

NEISSERIA GONORRHOEAE ANTIMICROBIAL RESISTANCE SURVEILLANCE



CONSOLIDATED GUIDANCE

PAHO



Pan American
Health
Organization



World Health
Organization
REGIONAL OFFICE FOR THE
Americas

Neisseria gonorrhoeae
Antimicrobial Resistance
Surveillance

Consolidated Guidance



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Neisseria gonorrhoeae Antimicrobial Resistance Surveillance: Consolidated Guidance

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Acronyms

AMR	antimicrobial resistance
AST	antimicrobial susceptibility testing
EGASP	Enhanced GASP
EQA	external quality assurance
GASP	Gonococcal Antimicrobial Surveillance Programme
GLASS	Global Antimicrobial Resistance Surveillance System
IM	intramuscular
MIC	minimum inhibitory concentration
MSM	men who have sex with men
NAAT	nucleic acid amplification test
NCC	National Coordinating Center
NRL	national reference laboratory
PAHO	Pan American Health Organization
ReLAVRA	Latin American Surveillance Network of Antimicrobial Resistance
R&D	research and development
SDG	Sustainable Development Goal
SOP	standard operating procedure
STI	sexually transmitted infection
WHO	World Health Organization

1.

Introduction

In 2016, the World Health Organization (WHO) published its Global Health Sector Strategy on sexually transmitted infections (STIs) (2016–2021), proposing a priority focus on two areas: securing better data on STI burden, to measure progress toward the control of these infections; and the identification of priority areas for action. The Global Health Sector Strategy on STIs focuses primarily on three STIs, which require immediate action for control, can be monitored, and for which cost-effective interventions exist. These are *Neisseria gonorrhoeae* infection (gonorrhea), *Treponema pallidum* infection (syphilis), and human papillomavirus infection (genital warts and cervical carcinogen).

N. gonorrhoeae infection was included among these priority STIs because of the rising risk of untreatable gonorrhea (owing to antibiotic resistance) and the “high risk of coinfection with other STIs including *Chlamydia trachomatis*” (1).

The Global Strategy has set targets for the reduction of these infections by 2030, in line with the United Nations Sustainable Development Goals (SDGs). For *N. gonorrhoeae* infection, the target is 90% global reduction in incidence from the 2018 baseline, by the year 2030 (1). To achieve these targets the Global Strategy established milestones for 2020, including 70% of countries having STI surveillance systems in place (to monitor progress toward the targets), and 70% of countries reporting on antimicrobial resistance (AMR) in *N. gonorrhoeae* (Box 1).

Gonococcal infections is caused by the Gram-negative bacteria *N. gonorrhoeae* and is associated with high morbidity worldwide (1). The 2013 Global Burden of Disease study estimates that *N. gonorrhoeae* infections is associated with 225,400 years lived with disability (YLD), and 313,900 disability-adjusted life years (DALYs) (2). This is because most *N. gonorrhoeae* infections may go untreated due to mild or asymptomatic presentation (especially in women). While some of the untreated infections may resolve spontaneously, many progress, leading to lifelong complications such as recurrent pelvic inflammatory disease, ectopic pregnancy, and infertility in women; and recurrent epididymitis in men (3). Gonorrhea also increases the risk of acquiring HIV (3).

The global burden of *N. gonorrhoeae* has been complicated by the increase in AMR emergence and propagation to traditional anti-gonococcal antibiotics (4). While this phenomenon is not new, the rapid increase in the resistance to some of the remaining effective mono-therapeutic option—the broad spectrum third-generation cephalosporins like ceftriaxone—has led to a growing concern globally, as it leaves fewer options for treatment (4, 5). As a result, the WHO has changed its recommendation for the empiric treatment to dual antibiotic therapy (ceftriaxone plus azithromycin) when local AMR surveillance is not available to inform national treatment guidelines (6).

> For more information refer to:

- World Health Organization. Global health sector strategy on sexually transmitted infections 2016-2021: toward ending STIs. Geneva: WHO; 2016. Available from: <https://www.who.int/reproductivehealth/publications/rtis/ghss-stis/en/>

Box 1. Global targets to ending STI epidemics by 2030

Targets established by the *WHO Global Health Sector Strategy on STIs to ending STI epidemics as public health concerns by 2030* (in line with the SDGs):

- > 90% reduction of *T. pallidum* incidence globally (2018 global baseline);
- > 90% reduction in *N. gonorrhoeae* incidence globally (2018 global baseline);
- > 50 or fewer cases of congenital syphilis per 100,000 live births in 80% of countries;
- > Sustain 90% national coverage and at least 80% in every district (or equivalent administrative unit) in countries with the human papillomavirus (HPV) vaccine in their national immunization program.

2020 milestones established by the *WHO Global Health Sector Strategy to facilitate meeting the above targets*:

- > 70% of countries have surveillance systems for STIs in place that are able to monitor progress toward the relevant targets;
- > 70% of countries have at least 95% of pregnant women screened for HIV and syphilis; 95% of pregnant women screened for HIV and syphilis with free, prior, and informed consent; 90% of HIV-positive pregnant women receiving effective treatment; and 95% of syphilis-seropositive pregnant women treated with at least one dose of intramuscular benzathine penicillin or other effective regimen;
- > 70% of key populations for HIV have access to a full range of services relevant to STIs and HIV, including condoms;
- > 70% of countries provide services for STIs or links to such services in all primary, HIV, reproductive health, family planning, and antenatal and postnatal care services;
- > 70% of countries deliver HPV vaccines through the national immunization program;
- > 70% of countries report on antimicrobial resistance in *N. gonorrhoeae*;
- > 90% national coverage sustained and at least 80% in every district (or equivalent administrative unit) in countries with the human papillomavirus vaccine in their national immunization program.

2.

Justification

Prevention, early diagnosis, and effective treatment are essential for the control and elimination of *N. gonorrhoeae* as a public health problem. Currently, in Latin America and the Caribbean, treatment for gonococcal infections is largely empiric, based on clinical diagnosis.

In the Americas, the high burden of new *N. gonorrhoeae* infections (estimated at 11 million new cases a year) (7), the complexity of the disease epidemiology, and in many countries the limited resources, make it difficult to fully understand the burden of disease and the AMR burden in *N. gonorrhoeae*.

Hence, the monitoring of *N. gonorrhoeae* AMR at the national level is an important part of gonorrhea surveillance.

In order to achieve this ambitious goal, a deliberate effort to integrate STI surveillance and AMR surveillance is needed.

The Pan American Health Organization (PAHO) has developed this document for public health professionals to facilitate the navigation of available guidance and recommendations to help countries in strengthening and/or developing AMR surveillance in *N. gonorrhoeae*.

The document contains a summarized compilation of key information published by WHO and PAHO by topic of interest and provides links to the relevant documents for more detailed information. Additional useful resources are also referenced at the end of the guidance.

3.

Objective

The main objective is to consolidate and streamline existing operational guidance on AMR surveillance for *N. gonorrhoeae* from manuals and other documents published by WHO and PAHO.

4.

Target audience

Public health and health care professionals, at the national and subnational levels, involved in designing, implementing and/or strengthening AMR surveillance in *N. gonorrhoeae* and overall STI surveillance.

5.

Antimicrobial resistance in *N. gonorrhoeae*

Emergence of gonococcal resistance to penicillin was documented almost immediately after the drug's discovery in the 1940s, though penicillin remained effective treatment for the following three decades. A rise in resistance levels to penicillin and tetracyclines was first documented in Asia during the 1970s (4). Resistance of *N. gonorrhoeae* to quinolones (e.g., ciprofloxacin) started to become a problem in the mid-2000s in several regions (4). Today the infection that was once almost uniformly susceptible to sulfonamides, penicillin, tetracyclines, macrolides, and fluoroquinolones, is no longer, and none of these drug classes is suitable on its own for treatment of gonorrhoea (4, 5).

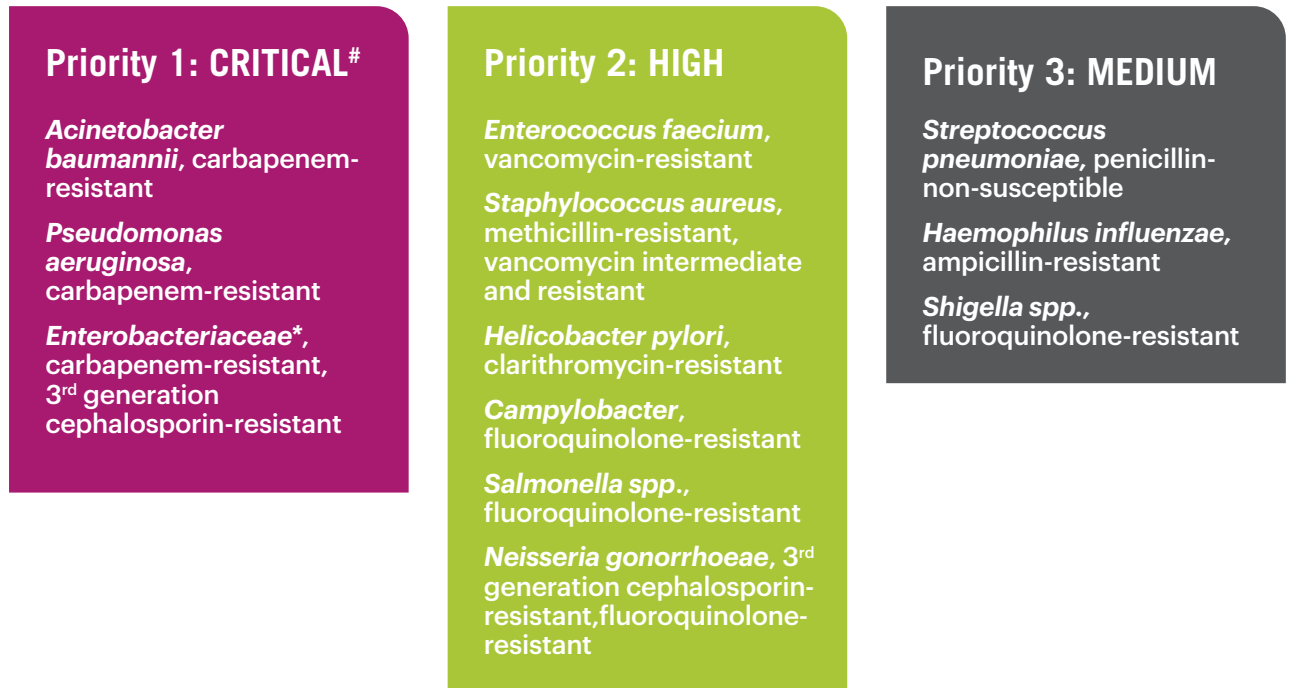
As a result, third-generation cephalosporins (e.g., ceftriaxone and cefixime) became the recommended gonorrhoea treatment regimens in many countries (5). However, the reports of *N. gonorrhoeae* isolates with increased minimum inhibitory concentrations (MICs) for cephalosporins have also been on the rise since the late 2000s, indicating that resistance to cephalosporins is emerging and increasing (8). In 2016, WHO changed its recommendation for empiric treatment to dual antibiotic therapy (first line: ceftriaxone plus azithromycin) in the absence of local epidemiological surveillance data for AMR in *N. gonorrhoeae* (5).

In 2017, WHO published a list of resistant “priority pathogens” from 12 families of bacteria categorized into three priority categories (i.e., critical, high, and medium) based on the threat they pose to human health in terms of resistance (Figure 1). The list aims to guide and promote research and development of new antibiotics for these pathogens. ***N. gonorrhoeae* was classified as a high priority pathogen (9, 10).**

> **For more information refer to:**

- World Health Organization. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. Geneva: WHO; 2017. Available from: <https://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/>
- World Health Organization. WHO guidelines for the treatment of *Neisseria gonorrhoeae*. Geneva: WHO; 2016. Available from: <https://www.who.int/reproductivehealth/publications/rtis/gonorrhoea-treatment-guidelines/en/>

Figure 1. WHO priority pathogens list for research and development of new antibiotics



[#] Mycobacteria (including *Mycobacterium tuberculosis*, the cause of human tuberculosis) was not subjected to review for inclusion in this prioritization exercise as it is already a globally established priority for which innovative new treatments are urgently needed.

^{*} Enterobacteriaceae include: *Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacter spp.*, *Serratia spp.*, *Proteus spp.*, and *Providencia spp.*, *Morganella spp.*

Source: World Health Organization. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. Geneva: WHO; 2017, page 5.

6.

Gonococcal infections and antimicrobial resistance in *N. gonorrhoeae* in Latin America and the Caribbean

Elimination of infections caused by *N. gonorrhoeae* is also a public health priority in the Americas, with 11 million estimated cases yearly (11). In Latin America and the Caribbean, multidrug resistant *N. gonorrhoeae* seems to be on the rise (12). Trend analysis of aggregate-level antimicrobial susceptibility testing (AST) data, obtained through the Latin American Antimicrobial Resistance Surveillance Network (Spanish: ReLAVRA), and results from the World Health Organization (WHO) Gonococcal Antimicrobial Surveillance Program (GASP) obtained between 2009 and 2014, and in 2016–2017, indicate an increase in resistance to penicillin, tetracycline, extended-spectrum cephalosporin (ESC) (cefixime and/or ceftriaxone) and ciprofloxacin among *N. gonorrhoeae* isolates (13). Reports of reduced antimicrobial susceptibility of *N. gonorrhoeae* to azithromycin were also reported by some countries in the Region (14).

The emergence and spread of isolates with decreased susceptibility to cefixime and ceftriaxone has been reported in Argentina from 2009 to 2013 (15). Further, a recently published report, detailing drug susceptibility testing results from *N. gonorrhoeae* isolates from seven Peruvian regions collected in 2016–2017, revealed high levels of resistance to ciprofloxacin (82.3%), tetracycline (54.2%), penicillin (51%), azithromycin (15.6%), and the first report of resistance to ceftriaxone in four isolates (4.2%) (16).

The results from a 2013–2014 global country survey published by WHO suggest that this rise in AMR in *N. gonorrhoeae* in the Region of

the Americas might be exacerbated by non-judicious use of antibiotics (17). The survey was part of a global assessment of strategies and structures in place to prevent and control AMR. The survey results also indicated that antimicrobial medicines were available without prescription in 51% of the countries in the Region of the Americas (17). The report found that during the survey time frame, only 17% of the participating countries had mechanisms for monitoring antimicrobial medicine use (17).

In February 2018, PAHO issued an epidemiological alert regarding cephalosporin resistance in *N. gonorrhoeae*, advising countries to strengthen AMR prevention and control measures including AMR surveillance, laboratory capacity, clinical management strategies, and communicating risk and raising awareness (18).

> For more information refer to:

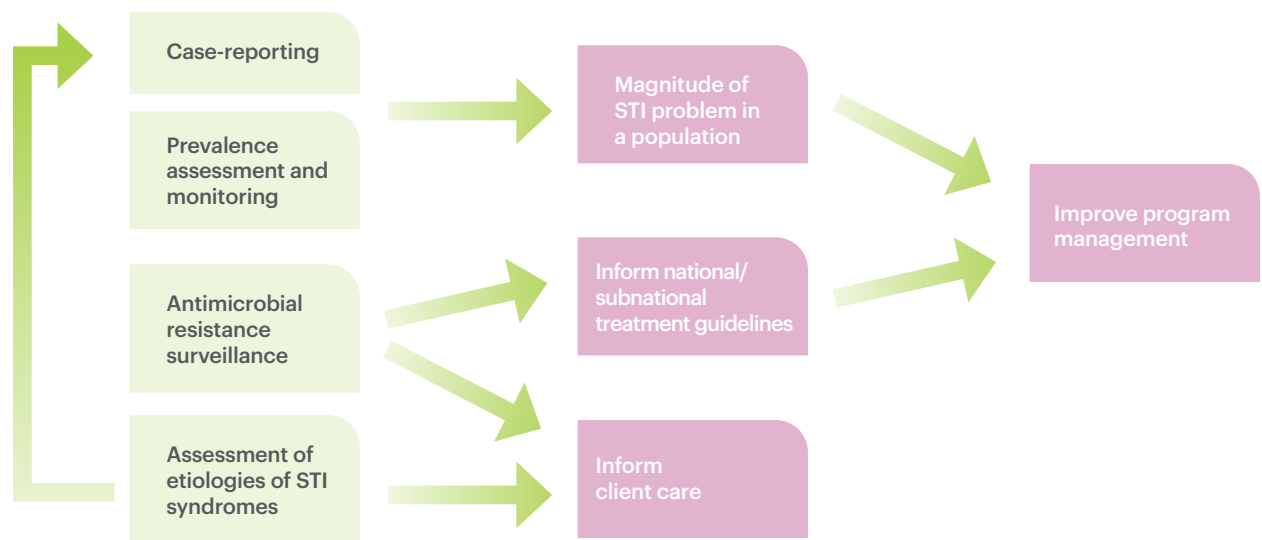
- World Health Organization. Country progress in the implementation of the global action plan on antimicrobial resistance: WHO, FAO and OIE global tripartite database. Geneva: WHO. Available from: <https://www.paho.org/en/topics/antimicrobial-resistance>
- Pan American Health Organization and Joint United Nations Programme on HIV/AIDS. HIV Prevention in the Spotlight: An Analysis from the Perspective of the Health Sector in Latin America and the Caribbean, 2017. Washington, D.C.: PAHO, UNAIDS; 2017. Available from: <https://www.paho.org/hiv-prevention-spotlight-2017/>

7. Core components of sexually transmitted infections surveillance

There are four core activities for STI surveillance: **case reporting; prevalence assessment and monitoring; AMR surveillance; and assessment of etiologies of syndromes** (Figure 2). This surveillance information can provide a comprehensive picture about gonorrhea

burden and trends, both collectively and by population of interest; AMR levels and trends; and guide national response. Figure 2 shows the relationship between the core components, and their relation to STI surveillance objectives.

Figure 2. STI surveillance core components and objectives



Adapted from the WHO's *Strategies and laboratory methods for strengthening surveillance of sexually transmitted infections*.

Case reporting

Case reporting together with prevalence assessment are used to define the magnitude of the STI problem in the population. WHO recommends syndromic and/or etiologic STI¹ reporting as one of the four components of any comprehensive STI surveillance system.

T. pallidum and *N. gonorrhoeae* infections are the two essential STIs that the WHO recommends for etiologic case reporting. In this context, all diagnosed laboratory-tested cases of *N. gonorrhoeae* should be reported (including, if possible, their AST results and basic epidemiologic information) to be able to analyze risk distribution in the population. Selective

¹ Etiologic case-reporting requires laboratory diagnosis. Depending on the specimen and the test used, cases may be classified as probable or confirmed. Either way, all probable and confirmed cases should be reported.

case reporting at sentinel sites is another valid option. If syndromic management is used, then, for surveillance purposes, WHO recommends, at minimum, reporting cases of **urethral discharge syndrome** in men (with or without dysuria), **genital ulcerative disease**, with **vaginal discharge** included in some situations. Further details available from:

> **For more information refer to:**

- UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. Strategies and laboratory methods for strengthening surveillance of sexually transmitted infection 2012. Geneva: World Health Organization; 2012. Available from: <https://www.who.int/reproductivehealth/publications/rtis/9789241504478/en/>

Prevalence assessment and monitoring

Prevalence surveys are cross-sectional surveys that establish the frequency of disease and other factors in a community. They are useful to estimate the number of people in a population who have the disease and can also identify differences in the frequency of diseases in different population groups. Prevalence is usually assessed from populations that are more or less representative of the general population (such as pregnant women), as well as populations considered to be at high risk of infection and transmission (sex workers, men who have sex with men [MSM], adolescents). An STI prevalence assessment is a determination of the number of persons infected with an STI among persons screened in defined populations. In addition to prevalence studies, behavioral studies may yield important information for interpreting surveillance data (health care seeking) and for planning and monitoring of primary prevention strategies (risk determinants). These studies are usually complex and strongly dependent on the respective society settings. Conducting surveys is a core STI surveillance activity, which will provide input for national-level STI prevalence estimates and contribute, together with case reporting, to informing trends—whether, and by how much, the prevalence is increasing or decreasing and which populations are affected—and helping a country monitor its epidemic and provide information on the effectiveness of prevention

and control measures. As resources allow, such point prevalence studies should be conducted every 3 to 5 years with populations of interest (e.g., pregnant women, and populations at higher risk of infection). As gonorrhea is frequently asymptomatic, prevalence assessment should aim to use the most accurate laboratory-validated *N. gonorrhoeae* diagnoses from the samples collected. Further details available from:

> **For more information refer to:**

- UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. Strategies and laboratory methods for strengthening surveillance of sexually transmitted infection 2012. Geneva: World Health Organization; 2012. Available from: <https://www.who.int/reproductivehealth/publications/rtis/9789241504478/en/>

> **For an example of a study protocol in antenatal care settings see:**

- World Health Organization. Standard protocol to assess prevalence of gonorrhoea and chlamydia among pregnant women in antenatal care clinics. Geneva: World Health Organization; 2018. Available from: <https://apps.who.int/iris/bitstream/handle/10665/275846/9789241514675-eng.pdf?ua=1>

Assessment of etiologies of syndromes

WHO recommends that the etiologies of STI syndromes be assessed periodically, to inform correct treatment recommendations and to estimate the disease burden when combined with syndromic case reports. This is especially relevant in countries that use syndromic management of STIs. This assessment should be conducted every 2–3 years. In the context of gonococcal infections, the main syndrome to study is urethral discharge syndrome in men (with or without dysuria). Accurate and laboratory-validated *N. gonorrhoeae* diagnoses are required for the samples collected in such assessments.

> **For more information refer to:**

- UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. Strategies and laboratory methods for strengthening surveillance of sexually transmitted infection 2012. Geneva: World Health Organization; 2012. Available from: <https://www.who.int/reproductivehealth/publications/rtis/9789241504478/en/>

***N. gonorrhoeae* AMR surveillance monitoring**

The main goal of AMR monitoring in *N. gonorrhoeae* is to determine the antimicrobial susceptibility of *N. gonorrhoeae* isolates to inform national or subnational treatment guidelines and prevent further rise in resistance. The objectives and principles of AMR surveillance in *N. gonorrhoeae* are detailed in the next section.

> Further details are available from:

- Pan American Health Organization. Red Latinoamericana de Vigilancia de la Resistencia a los Antimicrobianos – ReLAVRA Data. Washington, DC: PAHO. Available from: <https://www.paho.org/en/topics/antimicrobial-resistance>
- World Health Organization. National antimicrobial resistance surveillance systems and participation in the Global Antimicrobial Resistance Surveillance System (GLASS): a guide to planning, implementation, and monitoring and evaluation. Geneva: WHO; 2016. Available from <https://apps.who.int/iris/bitstream/handle/10665/251554/WHO-DGO-AMR-2016.4-eng.pdf?sequence=1&isAllowed=y>
- World Health Organization. Baseline report on global sexually transmitted infection surveillance 2018: Monitoring gonococcal antimicrobial susceptibility. The Gonococcal Antimicrobial Surveillance Program (GASP). Geneva: WHO. Available from: <https://www.who.int/reproductivehealth/topics/rtis/GASPnetwork.pdf?ua=1>
- World Health Organization. Global Antimicrobial Resistance Surveillance System (GLASS). Geneva: WHO. Available from: <https://www.who.int/glass/en/>
- UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. Strategies and laboratory methods for strengthening surveillance of sexually transmitted infection 2012. Geneva: World Health Organization; 2012. Available from: <https://www.who.int/reproductivehealth/publications/rtis/9789241504478/en/>

8.

N. gonorrhoeae antimicrobial resistance surveillance

Objectives and principles

The aim of AMR surveillance applied to *N. gonorrhoeae* is to collect and analyze data on infections, and report in a timely manner information on resistant organisms (4), to:

- > Determine etiologies and antimicrobial susceptibility of *N. gonorrhoeae* infections.
- > Understand changes over time and quantify the trends, magnitude, distribution, and impact of AMR on disease epidemiology.
- > Detect newly emerging resistance.
- > Inform local, regional, and global action and interventions for AMR prevention and control.
- > Update *N. gonorrhoeae* treatment guidelines and inform patient management to ensure quality care through optimal antimicrobial therapy.
- > Identify at-risk groups, and health practices, risk behaviors, or other factors affecting the epidemiology of the pathogen.
- > Identify needs, gaps, and opportunity for improvement.
- > Provide data to design, manage, and evaluate the impact of interventions.

These objectives should be defined and applied within each country's context. For the surveillance system to achieve its objectives and ensure efficiency, several principles should be applied (Figure 3). These principles, detailed in the WHO's Strategies and laboratory methods for strengthening surveillance of sexually transmitted infections, include:

- > **Feasibility** of adapting and integrating the *N. gonorrhoeae* AMR surveillance to the national health system's structure and capacity, including the integration into routine care management.
- > **Standardization and consistency** in processes, standard operating procedures (SOP), forms, etc., with minimum changes to the existing system.
- > **Confidentiality**, with written policy, confidential forms, and SOPs (e.g., using unique patient identifiers).
- > **Periodic monitoring and feedback** to all surveillance personnel.
- > **Continuity and sustainability** of structures, resources, and investment.

> For more details on general surveillance objectives and principles refer to:

- UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. Strategies and laboratory methods for strengthening surveillance of sexually transmitted infection 2012. Geneva: World Health Organization; 2012. Available from: <https://www.who.int/reproductivehealth/publications/rtis/9789241504478/en/>
- Declich S, Carter AO. Public health surveillance: historical origins, methods and evaluation. Bulletin of the World Health Organization. 1994;72(2):285.
- World Health Organization. Global action plan on antimicrobial resistance. Geneva: WHO; 2015. Available from: <https://www.who.int/antimicrobial-resistance/global-action-plan/en/>
- World Health Organization. Global Antimicrobial Resistance Surveillance System: manual for early implementation. Geneva: WHO; 2015. Available from: <https://www.who.int/antimicrobial-resistance/publications/surveillance-system-manual/en/>

Figure 3. Overview of *N. gonorrhoeae* AMR surveillance principles



Surveillance assessment

When establishing or developing a surveillance program (including *N. gonorrhoeae* AMR surveillance) one must first assess all existing relevant activities or programs (at all levels). This process is important to avoid redundancy and operational silos, and to ensure optimal program design and resource allocation. This step also helps in identifying existing gaps, and opportunities for program improvement. Such assessment is valuable in informing future planning and consolidation of existing surveillance programs including *N. gonorrhoeae* AMR surveillance. In the case of AMR laboratory surveillance, special attention must be given to laboratory capacity and quality assurance programs assessment.

> For more information refer to:

- PAHO/WHO. Rapid assessment tool for monitoring laboratory capacity for antimicrobial surveillance (including *N. gonorrhoeae*), available from: <https://www.paho.org/en/topics/antimicrobial-resistance>
- World Health Organization. A tool for strengthening STI surveillance at the country level. Geneva: WHO; 2015. Available from: <https://www.who.int/reproductivehealth/publications/rtis/sti-surveillance/en/>

There are three phases to situation analysis/surveillance assessment:

- > **Pre-assessment phase:** to estimate the needs, and identify potential support and partners, and ensure adequate capacity for assessment (preparation phase).
- > **Assessment phase:** assessment of the current system including capacity, gaps, challenges, and opportunities for improvement (regarding surveillance indicators, methods, and impact, etc.).
- > **Post-assessment phase:** to document findings from the assessment phase, including report writing, dissemination and implementation of recommendations with progress monitoring.

> For more information refer to:

- UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. Strategies and laboratory methods for strengthening surveillance of sexually transmitted infection 2012. Geneva: World Health Organization; 2012. Available from: <https://www.who.int/reproductivehealth/publications/rtis/9789241504478/en/om:https://www.who.int/reproductivehealth/publications/rtis/9789241504478/en/>

Structure and governance

National gonorrhea AMR surveillance should be supported by the national AMR surveillance system and include the following **three components** (as shown in Figure 4):

> A national coordinating center (NCC)

This is a public health institution designated by the ministry of health (MOH) to coordinate national AMR surveillance activities, including in *N. gonorrhoeae*. The NCC must have the capacity and expertise (epidemiological, clinical, and microbiological) to conduct and manage national surveillance. The NCC is also in charge of defining the surveillance

objectives and ensuring the adaptation of protocols, and coordinating the dissemination of such protocols. The NCC should also have the capacity for the monitoring and evaluation, data analysis, and reporting to all levels, as well as acting as a quality assurance program nationally.

> A national reference laboratory (NRL)

A resource and coordinating point, offering technical guidance and training for laboratory expertise and capacity building. The NRL also acts as a liaison with the NCC, developing and sharing relevant reference materials

and facilitating the participation in external quality assurance (EQA). The NRL should have the capacity for EQA review and feedback, confirmatory testing of resistant isolates, and microbiology research and synthesis.

> *N. gonorrhoeae* AMR sentinel surveillance sites

The sentinel surveillance site collect and manage the samples obtained from patients. Such sites could include outpatient health care facilities, including STI clinics, as well as acute care facilities (from the public and/or private sectors). The NCC designates the sentinel sites (see next section for site selection criteria) to report *N. gonorrhoeae* AMR surveillance data to the NRL. Testing, analyzing, and reporting of AST results of the samples may be performed in the laboratories serving these sites and/or by transport of samples to a reference laboratory. Epidemiological data of the patients at the sentinel sites should be linked to the isolate information by unique identifier codes.

The NCC and NRL provide oversight to the sentinel sites, including overseeing the microbiology laboratories.

Sites that lack the laboratory capacity for *N. gonorrhoeae* testing including AST, but meeting all other criteria for *N. gonorrhoeae* AMR sentinel surveillance, can be assigned as sentinel sites, provided they have the capacity for proper sample management (collection, processing, storage, and transport). This is important because *N. gonorrhoeae* is a sensitive organism, and samples can be compromised if not well managed. In these cases, the NRL (or any other offsite laboratory)

can be used to perform the necessary laboratory diagnostics and AST. This is particularly useful in resource-limited settings, where the sentinel sites most representative of the population or a subpopulation might lack laboratory capacity for AST.

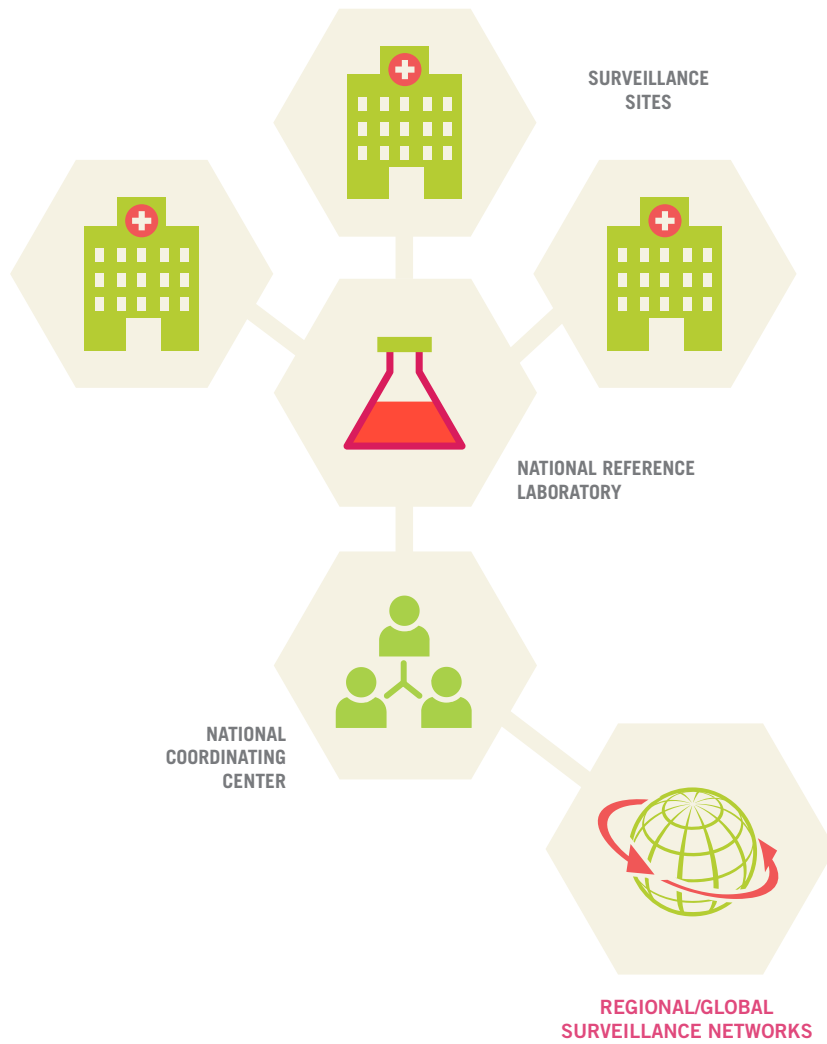
In either case, all designated sentinel sites must report, in a timely and regular manner, all relevant local data collected, to the NRL and/or NCC for further analyses and dissemination of information. This information will eventually be used to inform local and national guidelines for treatment and *N. gonorrhoeae* AMR control.

Note: In general, AMR surveillance should be based on using appropriate epidemiological methods and standardized protocols and quality-assurance systems, including monitoring and supervision of laboratories, and continuing education and capacity building for laboratory personnel and clinical providers.

> For more information refer to:

- World Health Organization. National antimicrobial resistance surveillance systems and participation in the Global Antimicrobial Resistance Surveillance System (GLASS): a guide to planning, implementation, and monitoring and evaluation. Geneva: WHO; 2016. Available from: <https://apps.who.int/iris/handle/10665/251554>
- UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. Strategies and laboratory methods for strengthening surveillance of sexually transmitted infection 2012. Geneva: World Health Organization; 2012. Available from: <https://www.who.int/reproductivehealth/publications/rtis/9789241504478/en/>

Figure 4. AMR surveillance structure



Note: The National Reference Laboratory may function as the National Coordinating Center in some countries.

Selection of sentinel sites for national *N. gonorrhoeae* antimicrobial resistance surveillance

N. gonorrhoeae AMR surveillance could be conducted through sentinel sites, representing various geographic locations and populations. When selecting sentinel sites, the following criteria should be considered:

> **Representativeness:** the population served is representative in terms of geographic, demographic, and risk distribution. To support representativeness and ensure national coverage, the combination of sites should serve patients from broad age groups, ethnicities, and sexual behaviors (i.e. men who have sex with women, MSM). For example, if the rate of new infections is higher in urban and semi urban areas, countries can select sentinel sites in these areas, with the percentage of sites in each area determined by the number of inhabitants or concentration of groups with greater burden of infection.

> **Type of health care facilities:** a combination of community STI health clinics and public hospitals, as well as relevant specialty private practices (e.g., infectious disease specialists, dermatologists, etc.), is ideal. The proportion of each type of health care facility is dependent on population size, proportion of STI patients the facility sees on average, location (urban vs. semi-urban), and the willingness and capacity for surveillance (see below). Countries that have many facilities in the same area can randomize selection of STI facilities/relevant specialty.

> **Technical capacity** for patient care and for *N. gonorrhoeae* AMR surveillance: sentinel sites should have the resources and technical diagnostic capacity to characterize, treat, and report cases.

> **Quality laboratory capacity** for diagnostics, characterization, confirmation, and antibiotic susceptibility testing. Sentinel sites that lack the laboratory capacity for *N. gonorrhoeae* AST must at least have the capacity for proper specimen management, storage, and transportation (to a secondary laboratory facility or a national laboratory).

> **Easy access** of the population to the sentinel health service.

> **Willingness for participation:** sites must be willing to participate in the surveillance activity. This is especially true for private practices. Financial compensation for STI reporting is not recommended, and may generate similar expectations for other disease reporting, or routine surveillance. Use of non-financial incentives for the sentinel surveillance is ideal (e.g., certificate for participation, sharing reports on trends involving practitioners as part of the working group, free access to medical journals, etc.).

> **Continuity** of reporting from the selected sentinel sites. Countries at the beginning stages of establishing an *N. gonorrhoeae* AMR surveillance system may start with few sentinel sites and gradually increase the number of sites to ensure population coverage and representativeness (19).

> **Sentinel site criteria questionnaire:** to better understand if a potential site is suitable for surveillance, an initial qualitative questionnaire must be completed by all participating sites on the characteristics of the sentinel sites (number of patients, number and type of staff, type of patients, services provided, capacity, etc.).

Sampling method and sample size

> **Number of isolates:** As mentioned before, the number of isolates to be collected and analyzed for the purpose of *N. gonorrhoeae* AMR sentinel surveillance will vary depending on the size and type of population, local epidemiology, risk distribution, and the availability of resources for diagnostics and AST, as well as the number of sentinel sites. The number of isolates that guarantees representativeness of the sample is recommended, with an established minimum sample size cut-off. WHO recommends a minimum of 100 isolates per country; however, to assure representativeness, the exact number should be determined based on the geographic distribution of the sites and the subpopulations under surveillance. Countries with large populations and a high percentage of groups with high burden should adjust their minimum sample size to ensure representativeness (20).

> **Surveillance criteria (case definition):** For *N. gonorrhoeae* AMR sentinel surveillance, a case definition including the denominator for the population under surveillance must be established.

Example for case definition: New patient with urethritis of unknown cause (i.e., inflammation of the urinary passage) presenting with one or more of the following: urgency, increased frequency (pollakiuria), dysuria, and/or discharge from the urethra, diagnosed clinically (without laboratory-confirmed diagnosis).

> **Population for sentinel surveillance:** Countries without well-established AMR surveillance systems may start with sites of greatest

technical capacity and interest. For example, countries can start with new cases of adult symptomatic men presenting with urethral discharge or urethritis from a small number of selected sites. This is because most symptomatic patients are males (gonococcal infections is typically asymptomatic in females) and the yield of viable isolates is higher with urethral discharge. It is important to stress that, if this approach is to be followed, when feasible, a stepwise plan should be in place for the inclusion of female patients (e.g., pregnant women) at a later stage.

> **Selection of cases:** To improve representativeness and achieve the desired sample size, a country should decide on an effective sampling method. For example, a country can choose to select consecutive patients meeting surveillance criteria, during certain days or weeks of the month, or all patients meeting surveillance criteria, as they present, until the sample size is reached. For example, sampling of the first 100 men presenting to a sentinel site with urethral discharge, or the first 10 men presenting to the site on first three days of each week. To reach the desired sample size, an additional percentage to account for lost or damaged samples should be included in the total number of *N. gonorrhoeae* isolates collected.

> ***N. gonorrhoeae* AMR** sentinel surveillance should be conducted systematically and regularly. The frequency of reporting must be determined by the national level (quarterly reporting is recommended) (21).

Laboratory samples and microbiological testing

N. gonorrhoeae can be diagnosed by culture or nucleic acid amplification tests (NAATs) and, in some instances, Gram stain. A drawback of currently available commercial NAATs is their inability to provide information on antimicrobial susceptibility. For diagnosis of *N. gonorrhoeae*, anatomical sites for specimen collection can depend on the sex, sexual practices of the individual, and clinical presentation of the infection. For example, in men and women with indicative clinical signs and/or sexual practice (oral and/or anal sex), additional samples from the oropharynx and rectum can be collected. The specimen is also determined by the capacity for collection and analyses, as well as of the diagnostic testing method to be performed.

For the purpose of AMR surveillance, sites must use gonococcal culture in lieu of—or in addition to—non-culture testing (such as NAAT), at least on male patients with urethritis. The following flow chart is recommended (Figure 5) (22). Ideally, samples will be pretreatment specimens.

It is important to keep in mind that *N. gonorrhoeae* is a highly vulnerable organism in vitro, and a sample exposed to adverse environmental elements can easily be compromised, if not collected and managed properly. Hence, we recommend that all sentinel sites must train involved staff on sample collection and management and keep an up-to-date detailed guidance/SOP on sample collection and management on-site (23).

> Specimen choice for AMR sentinel surveillance:

For *N. gonorrhoeae* AMR surveillance, the gold standard is to collect urethral swab specimens for culture from symptomatic adults (the majority of whom are likely males) presenting to the sentinel site² (20).

> **Specimen source:** A meatal swab can be collected from male patients presenting to the sentinel site with symptoms suggestive of *N. gonorrhoeae* urethral infection (e.g., urethritis, dysuria, urethral discharge). To ensure the viability of the sample, swabs with

plastic or wire shafts and rayon, Dacron tips, are recommended (24, 25). If the sample cannot be processed immediately, proper transport media must be used to maintain the viability. If multiple specimens are collected, the first specimen should be the one sent for culture (20, 23).

> **Diagnostic and susceptibility testing:** This includes Gram stain testing and culture. While a molecular test or a positive Gram stain of a urethral specimen from males is diagnostic for *N. gonorrhoeae* (highly specific and sensitive), culture remains essential for determination of susceptibility to antibiotics.

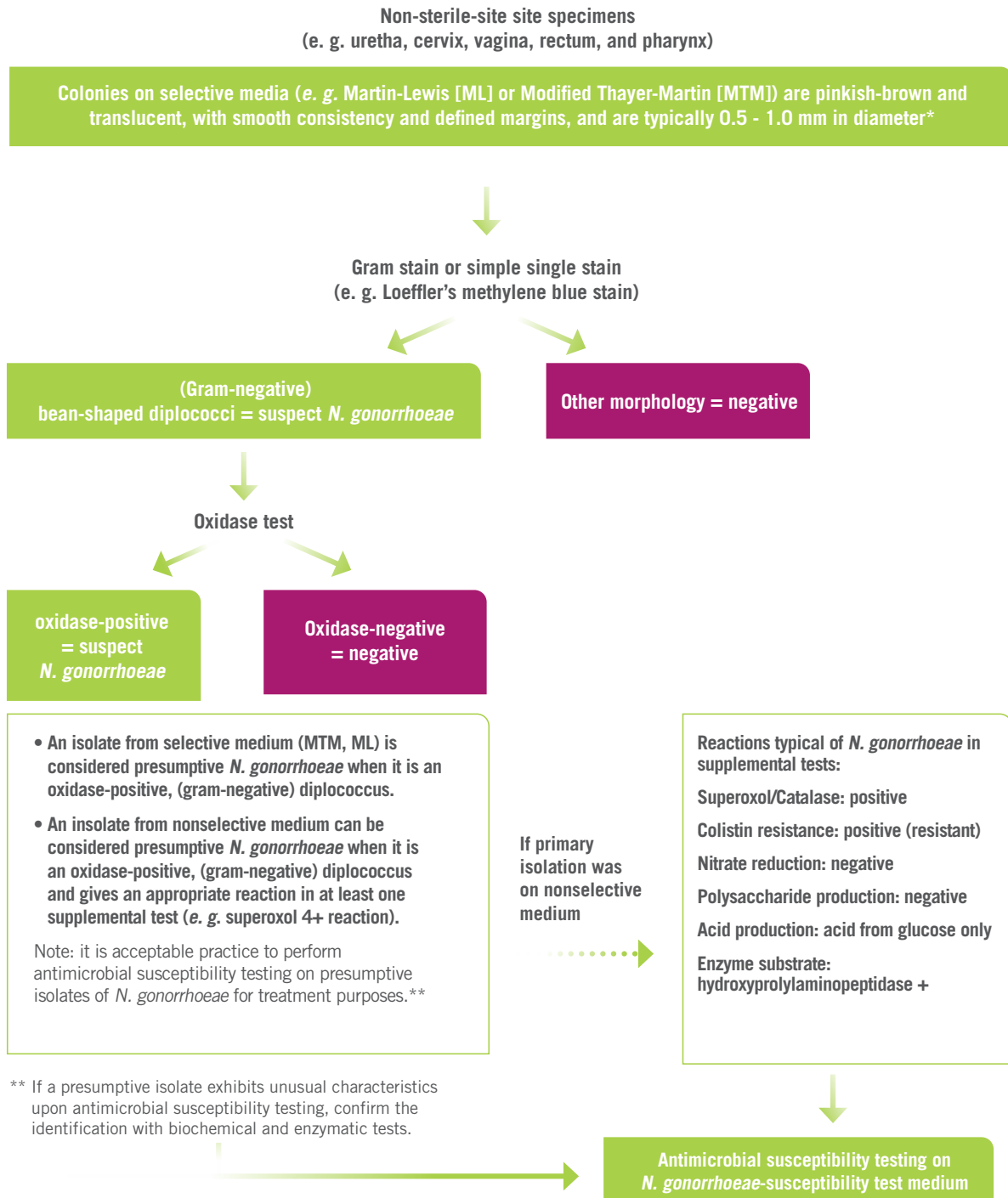
Note: Symptomatic patients are often prescribed antibiotics empirically, based on the history, clinical presentation, and/or the result of a positive Gram stain of a meatal swab or a urethral discharge. However, for *N. gonorrhoeae* AMR surveillance purposes, a culture of the meatal swab and antibiotic sensitivity must be performed. Although molecular testing is the gold standard for diagnostic testing of *N. gonorrhoeae*, culture allows for sensitivity testing.

> For more information on laboratory-related topics refer to:

- World Health Organization. Manual for the laboratory identification and antimicrobial susceptibility testing of bacterial pathogens of public health importance in the developing world: *Haemophilus influenzae*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Neisseria gonorrhoeae*, *Salmonella serotype Typhi*, *Shigella*, and *Vibrio cholerae*. Geneva: WHO; 2003. Available from: <https://apps.who.int/iris/handle/10665/68554>
- UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. Strategies and laboratory methods for strengthening surveillance of sexually transmitted infection 2012. Geneva: World Health Organization; 2012. Available from: <https://www.who.int/reproductivehealth/publications/rtis/9789241504478/en/>

² While a urethral specimen is the most frequently collected sample, the type of specimen collected—and test performed—might vary depending on the age, gender, clinical presentation, and risk factors of the patient.

Figure 5. Flow chart for isolation and presumptive identification of *N. gonorrhoeae*



Adapted from World Health Organization. Manual for the laboratory identification and antimicrobial susceptibility testing of bacterial pathogens of public health importance in the developing world: *Haemophilus influenzae*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Neisseria gonorrhoeae*, *Salmonella* serotype Typhi, *Shigella*, and *Vibrio cholerae*. Geneva: WHO; 2003: Chapter 6, Figure 19, page 66. Available from: https://apps.who.int/iris/bitstream/handle/10665/68554/WHO_CDS_CSR_RMD_2003.6.pdf?sequence=1&isAllowed=y

* Fastidious strains of *N. gonorrhoeae* may produce small, ~0.25-mm "pinpoint" colonies

External quality assessment

Assessment is a critical aspect of laboratory quality management, and it can be conducted in several ways. One of the commonly employed assessment methods is that of external quality assessment (EQA).

External refers to the fact that an organizer outside of the laboratory's organization provides a statement of quality to the laboratory. EQA (sometimes referred to as proficiency testing, or PT) allows for standardized comparison of a laboratory's testing procedures to other laboratories—in the country, region, or globally. This comparison can be made to the performance of a peer group of laboratories or to the performance of a reference laboratory.

Participation in an EQA scheme allows a laboratory (or the coordinating NRL/center) to gather valuable data about its performance. These data can be used in a variety of ways:

- Enables comparison of performance between laboratories;
- Provides an early warning for systematic errors;
- Highlights opportunities for improvement;
- Provides evidence for quality;
- Identifies gaps and training needs;
- Detects faulty equipment, reagent problems;
- Evaluates the reliability of materials and equipment; and
- Compares performance to different standard analytical methods.

There are several EQA methods/processes that are commonly used. These include:

> **Proficiency testing:** external provider sends unknown samples for testing to a set of laboratories, and the results of all laboratories are analyzed, compared, and reported to the laboratories.

> **Rechecking or retesting:** strains that have been tested in a laboratory are rechecked by a reference laboratory; allowing for interlaboratory comparison.

> **On-site evaluation:** usually done when it is difficult to conduct traditional proficiency testing or to use the rechecking/retesting method.

> **Sample exchange:** another method of interlaboratory comparison is the exchange of samples among a set of laboratories, usually reserved for specialized tests for which no proficiency testing is available. This method is used either by very specialized or sophisticated laboratories.

EQA provides assurance to both staff and customers that testing taking place at a laboratory provides accurate and reliable results. Problems can be identified early on and corrective action can be taken. The reliability of methods, materials, and equipment can be evaluated, and training can be developed, and its impact monitored.

In most EQA schemes, laboratories receive scores for their results. The most popular method is the Z-score, also called the standard deviation index (SDI). The score is given per analyte and per test item.

> **For more information on EQA for AST in *N. gonorrhoeae*, refer to:**

- Cole MJ, Quaye N, Jacobsson S, Day M, Fagan E, Ison C, et al. Ten years of external quality assessment (EQA) of *Neisseria gonorrhoeae* antimicrobial susceptibility testing in Europe elucidate high reliability of data. *BMC Infectious Diseases*. 2019 Dec;19(1):281. Available from: <https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-019-3900-z>
- Sawatzky P, Martin I, Galarza P, Carvallo ME, Rodriguez PA, Cruz OM, et al. Quality assurance for antimicrobial susceptibility testing of *Neisseria gonorrhoeae* in Latin American and Caribbean countries, 2013–2015. *Sexually Transmitted Infections*. 2018 Nov 1;94(7):479-82.

Treatment of gonococcal infections based on antimicrobial resistance data

WHO recommends that the choice of therapy should be determined by local epidemiology and AMR data. In settings where local resistance data are not available, the WHO guidelines for the treatment of *N. gonorrhoeae* should be followed (Box 2). For more details on the clinical management of *N. gonorrhoeae* infections, refer to:

> **For more information on treatment refer to:**

- World Health Organization. WHO guidelines for the treatment of *Neisseria gonorrhoeae*. Geneva: WHO; 2016. Available from: <https://www.who.int/reproductivehealth/publications/rtis/gonorrhoea-treatment-guidelines/en/>

Box 2. Gonococcal infections: most common clinical picture and WHO-recommended antibiotic treatment

Gonorrhea: The gonococci are mainly transmitted through sexual contact. There can be perinatal transmission through the birth canal during delivery.

N. gonorrhoeae infections primarily affect the mucous membranes of the urethra and the cervix, as well as the mucous membranes of the oropharynx, rectum, and conjunctivae. The incubation period ranges from 1–14 days, although the disease is typically manifested in 2–5 days. The most common uncomplicated infection in men is acute urethral infection (23). Male patients usually present with urethral discharge and painful urination (dysuria). Most infected women present with milder symptoms and many are asymptomatic (23, 26). Asymptomatic *N. gonorrhoeae* infections occur in both sexes and may go untreated. Infections may resolve spontaneously or lead to complications such as pelvic inflammatory disease, ectopic pregnancy, and infertility in women, and epididymitis in men (23). Rectal infections occur predominantly among men who have sex with men (MSM) (23, 24). Pharyngeal gonococcal infections are often transmitted through oral sex and are more common among MSM and heterosexual women (24, 27), but are largely asymptomatic (23, 24). Gonococcal conjunctivitis is most common in newborns who contract the gonococci from their infected mother during childbirth. Patients present with purulent ocular discharge and swollen eyelids; if untreated, gonorrhea may lead to scarring and blindness (23). Disseminated gonococcal infections may also cause skin lesions; asymmetrical arthropathies, tenosynovitis, or septic arthritis; and rarely, meningitis or endocarditis. Disseminated infections are more common in immunocompromised patients (28).

Treatment for urethral discharge³:

For the treatment to be more effective, the local resistance pattern must be taken into account. In the absence of local data, the 2016 WHO treatment recommendation for gonorrhea recommends a dual therapy over single therapy for genital or anorectal gonorrhea. The current WHO gonorrhea treatment guidelines (6) are:

Dual therapy (one of the following)

- ceftriaxone 250 mg intramuscular (IM) as a single dose PLUS azithromycin 1 g orally as a single dose;
- cefixime 400 mg orally as a single dose PLUS azithromycin 1 g orally as a single dose.

Single therapy (one of the following, based on recent local resistance data confirming susceptibility to the antimicrobial)

- ceftriaxone 250 mg IM as a single dose;
- cefixime 400 mg orally as a single dose;
- spectinomycin 2 g IM as a single dose.

³ For other treatment schemes, please see: World Health Organization. WHO guidelines for the treatment of *Neisseria gonorrhoeae*. Geneva: WHO; 2016. <https://apps.who.int/iris/bitstream/handle/10665/246114/9789241549691-eng.pdf>

Data analyses

> Data requirement

Select demographic and clinical data should be submitted for each sample, including age, gender, ethnicity, site and date of specimen collection, primary/secondary treatment for gonorrhea, and sexual practices (sex with women, men, and/or transgender women). Demographic and behavioral elements are critical to better understand the trends of AMR in *N. gonorrhoeae*. Further information can be found in the Enhanced GASP (EGASP) protocol and other available WHO guidance (29, 30).

> Data collection

It is important for any surveillance system to have a data collection methodology that is efficient, cost-effective, and clear. It is also important to determine a clear case definition for the population sampled (see section “Selection of sentinel sites for national *N. gonorrhoeae* AMR surveillance”) (17, 18). Data must be reported in a timely manner and must meet criteria for confidential reporting. A written standard guidance for reporting must be provided to each site. The guidance must ensure accuracy and patient privacy. For this, examples include the use of unique identifiers, passwords, and limiting the access to passwords. The following is an example tool for AMR data collection, management, and interpretation:

> For more information refer to:

- World Health Organization. The microbiology laboratory database software. Geneva: WHO. Available from: <http://www.whonet.org/>
- Clinical and Laboratory Standards Institute. Analysis and presentation of cumulative antimicrobial susceptibility test data. Wayne, PA: CLSI; 2019. Available from: <https://clsi.org/>

The sensitivity of STI data is of special importance; great care and a high degree of confidentiality must be exercised when

collecting and reporting the patients’ data at all levels. A confidentiality agreement in line with the country’s law on patient privacy and data protection must be signed by participating sites and laboratories. Staff must be educated regarding patients’ rights, privacy, and data handling for confidential reporting. Permissions must also be obtained from patients, after explaining the purpose of the surveillance and their privacy rights.

> Data quality and validation

Data must be validated for completeness, timeliness, errors, and biases. Laboratory data must also be validated for methodology and adherence to guidelines in methodology and interpretation (e.g., interpretation of AST results).

> Data analyses

AST data analysis—thus the analysis of isolates’ susceptibility—is the basic piece of data analysis from a laboratory perspective. For this analysis to have public health significance, however, the analysis of the characteristics of the samples collected needs to be incorporated into the surveillance, including the isolate level information. The latter will provide information on the epidemiologic characteristics of the sampled population and its representativeness, and will guide policy and programmatic decisions on *N. gonorrhoeae* management. For example, analysis of variables such as age, ethnicity, sexual behavior (% MSM), and prior treatment—by each site—is important for AMR surveillance.

AST for *N. gonorrhoeae* should be analyzed each year to inform treatment guidelines for *N. gonorrhoeae* infections.

Depending on the number of samples per site, yearly data can be analyzed by single sentinel facility, by multiple facilities, where appropriate, by region, and nationally (depending on the homogeneity and the

representativeness of the population under surveillance).

The use of local yearly data is recommended to update treatment guidelines and tailor therapy decisions. Local data should be representative, complete, and of good quality, size, and scope in order to draw conclusions. The data must also always be interpreted in the national and global context to provide an insight into local resistance findings (31). The interpretation of sensitivity results must also

be in line with standardized evidence-based global guidance (e.g., Clinical and Laboratory Standards Institute [CLSI]) (32).

Examples of relevant analysis among sites include: percentage of isolates with penicillin, tetracycline resistance; percentage of isolates with intermediate resistance or resistance to ciprofloxacin; in addition, distribution of ceftriaxone MICs; and distribution of cefixime MICs.

Dissemination and communication of results

The analysis of the *N. gonorrhoeae* AMR surveillance data needs to be disseminated at all levels of surveillance (local, national, regional) in a timely manner, to facilitate appropriate and effective public health responses based on *N. gonorrhoeae* surveillance reported information. Based on the new information, treatment guidelines should be updated, and used for training of health care providers and for advocacy. This is specifically crucial for annual accumulative AST of *N. gonorrhoeae*.

Beyond the accumulative annual AST reporting, the national STI program or epidemiology unit should develop and implement a plan to effectively communicate surveillance results. This can be in the format of epidemiology bulletins or reports, and in additional formats including electronic health communications, dissemination of predesigned summaries and visualizations, to communicate the results for action to all stakeholders. Examples include the following:

> **Epidemiological bulletins or annual gonorrhea surveillance reports:** including case numbers, rates and trends by geographical areas and demographic variables, and prevalence data by population;

> **Fact sheets:** data-based, with tables and graphs, which can be posted at health department offices and clinics, or provided in response to ad hoc enquiries, or included in guidelines and technical manuals;

> **Regular newsletters:** to clinicians, laboratory personnel, and others, may include brief reports of surveillance data along with updated information on patient management;

> **Press releases:** highlighting disease burden and trends, can be used as part of public information campaigns;

> **Educational materials:** charts and posters developed using the data provided by surveillance case reports;

> **Verbal feedback:** during meetings and supervisory visits;

> **Electronic media:** summary data published on a website.

A feedback system from health care providers and institutions that participate in *N. gonorrhoeae* surveillance should be in place to assist the gonorrhea surveillance program to review its activities and make the necessary changes to improve the system.

10.

International coordination and surveillance networks

The control of AMR emergence and spread is one of the main goals of WHO and PAHO global and regional action plans for containment of AMR. The plans include five strategic lines, including the need for strengthened AMR surveillance. Regional

and global AMR surveillance networks collect crucial information from participant countries; in turn, countries can utilize these platforms by participating in them. Box 3 contains examples of regional and global networks.

Box 3. Regional and Global AMR surveillance networks

Latin American Surveillance Network of Antimicrobial Resistance (ReLAVRA)

The Latin American Surveillance Network of Antimicrobial Resistance (*Red Latinoamericana de Vigilancia de la Resistencia a los Antimicrobianos*, or ReLAVRA)—created, supported, and coordinated by PAHO—is a Latin American regional surveillance system operating since 1996, based on standardized principles and horizontal cooperation between participant countries (33). Nineteen countries currently participate in the ReLAVRA network: Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Uruguay, and Venezuela. The national reference laboratory in Argentina, ANLIS Malbrán (Administración Nacional de Laboratorios e Institutos de Salud), plays a crucial role among ReLAVRA participating countries, serving as the regional reference laboratory for quality assessment, assurance, and trainings (34). The regional reference laboratory in Argentina is designated as a WHO collaborating center and works in coordination with PAHO.

Annual AMR reports are issued by ReLAVRA, available on their website is a downloadable rapid assessment tool (in English or Spanish) to help monitor and evaluate bacteriology laboratory capacity in the Americas, for use in printed form or electronically by an Epi Info-based software (35).

ReLAVRA uses free software available from WHO (WHONET) for managing and analyzing antimicrobial susceptibility data, and surveillance of *N. gonorrhoeae* AMR has been part of ReLAVRA since 2005. In the WHO Region of the Americas, national reference laboratories for testing sensitivity to antibiotics were present in 25 (71%) countries in 2015 thanks to ReLAVRA's strengthening of laboratory networks; however, only 13 countries (37%) had prepared reports on AMR surveillance.

- Pan American Health Organization. Latin American Surveillance Network of Antimicrobial Resistance (ReLAVRA) database 2005–2015. ReLAVRA. Washington, DC: PAHO. Available from: https://www.paho.org/hq/index.php?option=com_content&view=article&id=13682:relavra-home&Itemid=42427&lang=en

Global Antimicrobial Resistance Surveillance System (GLASS)

GLASS was launched by WHO in 2015 to support the implementation of the Global Action Plan on AMR by enabling standardized, comparable, and validated data on AMR to be collected, analyzed, and shared with all countries and partners, all based on countries' national AMR surveillance. Thus, a main goal of GLASS is to encourage and facilitate the establishment of reliable national AMR surveillance systems to gather and disseminate data to inform decision-making; drive local, national, and regional action; and provide the evidence base for action and advocacy. Specific objectives include the following:

- > foster national surveillance systems and harmonized global standards;
- > estimate the extent and burden of AMR globally by selected indicators;
- > analyze and report global data on AMR on a regular basis;
- > detect emerging resistance and its international spread;
- > inform implementation of targeted prevention and control programs; and
- > assess the impact of interventions.

GLASS combines patient, laboratory, and epidemiological surveillance data to enhance understanding of the extent and impact of AMR on populations. Countries should consider gradual implementation of surveillance standards proposed in the GLASS manual based on local priorities and resources (36).

- <https://www.who.int/glass/en/>

Gonococcal Antimicrobial Surveillance Programme (GASP)

GASP is a worldwide laboratory network coordinated by WHO focal points and regional coordinating centers. GASP has been collecting gonococcal antimicrobial susceptibility data from participating countries since 1992 to inform national, regional, and global treatment guidelines. However, testing and reporting delays, as well as varied and changing sampling strategies, laboratory methodologies, and quality assurance procedures, make it difficult to compare data between countries and assess trends over time. In order to address these weaknesses, the Enhanced GASP (EGASP) program is being developed as a collaboration between the ministries of health of specific countries, the U.S. Centers for Disease Control and Prevention (CDC), and WHO. EGASP analyses are based on demographic, behavioral, and clinical data from male patients attending the sentinel clinics who have been identified to have a positive urethral culture for *N. gonorrhoeae* and antimicrobial susceptibility data from these urethral isolates. To select the centers, coordinators from GASP first conduct an assessment comprising a visit to sites in selected countries based on *N. gonorrhoeae* morbidity, ease of access to health care providers, competent laboratory services, government engagement, and availability of local partners. Countries with documented high rates of identified gonorrhea cases are prioritized. Once ready, countries enter EGASP data into the GLASS system, and the surveillance data will be submitted directly to WHO.

- World Health Organization. The Gonococcal Antimicrobial Surveillance Programme (GASP). Geneva: WHO. Available from: https://www.who.int/reproductivehealth/topics/rtis/gonococcal_resistance/en/

11.

Conclusions

The antimicrobial resistance of *N. gonorrhoeae* is rapidly increasing to commonly used antibiotic causing a growing global concern, as fewer options are available for treatment. Thus, the WHO has changed its recommendation for the empiric treatment to dual antibiotic therapy (ceftriaxone plus azithromycin) when local AMR surveillance is not available to inform national treatment guidelines. In Latin America and the Caribbean, treatment for gonococcal infections is largely based on clinical diagnosis, in addition to the lack of systematic gonorrhoea surveillance to provide national level burden of disease.

This document compiles and summarizes available operational guidance and

recommendations from PAHO/WHO to help countries in strengthening and/or developing AMR surveillance systems for *N. gonorrhoeae*. Routine prevention interventions, early diagnosis, and effective treatment, considering local levels of AMR are essential for the control and elimination of *N. gonorrhoeae* as a public health problem by 2030.

In this sense, PAHO/WHO reinforce the recommendation for countries in Latin America and the Caribbean to prioritize the implementation of AMR monitoring in *N. gonorrhoeae* as a key component of their STI surveillance system.

12.

Resources

Pan American Health Organization. Latin American Surveillance Network of Antimicrobial Resistance (ReLAVRA) database 2005–2015. PAHO/WHO; 2019.

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<https://www.who.int/glass/resources/publications/early-implementation-report/en/>

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World Health Organization, Regional Office for Europe. Fact sheets on Sustainable Development Goals: health targets; AMR (SDG target 3.3). Copenhagen: WHO EURO; 2017.

World Health Organization. Global action plan on antimicrobial resistance. Geneva: WHO; 2016.

<https://www.who.int/antimicrobial-resistance/global-action-plan/en/>

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Prevention, early diagnosis, and effective treatment are essential for the control and elimination of *Neisseria gonorrhoeae* infections as a public health problem. Currently, in Latin America and the Caribbean, treatment for gonorrhea is largely empiric and based on clinical diagnosis. In the Americas, the high burden of new *N. gonorrhoeae* infections (estimated at 11 million new cases a year), the complexity of the disease epidemiology, and in many countries the limited resources, make it difficult to fully understand the burden of disease and the burden of antimicrobial resistance (AMR) in *N. gonorrhoeae*.

PAHO has developed this document to facilitate the navigation of available guidance and recommendations for *N. gonorrhoeae* AMR surveillance by public health and health care professionals, at the national and subnational levels, involved in designing, implementing, and/or strengthening AMR surveillance of *N. gonorrhoeae* and overall surveillance of sexually transmitted infections. This document aims to consolidate guidance on AMR surveillance of *N. gonorrhoeae* from documents published by PAHO/WHO, and strives to assemble relevant information in a summarized manner to help countries in strengthening and/or developing AMR surveillance systems in *N. gonorrhoeae*.

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