with a laboratory-based nucleic-acid amplification test (sensitivity 95% and specificity 98%), screening with a high-performance point-of-care test (90% and 95%), screening with a lower-performance point-of-care test (80% and 90%), screening with Gram stain and use of risk assessment before test. The impact of each scenario was assessed using several outcome indicators in nine populations. Web Annex B describes the assumptions in and structure of the model in detail. Briefly, the model operates in a static manner and therefore does not assess the evolving impact of screening initiatives over time at the population level. *N. gonorrhoeae* and *C. trachomatis* are treated as a single entity in infection for testing purposes. The model assumes uniformity in the probability of symptom development and between infections. The probability of clinical outcomes between men and women, regardless of the infecting pathogen, is equivalent. Additionally, the model assumes that all people screened are treated and that treatment is successful.

2.5 Assessment and presentation of the evidence

The certainty of the evidence for each outcome from the review of primary studies and from the model were assessed separately using the GRADE approach based on the domains for risk of bias, inconsistency, indirectness, imprecision, publication bias, effect size, dose response and opposing confounding (15,16).

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; and
- 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 (tables to facilitate decision-making for the updated recommendations) were drafted before the Guideline Development Group meeting using the GRADEpro software (17) (see Web Annexes A–D for the evidence-to-decision frameworks for each recommendation).

2.6 Making recommendations

Because of the complexity of developing these recommendations, several subgroup virtual meetings were initiated in 2022 to review the evidence. The Guideline Development Group subgroup proposed collecting additional evidence, including risk factors for *N. gonorrhoeae* and *C. trachomatis* infections and asymptomatic and symptomatic gonococcal and chlamydial infections and to model the cost and effectiveness of different strategies of diagnosing *N. gonorrhoeae* and *C. trachomatis* infections in 2023. A series of virtual meetings followed to discuss the evidence and propose draft recommendations for the various syndromes.

A virtual Guideline Development Group meeting was organized in April 2024 to support the development of the recommendations. Before this meeting, the draft recommendations and evidence-to-decision tables were circulated to the Guideline Development Group via the GRADEpro application to obtain feedback. In April 2024, the Guideline Development Group reviewed feedback, the evidence-to-decision tables and summaries of the evidence again to make judgements about the effects of the screening strategies in different populations and decide on whether to make strong or conditional recommendations for or against screening. The Guideline Development Group agreed by consensus, and there were no disagreements requiring voting. The recommendations and evidence-to-decision tables were finalized electronically via GRADEpro in June 2024.

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 Guideline Development Group that the desirable consequences (such as beneficial health outcomes) of the recommendations outweigh the undesirable consequences (such as adverse effects) and considers 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 Guideline Development Group is confident that the desirable consequences of adhering to the recommendation outweigh the undesirable consequences.
2. A conditional recommendation is one for which the Guideline Development Group concluded that the desirable consequences of adhering to the recommendation probably outweigh the undesirable consequences but is not confident about these trade-offs (15).

Table 2.2 explains the implications of the differing strengths of recommendations for patients, clinicians and policy-makers. Remarks were added to the recommendations 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 Guideline Development Group and the External Review Group for comments and feedback. All input was considered and the guidelines were revised. External peer review was completed in June 2024, and the text was edited, but neither of these processes affected 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.	Most individuals in this situation would want the suggested course of action, but some 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.

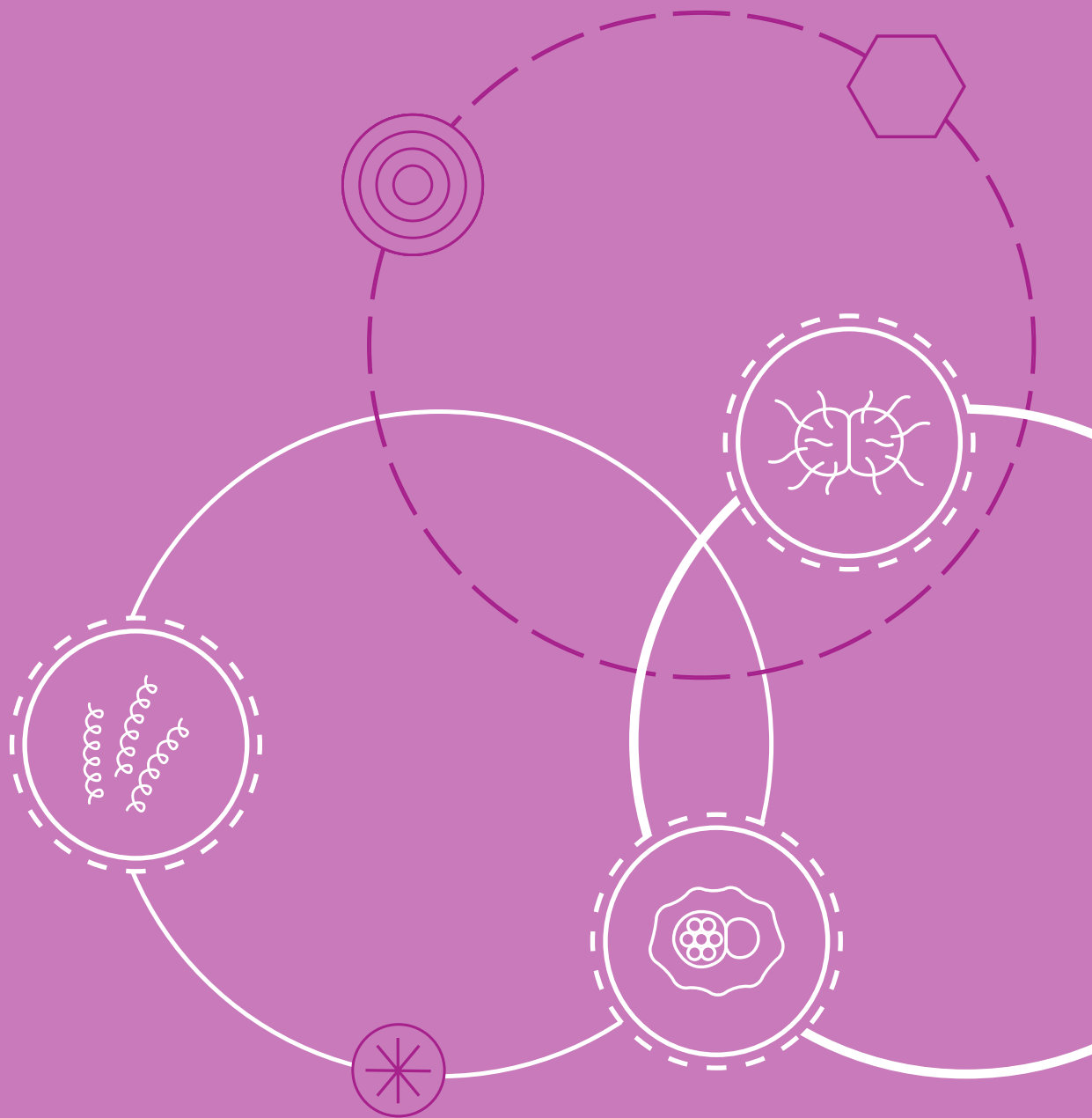
Source: WHO handbook for guideline development (15).

2.7 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 by WHO experts were implemented. Declaration of interests statements were obtained from all members of the Guideline Development Group and the External Review Group before they assumed their roles. At the beginning of the Guideline Development Group meetings, including subgroup meetings, the members disclosed their declared interests and any new ones. Annex 2 summarizes the declaration of interests statements.

Eleven members of the Guideline Development Group declared interests. All were deemed to be able to fully participate since conflict was not related to diagnostics or screening of asymptomatic infections.

3. Updated and new recommendations



3. Updated and new recommendations

This section provides recommendations for screening for *N. gonorrhoeae* and *C. trachomatis* for pregnant women, adolescents and young people, sex workers and men who have sex with men, with no symptoms of an STI who are accessing a health-care service.

The recommendations are based on the combined prevalence of *N. gonorrhoeae* and *C. trachomatis* at the population level. For sexually active adolescents and young people, a high prevalence in a setting is suggested to be about 15–20% combined for both infections. For pregnant women, because of the adverse health effects on infants, a combined prevalence of 10% in a setting may be considered high. Decision-makers may have access to prevalence data from countries, programmes or clinics, which can be used to determine whether screening should be implemented for the population addressed in the recommendation. Note that the recommendations are intended to be applied based on population-level prevalence and do not involve assessment of an individual's risk of infection.

3.1 Pregnant women

Recommendation (new 2024)

WHO suggests that pregnant women who have no symptoms of a sexually transmitted infection and are accessing health-care services for antenatal visits be screened for *N. gonorrhoeae* and/or *C. trachomatis* in settings where prevalence is high and resources and capacity are available. Recommendations for the management of symptomatic sexually transmitted infections should continue to be followed.^a

Conditional recommendation, low certainty in evidence of effects

Remarks: This recommendation applies to population-level prevalence rather than individual risk assessments, which have been shown to lack accuracy. This recommendation also applies to screening with either a quality-assured molecular assay, such as nucleic-acid amplification testing or a rapid test with a minimum sensitivity of 80% and specificity of 90%, where treatment is available.

Screening should be voluntary with informed consent. Treat for *N. gonorrhoeae* and/or *C. trachomatis* based on the results of the quality-assured test using the national treatment guidelines. Sexual partners of people testing positive should also be tested and treated, if positive.

^aGuidelines for the management of symptomatic sexually transmitted infections (11).

Summary of the evidence

Overall, the certainty in the evidence is low for small or moderate benefits and trivial harm of different screening strategies to screen pregnant women who have no symptoms of an STI and are accessing health-care services for antenatal visits (see the evidence-to-decision table in Web Annex A). The evidence for benefits and harm was based on a search for evidence up to April 2024 (see Web Annex E for the systematic review of the literature) and the results from the decision model (see Web Annex F). We found a randomized controlled trial (18) and a non-randomized study (19,20) and used results from the decision model. Both primary studies occurred in low- and middle-income countries, where the prevalence of the STIs was 23% and 25%. The Guideline Development Group judged that there is likely little to no difference in premature birth and/or low birthweight between screening with a point-of-care test and no screening. Based on the modelled results, the critical benefit of screening (and where the greatest value was placed) is reducing the transmission of *N. gonorrhoeae* and *C. trachomatis* to infants, which can lead to conjunctivitis or pneumonia. In settings where prevalence is high (such as greater than 20%), screening could lead to a significant reduction in infections

(about 25 per 1000 fewer). However, the reduction is smaller where prevalence is lower (about 12 per 1000 fewer). There remains uncertainty about whether antimicrobial resistance may slightly increase (due to higher antibiotic consumption) and the long-term consequences of asymptomatic infections.

A review of the acceptability and feasibility of rapid screening and treatment of pregnant women with STIs in six low- and middle-income countries found that acceptability ranged from 85% to 99% and feasibility from 91% to 100% (21). Barriers to access and acceptability include logistical barriers and knowledge about STIs and stigma (22). The Guideline Development Group agreed that screening is probably acceptable to pregnant women and feasible. However, the resources and costs of nucleic-acid amplification tests or point-of-care tests to screen are moderate, and these tests may not be available in some settings. The Guideline Development Group therefore agreed that there may be greater benefits over undesirable consequences in settings where the prevalence is greater than 20%, but where prevalence is lower, the benefits may not outweigh the costs and required resources.

3.2 Adolescents and young people

Recommendation (new 2024)

WHO suggests that sexually active adolescents and young people (10–24 years old) who have no symptoms of a sexually transmitted infection and are accessing health-care services be screened for *N. gonorrhoeae* and/or *C. trachomatis* in settings where prevalence is high and resources and capacity are available. Recommendations for management of symptomatic sexually transmitted infections should continue to be followed.^a

Conditional recommendation, low certainty in evidence of effects

Remarks: When balancing resources and benefits of screening, adolescent girls and young women may be prioritized. This recommendation applies to population-level prevalence rather than individual risk assessments, which have been shown to lack accuracy. However, exploring sexual activity in the past 12 months prior to screening is essential. This recommendation also applies to screening with either a quality-assured molecular assay, such as nucleic-acid amplification testing, or a rapid test with a minimum sensitivity of 80% and specificity of 90%, where treatment is available.

Screening should be voluntary with informed consent. Treat for *N. gonorrhoeae* and/or *C. trachomatis* based on the results of the quality-assured test using the national treatment guidelines. Sexual partners of people testing positive should also be tested and treated, if positive.

^aGuidelines for the management of symptomatic sexually transmitted infections (11).

Summary of the evidence

Overall, the certainty in the evidence is low for moderate benefits and small harm of screening strategies to screen sexually active adolescent girls and young women and young people who have no symptoms of an STI and low for trivial benefits and small harm for adolescent boys and young men (see the evidence-to-decision table in Web Annex B). The evidence for benefits and harm was based on a search for evidence up to April 2024 (see Web Annex E for the systematic review of the literature) and the results from the decision model (see Web Annex F). We found a systematic review (23) of four randomized controlled trials and two recently published studies, one case series in a low- and middle-income country (24) and one randomized controlled trial (25). The prevalence of *N. gonorrhoeae* and *C. trachomatis* combined was 10.4% for males, and 20.5% for females in the case series in a low- and middle-income country and 20% in the model. The benefits for both males and females could include reducing transmission of STIs which could reduce their incidence, but there was no evidence reporting this outcome. For males, the Guideline Development Group agreed that infection may cause little to no difference in the incidence of epididymitis based on the modelled evidence (8 fewer per 1000). For females, the model estimated that the risk of pelvic inflammatory disease may be reduced by about 20 people per 1000, but the review of randomized controlled trials found about 2 fewer. The estimate from the model found that infertility may be reduced by 5 per 1000. The recently published randomized controlled trial found that prevalence may be slightly reduced (0.5%). The Guideline Development Group agreed that stigma and its consequences may be a small harm for both males and females. There is also uncertainty about the long-term consequences of asymptomatic infection or whether antibiotic resistance caused by greater

antibiotic consumption may be slightly increased with screening. The Guideline Development Group placed greatest value on the potential for reducing the transmission of STIs and adverse outcomes and therefore agreed that the benefits would outweigh the harm, especially for females.

A review of four studies reporting acceptability found that testing is probably acceptable, but there are barriers, such as cost, lack of knowledge about risk and embarrassment (24,26,27). The resources and costs of nucleic-acid amplification tests or point-of-care tests to screen are large, especially considering the large number of adolescents and young people that would need to be screened. Screening tests (molecular assay such as nucleic-acid amplification testing or rapid tests) may not be available in some countries, potentially reducing equity. Consequently, screening may not be feasible in many countries. The Guideline Development Group agreed that there may be greater benefits over undesirable effects in settings where prevalence is greater than 20%, and more so in adolescent girls and young women, who should be given priority for screening when resources and capacity could be available.

3.3 Sex workers

Recommendation (updated 2024)

WHO suggests that sex workers accessing health-care services who have no symptoms of a sexually transmitted infection be screened for *N. gonorrhoeae* and/or *C. trachomatis*. Recommendations for the management of symptomatic sexually transmitted infections should continue to be followed.^a

Conditional recommendation, low certainty in evidence effects

Remarks: This recommendation also applies to screening with either a quality-assured molecular assay, such as nucleic-acid amplification testing, or a rapid test with a minimum sensitivity of 80% and specificity of 90%, where treatment is available. The anatomical site depends on sexual behaviour and pooling samples can reduce cost and increase yield, depending on the resources available.

Screening should be voluntary with informed consent. Treat for *N. gonorrhoeae* and/or *C. trachomatis* based on the results of the quality-assured test using the national treatment guidelines. Sexual partners of people testing positive should also be tested and treated, if positive.

^aGuidelines for the management of symptomatic sexually transmitted infections (11).

Summary of the evidence

Overall, the certainty in the evidence is low for moderate benefits (such as reduction in STI transmission) and trivial harm of screening strategies to screen sex workers who have no symptoms of an STI (see the evidence-to-decision table in Web Annex C). This evidence was assessed as applicable to sex workers defined as female, male, trans and gender-diverse adults (18 years of age and older) who receive money or goods in exchange for sexual services, either regularly or occasionally. The evidence for benefits and harm was based on a search for evidence up to April 2024 (see Web Annex E for the systematic review of the literature) and results from the decision model (see Web Annex F). We found a recent randomized controlled trial (28) and a review of evidence from previously published WHO guidelines in 2012 (29). Evidence from the 2012 guidelines included eight non-comparative studies and one randomized controlled trial that reported HIV, *N. gonorrhoeae* and *C. trachomatis* acquisition with screening provided in combination with other interventions (such as condom promotion, education and STI treatment). Most studies found reductions in the prevalence of infections over time. The more recent randomized controlled trial in a low- and middle-income country found that the prevalence of *C. trachomatis* was lower by 3.7% and *N. gonorrhoeae* by 0.7% with screening versus no screening. Other benefits for female sex workers estimated in the model included reduction in pelvic inflammatory disease (20 fewer per 1000) and infertility (5 fewer per 1000). The Guideline Development Group placed the greatest value on the potential to reduce onward transmission of STIs, although this was not measured in studies. There is uncertainty about the harm (such as whether antibiotic resistance may be slightly increased because of greater antibiotic consumption or about the long-term consequences of asymptomatic infection). Overall, the health benefits of screening outweighed harm for sex workers.

Other factors did not change favouring screening in this population. We found a systematic review of 14 studies in low- and middle-income countries and high-income countries assessing the facilitators and barriers to screening by female sex workers (30). It found that a greater number of sex clients or partners, awareness of STIs, trained peers and emotional support may increase the uptake of testing. Barriers may be lack of awareness of risk of STIs or of the availability of testing, time constraints and long waiting lists, cost, judgemental attitudes of health-care providers, stigma and criminalization of sex work. The Guideline Development Group agreed that screening is probably acceptable to female sex workers, but they may experience multiple barriers. The Guideline Development Group also agreed that the resources and costs of nucleic-acid amplification tests or point-of-care tests to screen are moderate, and screening may not be feasible in many countries that currently do not have these tests.

3.4 Men who have sex with men

Recommendation (updated 2024)

WHO suggests that men who have sex with men accessing health-care services who have no symptoms of a sexually transmitted infection be screened for *N. gonorrhoeae* and/or *C. trachomatis*. Recommendations for the management of symptomatic sexually transmitted infections should continue to be followed.^a

Conditional recommendation, low certainty in evidence of effects

Remarks: This recommendation applies to screening with either a quality-assured molecular assay, such as nucleic-acid amplification testing, or a rapid test with a minimum sensitivity of 80% and specificity of 90%, where treatment is available. The anatomical site depends on sexual behaviour, and pooling samples can reduce cost and increase yield, depending on the resources available.

Screening should be voluntary with informed consent. Treat for *N. gonorrhoeae* and/or *C. trachomatis* based on the results of the quality-assured test using the national treatment guidelines. Sexual partners of people testing positive should also be tested and treated, if positive.

^aGuidelines for the management of symptomatic sexually transmitted infections (11).

Summary of the evidence

Overall, the certainty in the evidence is low for small benefits and trivial harm of screening strategies to screen men who have sex with men who have no symptoms of an STI (see the evidence-to-decision table in Web Annex D). The evidence for benefits and harm was based on a search for evidence up to April 2024 (see Web Annex E for the systematic review of the literature) and results from the decision model (see Web Annex F). We found a systematic review of 12 non-randomized studies (31), a recently published study of men who have sex with men using HIV PrEP in high-income countries (32) and evidence from a previously published WHO guideline (33). Evidence from the guideline included five observational studies in low- and middle-income countries providing data for sensitivity and specificity of different tests and prevalence of urethral and rectal *N. gonorrhoeae* and *C. trachomatis* but did not measure outcomes or the effect of screening. The systematic review found that the prevalence of *N. gonorrhoeae* and *C. trachomatis* at various sites was increased or unchanged in 10 and reduced in six sites over time with screening. Incidence was reported in the randomized controlled trial and found little to no difference (0.5 infections per 1000 person-days). The Guideline Development Group agreed that these benefits of screening may be trivial, but HIV acquisition and transmission to heterosexual populations were not measured in studies. Given the increased risk of HIV acquisition with STIs and the risk of transmission to heterosexual populations, the Guideline Development Group agreed that the benefits are small. Regarding harm, there is uncertainty about whether antibiotic resistance may be slightly increased because of greater antibiotic consumption and about the long-term consequences of asymptomatic infection.

Two studies (32,34) assessed the acceptability of screening and found mixed reactions to screening: some wanted to treat infections and not prevent infections; others wanted asymptomatic infections treated. Evidence on the frequency of screening was also considered from a systematic review of 46 studies (35), of which none directly compared less frequent to more frequent. Although fewer people tested positive when screened every 2–3 months than every 4–6 months, confounding between the populations could be responsible for the difference. The Guideline Development Group agreed that screening is probably acceptable to and feasible for men who have sex with men. The resources and costs of nucleic-acid amplification tests or point-of-care tests to screen asymptomatic men who have sex with men are moderate, and screening may not be feasible in many countries that currently do not have the tests available.

3.5 Research needs

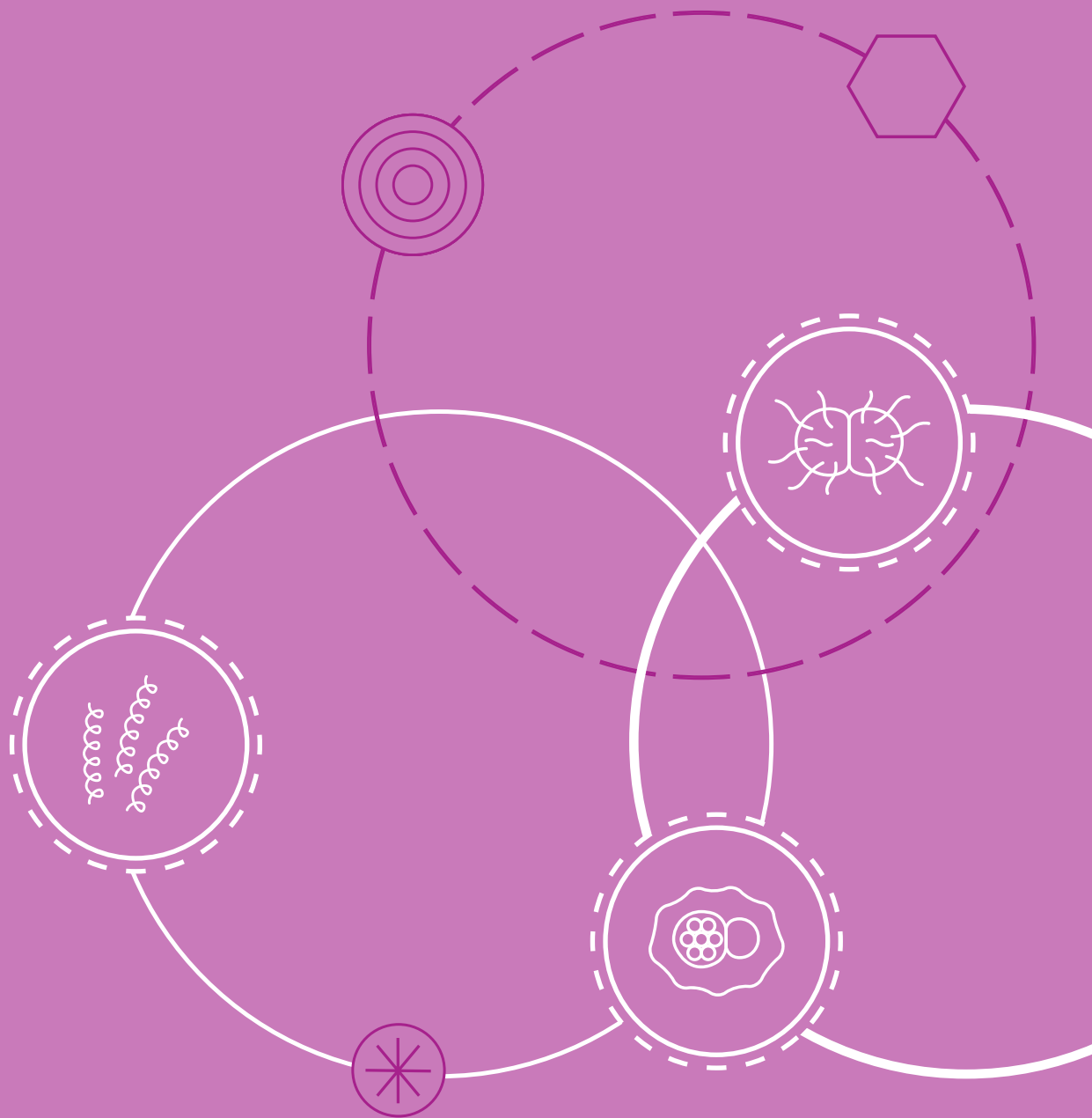
To address the gaps in the certainty of evidence in effects of the asymptomatic screening of STIs, particularly of *N. gonorrhoeae* and *C. trachomatis*, more randomized controlled trials and/or hybrid efficacy and implementation science studies are essential, especially in low- and middle-income countries and among diverse populations. These studies should aim to measure how asymptomatic screening affects the outcomes of transmission, including onward STI transmission, HIV acquisition and transmission, adverse events associated with these infections among pregnant and non-pregnant people and their broader impact on incidence and population health. Implementation outcomes should also be documented as asymptomatic screening procedures are incorporated into clinical services.

Antimicrobial resistance represents a significant area of concern and should be given priority in research efforts to detect any rise in resistance among the pathogens being screened. Collaborative efforts with other sectors should also monitor antimicrobial resistance in non-STI-related organisms. Further studies are necessary to elucidate the role of asymptomatic STIs in transmission to sexual partners and the associated morbidity of untreated infections.

In addition, the development of low-cost, rapid point-of-care tests with high specificity and sensitivity is critically needed. Implementation research focused on the use of point-of-care and nucleic-acid amplification tests for screening is vital to optimize these approaches. Emerging testing technologies should be rigorously evaluated and incorporated into screening programmes in a learn-as-you-go approach.

When screening programmes for asymptomatic infections are implemented, gathering data on potential harm, acceptability and feasibility within various settings and populations is crucial. Moreover, research should explore the sustainability of these programmes, identifying factors contributing to the discontinuation or inefficacy of screening strategies, especially those that fail to achieve high coverage or reach the intended populations.

4. Other recommendations related to asymptomatic screening of STIs



4. Other recommendations related to asymptomatic screening of STIs

4.1 Syphilis

Syphilis is a bacterial STI caused by *T. pallidum* that 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 when maternal infection is not detected and treated sufficiently early in pregnancy. Syphilis, if not treated, results in substantial morbidity and mortality. Syphilis in pregnancy, if untreated, can lead to stillbirth, neonatal death, prematurity, low birthweight, malformations in bones and serious neurological issues. When untreated among 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, and late syphilis comprises 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 (36).

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 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. Further information about syphilis diagnosis is available in *Laboratory and point-of-care diagnostic testing for sexually transmitted infections, including HIV* (12).

WHO has a number of existing recommendations on the screening of asymptomatic syphilis for different populations (Box 4.1).

Box 4.1. Existing WHO recommendations on screening for asymptomatic syphilis infection

Pregnant women (37,38)

- *Recommendation:* WHO recommends screening all pregnant women for syphilis at least once and as early as possible, ideally at the first antenatal care visit (*strong recommendation, moderate-certainty evidence*).

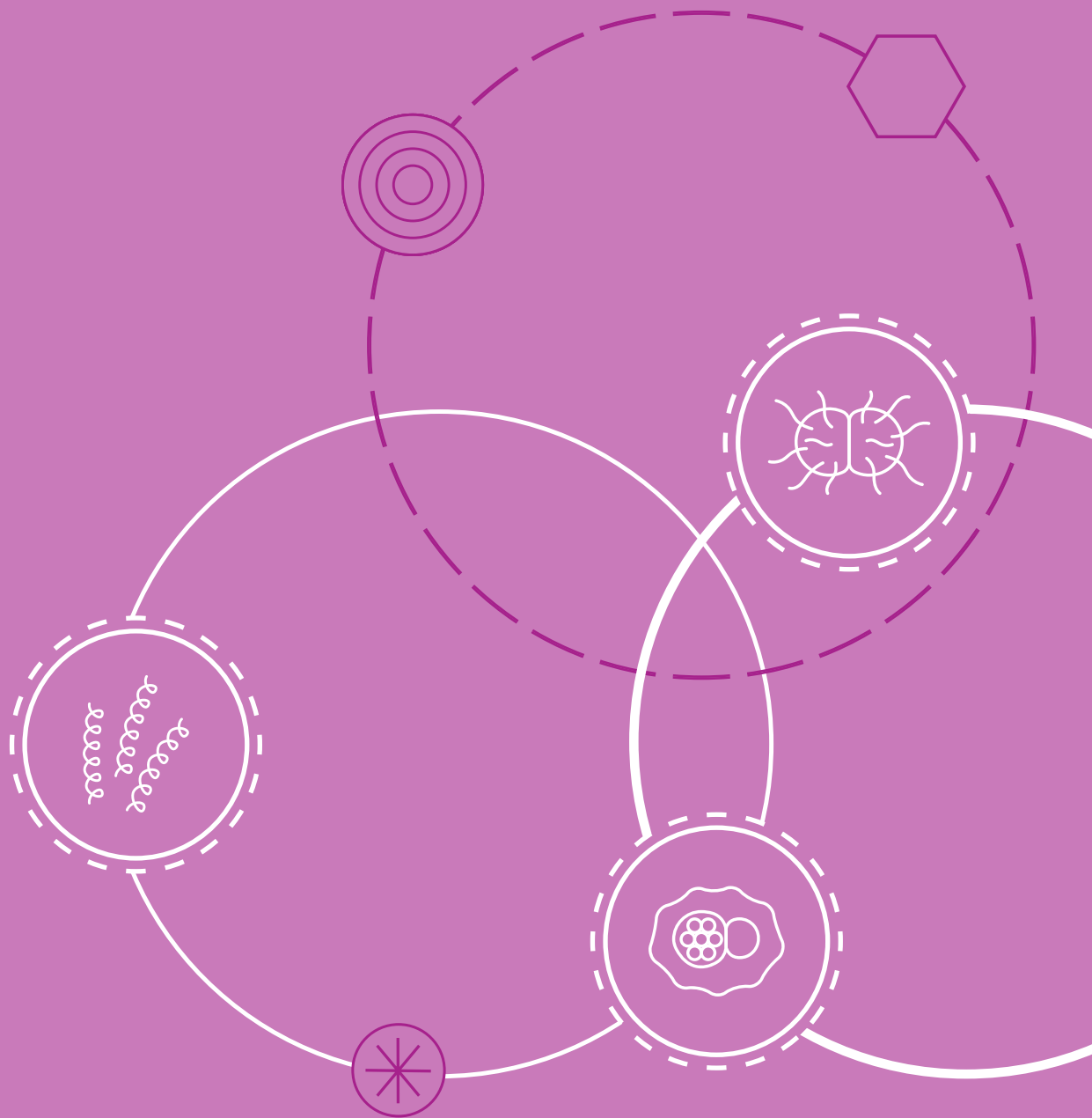
Key populations (39)

- *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*).
- *Recommendation:* WHO suggests offering periodic screening for asymptomatic syphilis infection to sex workers (*conditional recommendation, low certainty of evidence*).

People with STI symptoms (11)

- *Good practice statement:* For people with symptoms of: (1) urethral discharge from the penis; (2) vaginal discharge; (3) lower abdominal pain (among sexually active women); (4) genital ulcers (including anorectal ulcers); or (5) anorectal discharge, good practice includes offering HIV and syphilis testing.

5. Implementation considerations for the management of asymptomatic STIs



5. Implementation considerations for the management of asymptomatic STIs

5.1 Definition of screening

In the context of screening for asymptomatic STIs, especially *N. gonorrhoeae*, *C. trachomatis*, syphilis and HIV, the person being screened would be well and unaware that they may have an infection. Screening, therefore, can be defined as the presumptive identification of unrecognized infection or disease by applying tests, examinations or other procedures that can be applied rapidly to sort out apparently well people who probably have an infection or disease from those who probably do not.

Broadly, three types of screening exist:

- mass screening, with no selection of population, such as checking all infants for hearing problems;
- selective screening, categorized, for example, by age, sex or sexual risk for a specific infection; and
- multi-phased screening, performed periodically, such as annual health examinations.

For STIs, depending on the infection being screened for, the latter two types of screening may be more appropriate. For example, it is generally accepted that *C. trachomatis* is more prevalent in adolescents and young people, and they would, therefore, be an appropriate target population for this pathogen. Key populations, such as men who have sex with men and sex workers, may also be offered screening for STIs including syphilis and HIV. For pregnant women, it is important to exclude syphilis and HIV or, if detected, be offered prompt treatment to prevent adverse pregnancy outcomes and reduce risk of infant infection.

For pregnant women, the screening may be multi-phased and conducted in the first trimester and again near delivery to exclude, or pick up, any infection that may have been acquired in the nine months of pregnancy.

5.2 Rationale and objectives for establishing screening programmes for asymptomatic STIs

Justifying the screening strategy requires that the infections in question constitute a significant public health problem in terms of the morbidity and mortality they may cause and should be amenable to effective treatment that is available and accessible and with a potential for cure.

People may have the most common bacterial and viral STIs (*C. trachomatis*, *N. gonorrhoeae*, HIV, herpes simplex virus and human papillomavirus) and *Trichomonas vaginalis* without symptoms. Some individuals, such as biological women, may have asymptomatic gonococcal and chlamydial infections of the cervix in about 50–97% of cases (40,41). In anatomical sites other than the urethra and the cervix, such as the anorectal and oropharyngeal sites, symptoms are usually minimal to absent in up to about 85% of cases (42).

Asymptomatic infections, especially in anatomical sites such as the pharynx or rectum, may be reservoirs for the selection of antimicrobial resistance when antimicrobial agents are taken for other conditions but at below the minimal inhibitory concentration for the pre-existing STI pathogens (43).

Since about 50–97% of STI infections may be asymptomatic, people with symptomatic infections represent the tip of the iceberg. Ignoring asymptomatic infections is imprudent since people who are infected but without symptoms have been documented to transmit the STI pathogens to their sexual partners (44,45). Asymptomatic STIs can cause significant ill health and mortality as precursors for cancer, including cervical, penile, anal and hepatic cancer. Further, untreated asymptomatic infections can result in an increased risk of transmitting and acquiring HIV.

Before a screening programme is introduced for asymptomatic STIs at the national level, there should be common agreement on the objectives of the intervention, the screening tests to be used, the populations to be screened and the pathogens to be screened for. Considerations on which populations (such as pregnant women and adolescents and young people) to screen will depend on the prevalence, the value placed on the outcomes of not screening (such as infertility among young women, adverse pregnancy outcomes or increased STI transmission) and the cost of the test. The populations for which screening is implemented should be known to have a high prevalence of *N. gonorrhoeae* and *C. trachomatis*. Screening may be cost-effective if it can target population subgroups at higher risk based on available surveillance data. The frequency of screening should depend on sexual exposure, the rates of partner exchange and transmission and the cost of the test. The frequency of screening should be balanced against the cost and the number of cases detected and the consequences of not screening. Based on the evidence for frequency of screening among men who have sex with men, fewer people test positive when screened every 2–3 months than 4–6 months, confounded between populations (34). However, more frequent screening costs more. Sex workers and men who have sex with men should be screened at least annually or every six months.

The main objectives of a screening programme for asymptomatic STIs are:

- to detect the infection at a stage when treatment can be given before the person develops signs, symptoms and complications; and
- to interrupt the chain of transmission of STIs and the impact on the incidence and prevalence of STIs in the community.

5.3 Ethical considerations

Since screening is conducted on healthy people, the ethics of health care must be given priority. The following ethical principles should be observed:

- autonomy: in moral, political, and bioethical philosophy, people must have the capacity to make informed and uncoerced decisions regarding whether to undertake the screening test;
- non-maleficence: the principle of not causing harm or evil to people must be upheld;
- beneficence: the process should be conducted with the intent to do good; and
- justice: fairness must be ensured in how everyone involved is treated.

People also have a mental risk associated with learning that they have an STI, especially sexually active adolescents. Minimizing social risks by ensuring the confidentiality of results is essential. In addition, sexually active adolescents, like sex workers and men who have sex with men, may be vulnerable to coercion and undue influence. Procedures should be in place to ensure that people from these populations receive proper education about screening and that informed consent is obtained. People with positive STI results should receive counselling from trained personnel. Adolescents should be counselled about the potential benefits and risks of disclosing their positive STI status and empowered and supported to decide whether, when, how and to whom to disclose their status.

5.4 Selecting diagnostic tests for screening asymptomatic STIs

Screening tests are intended to determine whether an asymptomatic person has an infection that has not been recognized because lack of symptoms. The accurate identification of asymptomatic STIs depends on the availability of accurate diagnostic tests and a sound screening strategy.

The following guidance should be adhered to in selecting the tests to be used:

- validity: the test should be able to detect as many as possible of the infections in the asymptomatic state, to be determined by the performance characteristics of the test in terms of its sensitivity and specificity;
- reliability: the test should give consistent results with no random errors;
- acceptability and accessibility: the test should cause the least discomfort to the person and should have an affordable cost for the individual and/or the government; and
- the testing can be linked to care, treatment and follow-up.

High-quality diagnostic tests for STIs are available but are currently expensive, frequently labour intensive and currently not suitable for use as rapid point-of-care tests. A screening strategy therefore needs to be established to determine the targeted population and the specific pathogens to be screened. In settings where screening for syphilis and HIV is already established, assessments should be made to determine whether screening for the additional pathogens can be integrated into that population.

5.5 Acceptable performance characteristics of a screening test

To ensure the sustainability of a screening programme, the tests used should be inexpensive and easy to administer and should not cause discomfort that would deter the person from being tested. Further, the tests should be widely available and accessible to the target population. For the test to serve its purpose adequately, it should have acceptably good sensitivity and specificity.

The sensitivity of a screening test is its ability to detect a true positive: correctly identifying an infection among everyone infected. The specificity of a screening test is its ability to detect a true negative: correctly identifying people who do not have infection.

The predictive value is the probability of having the infection given the results of a test. Positive predictive value is the probability that a person with a positive test result has the infection, whereas a negative predictive value is the probability that a person with a negative test result is truly free from infection. Predictive values are determined by the sensitivity and specificity of the test and the prevalence of the infection in the population being tested.

For a screening programme, the specificity is especially important to a health-care provider because a positive test reduces the likelihood that the person tested is free from infection. When the prevalence of infection is low, the positive predictive value will also be low, even if the test has high sensitivity and high specificity. Increasing the positive predictive value in a screening programme therefore requires targeting those at high risk of infection.

The sensitivity and specificity of the test should be evaluated against a gold standard or a reference standard test, and policy-makers should ensure they have this information before selecting screening tests for a screening programme. Currently, the gold standard for diagnostic or screening tests for STIs is molecular-based testing, such as real-time polymerase chain reaction (PCR).

A highly sensitive test for asymptomatic infections would mean that the number of people with asymptomatic infection who are not diagnosed by the test decreases. The test would pick up a high proportion of those infected but may also have some false positives. A highly specific test would produce a small percentage of false-positive results. For a screening programme, high specificity may be desired over sensitivity, especially when the costs of overtreatment need to be avoided, including unnecessary use of antibiotics and

development of antimicrobial resistance. However, as indicated above, the predictive values depend on the prevalence of infection in the community being tested. Nevertheless, since specificity may never be 100%, the tested person should be informed that a negative screening result does not mean the infection is not present but, rather, that the likelihood of infection being present is low. Similarly, a highly sensitive screening test is unlikely to produce false-negative results, and people who test negative on that kind of screening test are therefore very unlikely to be infected. However, false positives, even if fewer, should be borne in mind.

Screening tests should be reliable and reproducible. This is important when point-of-care tests are used for screening since the traffic of people being tested may be high and the tests may be performed in a rush or by different health-care personnel or self-test. The frequent causes of variability of results are usually the following:

- anatomical site from which the sample was taken;
- intraobserver variability because of the differences in interpretation of a test at different times; and
- interobserver variability because of variation of interpretation of a test by two or more health-care providers.

Therefore, regardless of which test is selected for screening, training should be conducted, and standard operating procedures established covering preparation of the person and anatomical site to be tested, collecting and processing the specimen, conducting the test and how to interpret the result.

5.6 Treatment, antibiotic consumption and preparedness for the screening programme

All people testing positive for an STI should be treated based on the national guidelines. In addition, since a screening programme should also constitute part of a prevention strategy, the sexual partners of people testing positive should also be tested and treated, if positive. Testing sexual partners ensures that all antibiotic use is rational and adheres to the principle of antimicrobial stewardship.

An effective and successful screening programme will detect more infections requiring more treatment options than previously obtained for the management of symptomatic infections.

5.7 Screening as an integrated prevention intervention

Screening for asymptomatic STIs should be implemented as part of an integrated prevention intervention and not as a panacea for ending the STI burden on its own. In the general population and in any of the populations selected for targeted STI screening, other prevention interventions should be enhanced and scaled up to maximum coverage for impact. The prevention package for STIs includes the following interventions (46):

- information, education and communication activities aimed at fostering participants' knowledge of STIs and safer sex;
- use of male and female condoms;
- vaccines, currently for the human papillomavirus and hepatitis B;
- voluntary medical male circumcision; and
- suppressive therapy for genital herpes, which may prevent the transmission of herpes simplex virus 2 (HSV-2).

5.8 Ensuring early and effective treatment

All prevention interventions and screening services should be implemented in conjunction with accessible and acceptable STI services for treatment and care for the general population, adolescents and key populations and ensure the following in the process:

- promoting good STI health care-seeking behaviour;
- providing high-quality care for STIs, which ensures immediate treatment; and
- ensuring universal access to STI care for everyone who needs the services and thus putting the services to scale for adequate coverage for maximum impact.

5.9 STI services for key populations, adolescents and young people

The adaptation and implementation of these guidelines should be accompanied by efforts to promote and protect the human rights of people requiring STI care services. This includes ensuring that stigma and discrimination are prevented in service provision while promoting gender equity and ensuring that the use of services is voluntary. Since key populations are disproportionately affected by STIs, it is critical to increase access to STI services for key populations and people living with HIV, including adolescents and young people. In many settings, people from key populations may not disclose their identities or behaviour, particularly in contexts where sex work and certain sexual activities are criminalized. Therefore, services should be designed to be accessible and non-discriminatory, ensuring confidentiality and protection from legal or social repercussions.

The WHO *Consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment and care for key populations* provide recommendations and guidance (39). In addition, the following WHO guidance publications offer further implementation considerations for increasing access to and delivering STI services for key populations:

- *Implementing comprehensive HIV and STI programmes with sex workers: practical approaches from collaborative interventions* (47);
- *Implementing comprehensive HIV and STI programmes with men who have sex with men: practical guidance for collaborative interventions* (48);
- *Implementing comprehensive HIV and STI programmes with transgender people: practical guidance for collaborative interventions* (49); and
- *Implementing comprehensive HIV and HCV programmes with people who inject drugs: practical guidance for collaborative interventions* (50).

Adolescent-friendly health services should be provided, ensuring that they meet the specific needs of adolescents through community-based approaches and training for health-care providers. Services should maintain confidentiality, privacy and non-judgemental attitudes to create a supportive environment for those seeking care. Additional WHO guidance on providing high-quality health-care services for adolescents is available in the following publications:

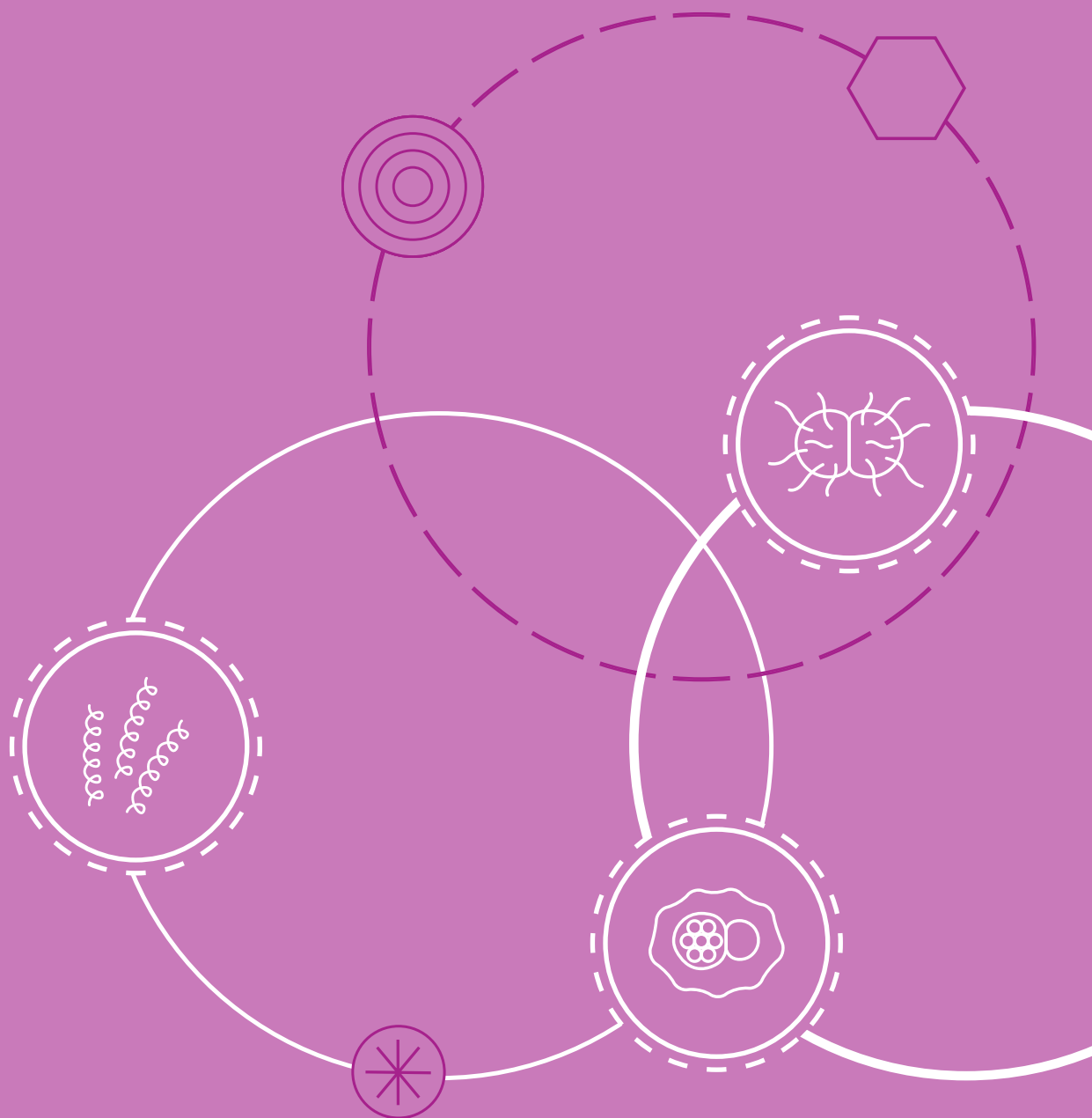
- *Global standards for quality health-care services for adolescents: a guide to implement a standards-driven approach to improve the quality of health-care services for adolescents* (51); and
- *Adolescent-friendly health services for adolescents living with HIV: from theory to practice* (52).

5.10 Antenatal screening for pregnant women

The *WHO recommendations on antenatal care for a positive pregnancy experience* (53) recommend maternal assessments to detect various conditions during pregnancy. These include anaemia, asymptomatic bacteriuria, intimate partner violence, gestational diabetes mellitus, tobacco use, substance use, HIV, syphilis and tuberculosis. All pregnant women should be tested for HIV, as well as syphilis and hepatitis B virus, at least once and as early as possible during pregnancy (38).

In settings with a high prevalence of infections (exceeding 15–20%), WHO also recommends to integrate screening for *N. gonorrhoeae* and *C. trachomatis* into maternal assessments to prevent adverse maternal and newborn outcomes from gonococcal and chlamydial infections.

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, implementing and monitoring the utility of these guidelines.

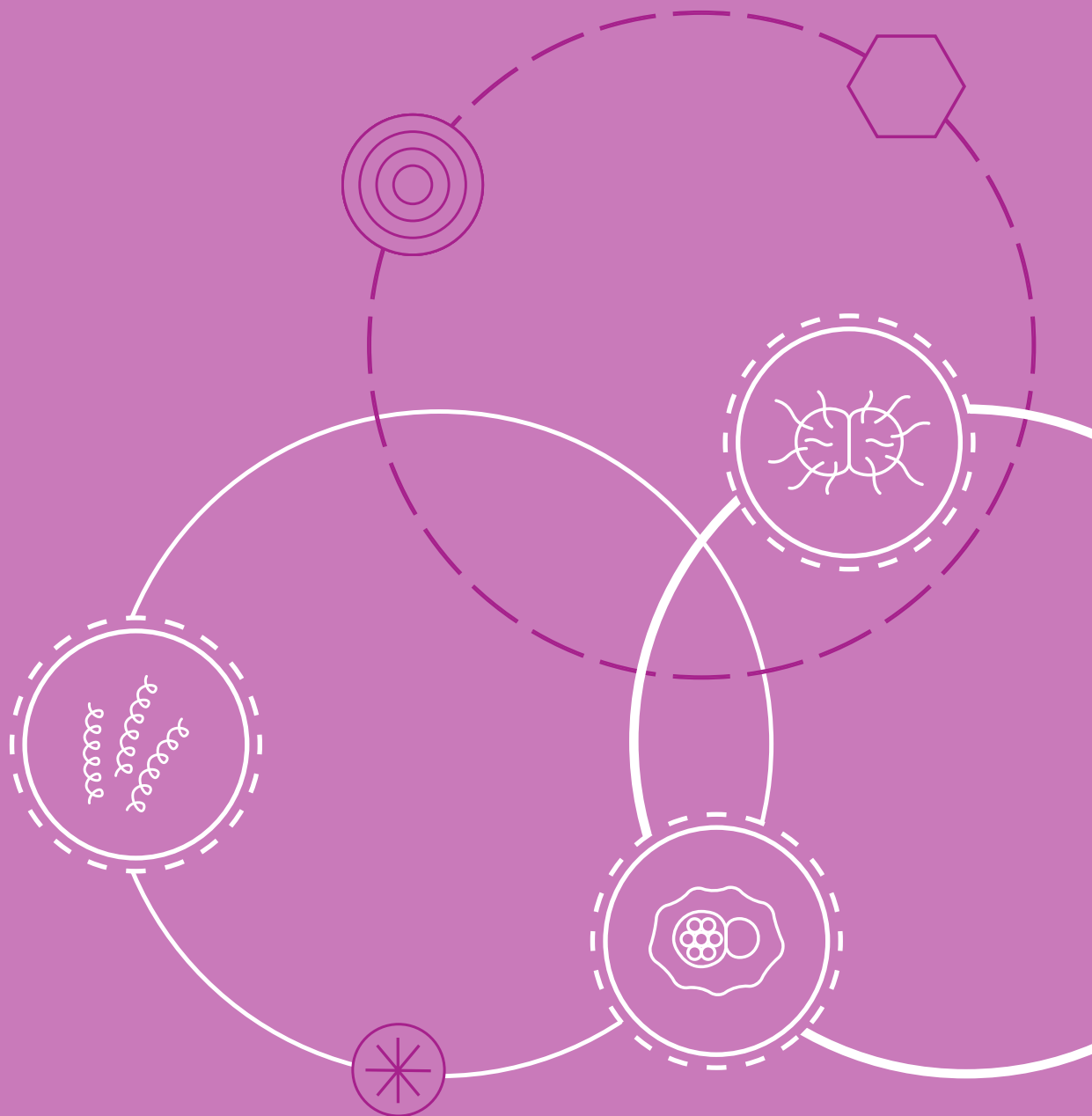
Every level of WHO (headquarters, regional offices and country offices) will work with regional and national partners – including the United Nations Population Fund (UNFPA), the United Nations Children’s Fund (UNICEF), the Joint United Nations Programme on HIV/AIDS (UNAIDS), nongovernmental organizations 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.

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. Some of the mechanisms will be by electronic communication. An electronic follow-up survey of key end-users of these guidelines will be conducted after they have been disseminated for one year. 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 service delivery for STIs and to identify topics or gaps in treatment that need to be addressed in future editions.

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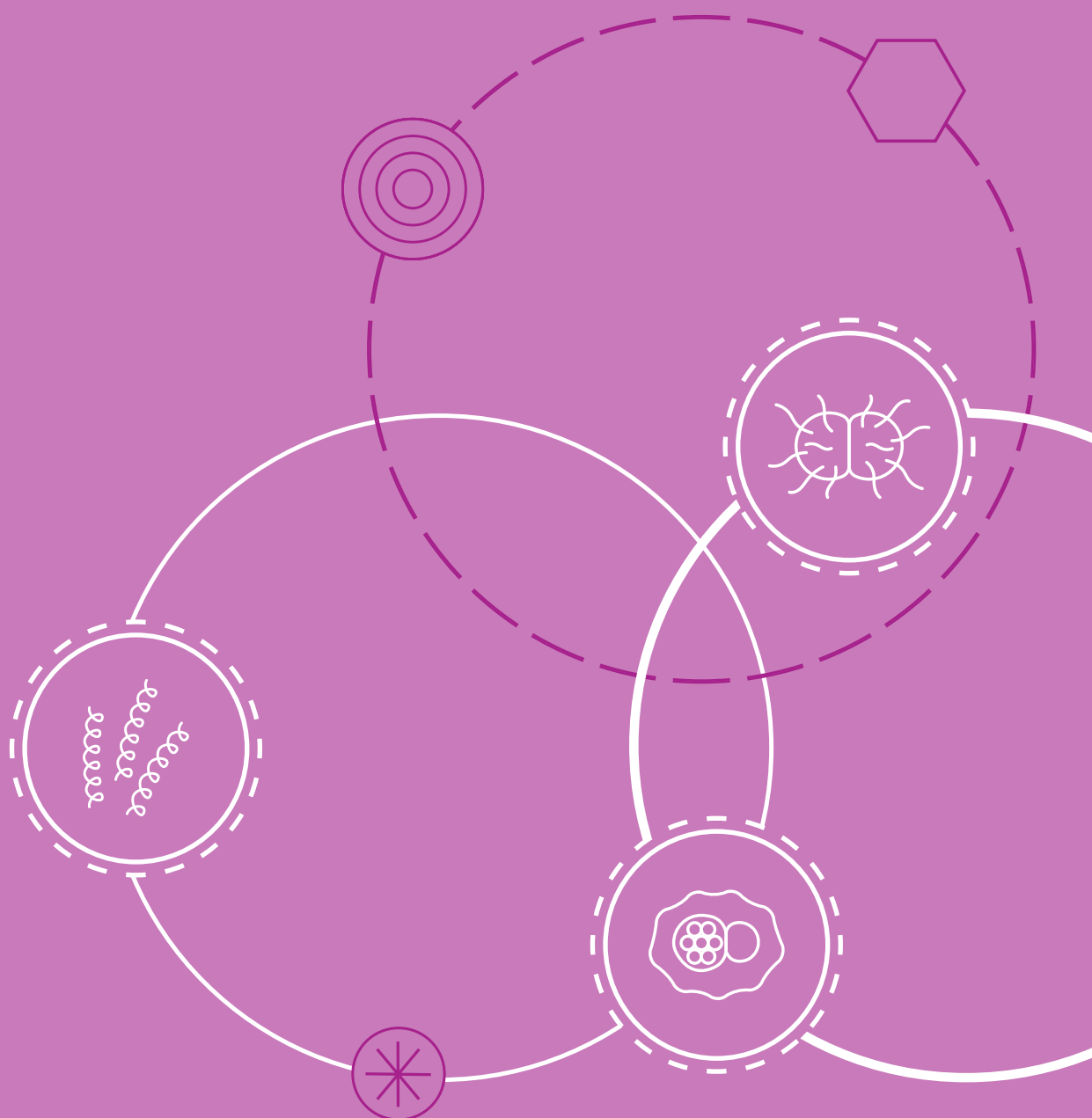
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Annex 1.

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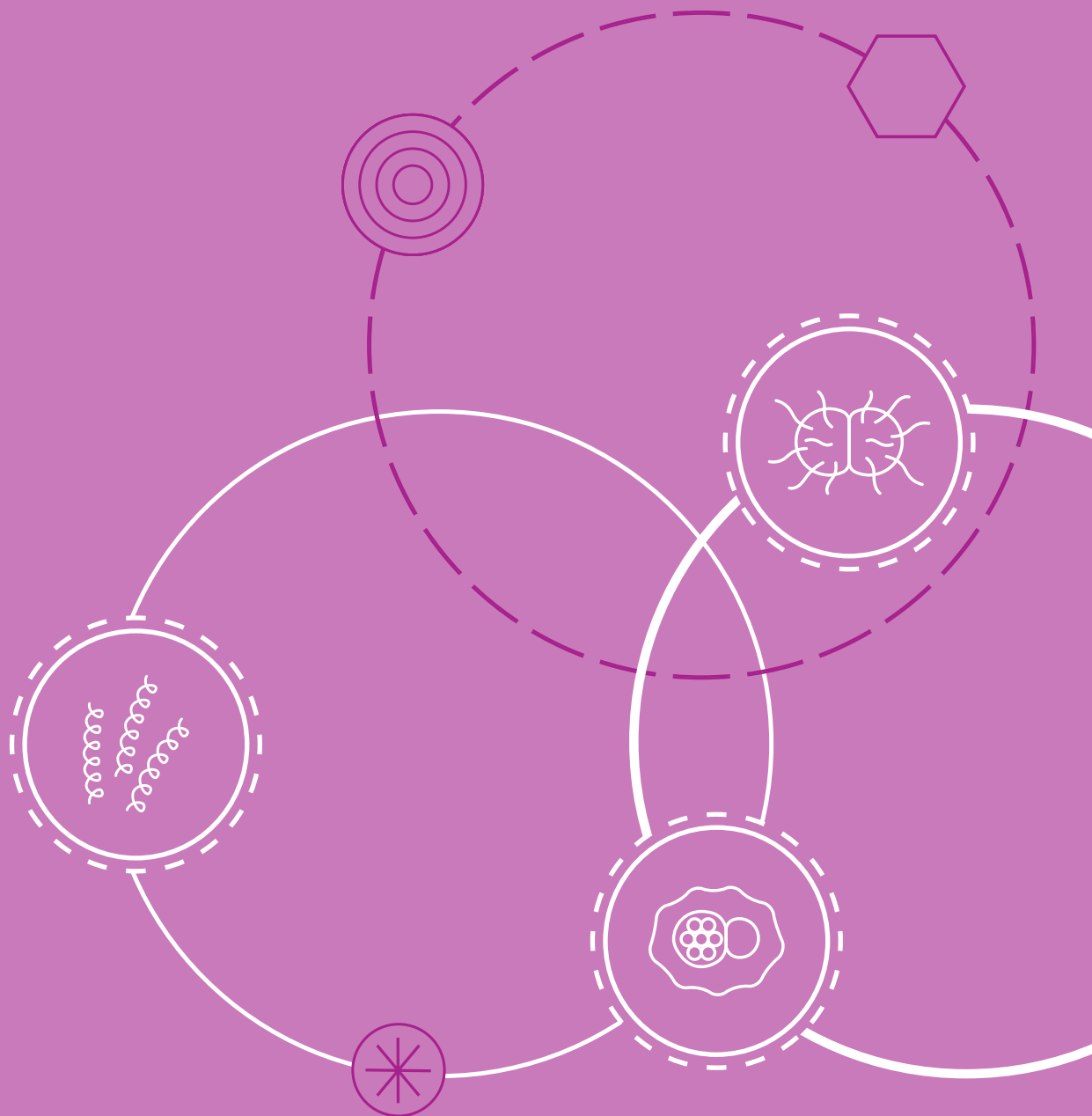
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Declarations of conflicts of interest

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Declarations of conflicts of interest



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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
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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 (3800 Australian dollars).	Australian Research Council Grant to Monash University that contains contributions from the government, two diagnostic companies (Speedx and Cepheid) and NGOs including Global Antibiotic Research and Development Partnership (GARDP) to support work on the development of resistance diagnostics and antimicrobial resistance (1.5 million Australian dollars). Diagnostic kits and GeneXpert platform donated for use in specific investigator-initiated research.	-	-	-	-	Declare. Direct finance not significant. Full participation
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Irith De Baetselier (Institute of Tropical Medicine, Belgium)	-	-	-	-	-	-	Full participation

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Patricia Garcia (Universidad Peruana Cayetano Heredia, Peru)	-	-	-	-	-	-	Full participation
William M. Geisler (University of Alabama at Birmingham, USA)	Consulting on <i>C. trachomatis</i> vaccine for Sanofi (ceased 2023), consulting on STI point-of-care tests for Visby (ceased 2023).	Research support from Hologic for study of <i>M. genitalium</i> prevalence and resistance in the USA (ceased 2023), speaking honoraria related to <i>M. genitalium</i> from Hologic, Roche Molecular Systems, and Abbott (ceased 2023).	-	-	-	-	Declare. None are active. Full participation
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Jeffrey D. Klausner (University of Southern California, USA)	Consulting and technical adviser with Visby Medical (ceased 2023), Biofire (ceased 2023), Cepheid (ceased 2022), and Roche (ceased 2021).	-	-	-	-	-	Declare. None are active. Full participation
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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
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