WHO global antimicrobial resistance surveillance for Neisseria gonorrhoeae 2017–18: a retrospective observational study

Magnus Unemo, Monica M Lahra, Martina Escher, Sergey Eremin, Michelle J Cole, Patricia Galarza, Francis Ndowa, Irene Martin, Jo-Anne R Dillon, Marcelo Galas, Pilar Ramon-Pardo, Hillard Weinstock, Teodora Wi

Summary

Background Gonorrhoea and antimicrobial resistance (AMR) in Neisseria gonorrhoeae are major health concerns globally. Increased global surveillance of gonococcal AMR is essential. We aimed to describe the 2017–18 data from WHO’s global gonococcal AMR surveillance, and to discuss priorities essential for the effective management and control of gonorrhoea.

Methods We did a retrospective observational study of the AMR data of gonococcal isolates reported to WHO by 73 countries in 2017–18. WHO recommends that each country collects at least 100 gonococcal isolates per year, and that quantitative methods to determine the minimum inhibitory concentration of antimicrobials, interpreted by internationally standardised resistance breakpoints, are used.

Findings In 2017–18, 73 countries provided AMR data for one or more drug. Decreased susceptibility or resistance to ceftriaxone was reported by 21 (31%) of 68 reporting countries and to cefixime by 24 (47%) of 51 reporting countries. Resistance to azithromycin was reported by 51 (84%) of 61 reporting countries and to ciprofloxacin by all 70 (100%) reporting countries. The annual proportion of decreased susceptibility or resistance across countries was 0–21% to ceftriaxone and 0–22% to cefixime, and that of resistance was 0–60% to azithromycin and 0–100% to ciprofloxacin. The number of countries reporting gonococcal AMR and resistant isolates, and the number of examined isolates, have increased since 2015–16. Surveillance remains scarce in central America and the Caribbean and eastern Europe, and in the WHO African, Eastern Mediterranean, and South-East Asian regions.

Interpretation In many countries, ciprofloxacin resistance was exceedingly high, azithromycin resistance was increasing, and decreased susceptibility or resistance to ceftriaxone and cefixime continued to emerge. WHO’s global surveillance of gonococcal AMR needs to expand internationally to provide imperative data for national and international management guidelines and public health policies. Improved prevention, early diagnosis, treatment of index patients and partners, enhanced surveillance (eg, infection, AMR, treatment failures, and antimicrobial use or misuse), and increased knowledge on antimicrobial selection, stewardship, and pharmacokinetics or pharmacodynamics are essential. The development of rapid, accurate, and affordable point-of-care gonococcal diagnostic tests, new antimicrobials, and gonococcal vaccines is imperative.

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Research in context

Evidence before this study
Gonorrhoea remains a major public health concern globally, and antimicrobial resistance (AMR) in Neisseria gonorrhoeae is compromising the management and control of the infection. It is concerning that gonorrhoea could become untreatable due to the high level of AMR, which would result in an increase in serious complications, including infertility, ectopic pregnancy, and increased transmission of HIV. Additionally, infection during pregnancy is associated with low birthweight and ophthalmia neonatorum in neonates, which can cause blindness. WHO and other public health organisations have stated that global surveillance of gonococcal AMR is essential. We searched PubMed on Nov 23, 2020, using the terms “Neisseria gonorrhoeae” AND “surveillance” AND “global” AND “antimicrobial susceptibility” OR “antimicrobial resistance” for articles published from June 14, 1970, to Nov 23, 2020. Only two published papers, both from WHO, have attempted to describe the AMR of N gonorrhoeae globally. Scarc AMR data from few countries, particularly in the eastern part of the WHO European region (eg, three of 67 surveyed countries in 2016), African region (six of 67 countries in 2016), and Eastern Mediterranean region (one of 67 countries in 2016), were available. Additionally, AMR testing methodologies varied, many countries examined low numbers of isolates, and further improvements were considered to be essential.

Added value of this study
We report the data on gonococcal AMR from 73 countries globally in 2017–18, which is the largest report on gonococcal AMR to date. The WHO Western Pacific region had the highest levels of resistance to ceftriaxone and ciprofloxacin. Globally, ciprofloxacin resistance is high, azithromycin resistance is increasing, and decreased susceptibility and resistance to ceftriaxone and cefixime continues to emerge. The number of countries reporting gonococcal AMR and AMR isolates, as well as the number of examined isolates, have substantially increased compared with the two earlier studies reporting available data on gonococcal AMR globally. Additionally, AMR testing methodologies have improved, resulting in results with increased reliability. Furthermore, we discuss the key priorities that are essential for effective future management and control of gonorrhoea.

Implications of all the available evidence
Gonorrhoea is difficult to treat and could become untreatable due to high AMR levels. AMR gonococcal strains are spreading internationally; therefore, enhanced global surveillance is essential. Data on gonococcal AMR are imperative to monitor AMR trends, to identify emerging AMR, and to inform refinements of global, international, and national clinical management guidelines and public health policies. Key priorities essential for effective future management and control of gonorrhoea should be implemented into international and national action or response plans. However, gonococcal AMR surveillance needs to continue to be expanded and improved internationally, and global collaborative actions are essential to strengthen this.

Methods
Study design
For this retrospective observational study, we used WHO GASP and GLASS data on gonococcal AMR reported by 73 countries (an increase from 67 in 2015–16) from isolates collected between January, 2017, and December, 2018 (appendix pp 1–3). 61 countries reported data to WHO GASP and GLASS on AMR from 73 countries globally, to make comparisons with 2015–16 data in particular, and to discuss national and international priorities that are essential for effective management and control of gonorrhoea.

For more on WHO GLASS see https://www.who.int/glass/en

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The structure, sampling and testing methodologies, and quality assurance and control practices (including use of
2016 WHO gonococcal reference strains for comparisons within and between laboratories) of WHO GASP have been previously described.4,5,11 Where feasible, WHO GASP recommends that at least 100 representative gonococcal isolates are collected per country per year, and that quantitative methods are used to determine the minimum inhibitory concentration (MIC) of modern therapeutic antimicrobials (eg, agar dilution method or MIC gradient strip tests). These MICs should be interpreted with internationally validated and standardised interpretative criteria (ie, clinical susceptibility and resistance breakpoints or ecological cutoff values [where clinical breakpoints are not available]), such as those recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) or the Clinical Laboratory and Standards Institute (CLSI). Unfortunately, complete details regarding AMR testing methodology, MICs (or zone diameters in rare countries that use the disk diffusion method), and susceptibility or resistance breakpoints used (including version) were not available from several countries. Additionally, the CLSI recommends that only susceptibility breakpoints are used for ceftriaxone and cefixime. Accordingly, decreased susceptibility and resistance had to be combined for ceftriaxone and cefixime. Furthermore, since 2019, no clinical resistance breakpoints have been stated by the EUCAST and CLSI for azithromycin, and an epidemiological cutoff value (MIC >1 mg/L) has been used for the identification of non-susceptible isolates with determinants of azithromycin resistance. Due to the paucity of complete information regarding the susceptibility or resistance breakpoints used (including version) from many countries, in this study, we have included the figures that the countries reported concerning isolates that were non-susceptible or resistant to azithromycin (for easy comparability with previous global studies,4,5 these are referred to as azithromycin-resistant isolates hereafter).

Role of the funding source
No specific funding body had any role in study design, data collection, data analysis, data interpretation, or writing of the report.

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Data are n (%). MIC=minimum inhibitory concentration. *Decreased susceptibility and resistance were combined for ceftriaxone and cefixime due to the different antimicrobial resistance testing methods (eg, MIC determination using agar dilution or MIC gradient strip tests, or disc diffusion methods) and breakpoints used, and because the Clinical Laboratory and Standards Institute recommends only susceptibility breakpoints for these antimicrobials. †Resistance level where WHO recommends to discontinue a first-line empirical antimicrobial regimen in gonorrhoea monotherapy. Arbitrary resistance level illustrating the extremely high level of ciprofloxacin resistance.
As in previous WHO GASP studies,\textsuperscript{4,5} in 2017–18, the WHO European region had the highest number of reporting countries (n=30; including 27 EU or European Economic Area countries), followed by the Western Pacific region with 14 countries, region of the Americas (including Latin America, the Caribbean, and North America with USA and Canada) with 13 countries, the Eastern Mediterranean region with seven countries, the African region with five countries, and the South-East Asian region with four countries (table). The total number of isolates reported for the different antimicrobials varied from 12,895 (cefixime) to 25,505 (ciprofloxacin) in 2017 and from 15,876 (cefixime) to 27,251 (ciprofloxacin) in 2018 (appendix pp 1–3).

In 2017–18, isolates with decreased susceptibility or resistance to ceftriaxone were reported by 21 of 68 reporting countries (31%; up from 24% in 2015–16) and to cefixime by 24 of 51 reporting countries (47%; up from 45% in 2015–16). Isolates with resistance to azithromycin were reported by 51 of 61 reporting countries (84%; up from 81% in 2015–16) and to ciprofloxacin by all 70 reporting countries (100%; also 100% in 2015–16).\textsuperscript{5} During 2017–18, the annual proportion of decreased susceptibility or resistance across the 51–70 countries ranged from 0% to 21% to ceftriaxone and from 0% to 22% to cefixime, and that of resistance ranged from 0% to 60% to azithromycin and from 0% to 100% to ciprofloxacin.

The WHO GASP and GLASS data from 2017 are summarised in the appendix (pp 6–10). In 2018, 62 countries reported AMR data for ceftriaxone, which can be compared with 51 countries in 2014\textsuperscript{4} and with 58 countries in 2016.\textsuperscript{1} However, the number of tested isolates varied widely, from one in Luxembourg to 9,006 in Australia, and 33 (53%) countries tested fewer than 100 isolates (appendix pp 1–3). Overall, 17 (27%) of these 62 countries reported isolates with decreased susceptibility or resistance to ceftriaxone (figure 1), which is an increase from 13 (22%) of 58 countries in 2016.\textsuperscript{1} 49 countries reported data on cefixime susceptibility, but the number of examined isolates ranged from one in Luxembourg to 5,160 in the USA (appendix pp 1–3). 27 (55%) countries tested fewer than 100 isolates for cefixime. Overall, 19 (39%) countries reported isolates with decreased susceptibility or resistance to cefixime (figure 2), a decrease from 19 (49%) of 39 countries in 2016.\textsuperscript{1}

In 2018, 3,299 isolates from 27 EU or European Economic Area countries in the WHO European region were tested in Euro-GASP.\textsuperscript{12} Three (0.09%) of the 3,299 isolates, from Germany (n=1) and Spain (n=2), had decreased susceptibility or resistance to ceftriaxone, compared with none in 2016 or 2017.\textsuperscript{12} Across non-EU or European Economic Area countries within the WHO European region, no isolates with decreased susceptibility or resistance to ceftriaxone were found in Belarus and Ukraine; however, two (2%) of 110 isolates were reported in Switzerland (figure 1). Isolates with decreased susceptibility or resistance to cefixime were detected in 12 (44%) EU or European Economic Area countries, but the overall prevalence was low at 1.4% (n=1.9%) in 2017 and 2.1% in 2016.\textsuperscript{12} Three (11%) EU countries reported decreased susceptibility or resistance to cefixime in at least 5% of isolates (Cyprus 20.0% [1/5], Greece 6.0% [5/83],

Figure 1: Percentage of isolates with decreased susceptibility or resistance to ceftriaxone reported to WHO Global Antimicrobial Surveillance Programme and Global Antimicrobial Resistance Surveillance System in 2018

For Bahrain, China, Ecuador, New Zealand, Tunisia, and Vietnam, data are from 2017 (no data reported in 2018). Due to the low number of isolates in several countries (appendix pp 1–3), interpretations of antimicrobial resistance levels in these countries should be done with great caution. Disputed territories (Western Sahara, Jammu, and Kashmir) were not applicable and no data were available from these regions. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
and Italy 5·0% [5/100]. Across non-EU or European Economic Area countries, no isolates with decreased susceptibility or resistance to cefixime were detected in Ukraine; however, at least 5% of isolates were detected in Belarus (16·0% [3/19]) and Switzerland (5·6% [3/54]; figure 2).

In the WHO Western Pacific region, decreased susceptibility or resistance to cefixime was reported by seven (70%) of ten countries reporting data on ceftriaxone from 10,488 isolates, a decrease from ten (83%) of 12 countries with data in 2016. Decreased susceptibility or resistance was reported in at least 5% of isolates in one country (Japan 19·0% [132/692]) and in less than 5% of isolates in six countries: Australia (0·1% [6/9006]), Laos (1·6% [1/64]), Mongolia (0·8% [1/129]), Malaysia (2·4% [4/170]), the Philippines (4·0% [4/99]), and Singapore (1·5% [3/200]). Only three countries (Fiji, Cambodia, and South Korea) reported ceftriaxone-susceptible isolates only (figure 1). Notably, in 2016, decreased susceptibility or resistance to cefixime was also confirmed in Peru (2·4%). In 2018, decreased susceptibility or resistance to cefixime was documented in Canada (0·5% [17/3122] vs 0·3% in 2016) and the USA (0·3% [15/5160] vs 0·3% in 2016). All isolates in Argentina, Chile, Dominican Republic, Peru, Paraguay, and Uruguay were susceptible to ceftriaxone (figure 1). Notably, in 2016, decreased susceptibility or resistance to ceftriaxone was also confirmed in Peru (2·4%). In 2018, decreased susceptibility or resistance to cefixime was documented in Canada (0·5% [17/3122] vs 0·3% in 2016) and the USA (0·3% [15/5160] vs 0·3% in 2016). All isolates in Argentina, Chile, Columbia, Cuba, Dominican Republic, Ecuador, Panama, Peru, Paraguay, and Uruguay were susceptible to cefixime (figure 2). In 2016, less than 5% of isolates with decreased susceptibility or resistance to cefixime were reported in Argentina (1·4%).

In 2018, only five (11%) of the 47 countries in the WHO African region provided data on ceftriaxone from 714 isolates, and no isolates with decreased susceptibility or resistance were reported from Côte d’Ivoire, Kenya, or South Africa. Nevertheless, less than 5% of isolates with decreased susceptibility or resistance were found in Madagascar (1·2% [1/81]) and Uganda (0·3% [1/340]; figure 1). No isolates with decreased susceptibility or resistance to cefixime were detected in Côte d’Ivoire, Kenya, or South Africa; however, less than 5% of isolates with decreased susceptibility or resistance were reported in Uganda (0·3% [1/340]; figure 2).

In 2018, five (24%) of 21 countries in the WHO Eastern Mediterranean region reported data on ceftriaxone for
163 isolates. Saudi Arabia reported less than 5% of isolates with decreased susceptibility or resistance (3·1% [2/64]), but all isolates in Oman, Pakistan, Qatar, and United Arab Emirates were susceptible to ceftriaxone (figure 1). Although no isolates with decreased susceptibility or resistance to cefixime were found in United Arab Emirates, more than 5% of isolates in Saudi Arabia had decreased susceptibility or resistance (17% [1/6]; figure 2).

For azithromycin, 58 countries reported AMR data in 2018. However, the number of examined isolates varied widely, from one in Luxembourg to 9006 in Australia, and 31 (53%) countries tested fewer than 100 isolates (appendix pp 1–3). Overall, 44 (76%) countries reported resistant isolates, which has decreased from 49 (83%) of 59 countries since 2016. Nevertheless, 40 (69%) countries reported that at least 5% of isolates had resistance to azithromycin (figure 3), which has increased from 29 (49%) of 59 countries since 2016. Using the outdated EUCAST clinical resistance breakpoint, azithromycin-resistant isolates were detected in 24 (89%) of 27 Euro-GASP countries in the WHO European region in 2018, compared with 21 (84%) of 25 countries in 2016. Of these 24 countries, 23 (96%) reported that at least 5% of isolates had resistance. Additionally, the overall resistance in the EU or European Economic Area in 2018 increased to 13·3% (438/3299) from 7·5% in 2016. However, since 2019, EUCAST has not recommended any clinical azithromycin resistance breakpoint, and use of the recommended epidemiological cutoff value (MIC >1 mg/L) meant that 7·6% (251/3299) of isolates in 2018 were considered to contain azithromycin-resistance determinants. No azithromycin-resistant isolates were reported in Ukraine or Belarus, but the azithromycin-resistance level in Switzerland was more than 5% (28% [21/74]; figure 3).

In the WHO Western Pacific region, five (71%) of seven countries with data on azithromycin reported azithromycin-resistant isolates in 2018, compared with nine (75%) of 12 countries in 2016. Four countries reported at least 5% resistance (Australia 6·2% [561/9006], Japan 26·0% [178/692], Mongolia 7·3% [19/262], and Singapore 6·8% [20/294]) and one country reported less than 5% resistance (South Korea 0·9% [1/115]). All isolates in Cambodia and the Philippines were susceptible to azithromycin (figure 3).

In the WHO South-East Asian region, azithromycin resistance was detected in two (50%) of the four countries reporting in 2018, compared with six countries (100%) in 2016. India reported at least 5% resistance (9·4% [3/32]), Sri Lanka reported less than 5% resistance 4·2% [1/24]), and Bhutan and Thailand reported susceptible isolates only (figure 3).

In the WHO region of the Americas, azithromycin resistance was identified in all nine countries reporting in 2018. Eight (89%) countries (Argentina, Canada, Chile, Columbia, Cuba, Ecuador, Peru, and Uruguay) reported at least 5% resistance, whereas one (11%) country (USA) reported less than 5% resistance (4·6% [235/5160] vs 3·6% in 2016; figure 3).

In the WHO African region, Kenya reported at least 5% azithromycin-resistant isolates in 2018 (5·3% [5/96]), whereas no azithromycin resistance was detected in

Figure 3: Percentage of isolates with resistance to azithromycin reported to WHO Global Antimicrobial Surveillance Programme and Global Antimicrobial Resistance Surveillance System in 2018

For China, New Zealand, and Vietnam, data are from 2017 (no data reported in 2018). Due to the low number of isolates in several countries (appendix pp 3–3), interpretations of antimicrobial resistance levels in these countries should be done with great caution. Disputed territories (Western Sahara, Jammu, and Kashmir) were not applicable and no data were available from these regions. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
Côte d’Ivoire, Madagascar, Uganda, or South Africa (figure 3). Notably, less than 5% resistance was reported in Côte d’Ivoire in 2016 (2.0%).

In the WHO Eastern Mediterranean region, at least 5% of isolates were reported to be resistant to azithromycin in Pakistan (8.5% [4/47]) and Saudi Arabia (16.7% [1/6]) in 2018, whereas all isolates in United Arab Emirates were susceptible (figure 3).

For ciprofloxacin, 66 countries reported AMR data in 2018. However, the number of tested isolates ranged from one in Luxembourg to 8895 in Australia, and 37 (56%) countries tested fewer than 100 isolates (appendix pp 1–3). The mean level of ciprofloxacin resistance in WHO regions ranged from 49% (European region) to 93% (South-East Asian region). Overall, 12 (19%) countries in five WHO regions reported more than 90% resistance to ciprofloxacin: Bhutan, Cambodia, Ecuador, India, South Korea, Madagascar, Pakistan, Peru, Saudi Arabia, Thailand, Tunisia, and Uganda.35 (53%) additional countries had ciprofloxacin resistance levels of 50–90%. Only four (6%) countries reported less than 30% resistance (United Arab Emirates 28.6% [2/7], Australia 25.9% [2303/8895], Fiji 2.0% [1/51], and Ukraine 10.0% [1/10]; figure 4).

Discussion

In 2017–18, WHO GASP and GLASS reported extremely high levels of ciprofloxacin resistance, increasing azithromycin resistance, and continued spread of decreased susceptibility and resistance to cefixime and ceftriaxone. The number of countries reporting to WHO GASP and GLASS, those reporting every year, and those reporting isolates with decreased susceptibility or resistance to examined antimicrobials, as well as the total number of examined isolates, have increased since 2015–16.5 However, despite how a low number of isolates per country has been shown to relatively closely reflect the national AMR situation,36 major concerns remain regarding the low numbers of isolates and countries examined in many WHO regions, mostly due to either use of syndromic management or molecular diagnostics. Many countries with limited gonococcal AMR surveillance have a high incidence of gonorrhoea, suboptimal diagnosis, over-the-counter access to antimicrobials, and limited availability of optimal antimicrobial treatment (eg, high-quality and high-dose ceftriaxone or dual therapy with ceftriaxone plus azithromycin). These factors create opportunities for the further emergence and spread of gonococcal AMR.15-18 Accordingly, expanded gonococcal AMR surveillance, with a focus on extended-spectrum cephalosporins and azithromycin, is especially urgent in the WHO African, Eastern Mediterranean, and South-East Asian regions, and in central America and the Caribbean and non-EU or European Economic Area European countries. Nevertheless, in the WHO Eastern Mediterranean region, seven (33%) countries reported some AMR data in 2017–18 (despite few isolates tested in most countries), compared with one (5%) country in 2015–16; and surveillance initiatives are ongoing in selected countries across the WHO African region. Further strengthening is also important in the WHO Western Pacific region, where most tested isolates are from Australia; however, many ceftriaxone-resistant and cefixime-resistant strains have originated in east Asian countries.3-7

Figure 4: Percentage of isolates with resistance to ciprofloxacin reported to WHO Global Antimicrobial Surveillance Programme and Global Antimicrobial Resistance Surveillance System in 2018

For Bahrain, China, New Zealand, El Salvador, Tonga, and Vietnam, data are from 2017 (no data reported in 2018). Due to the low number of isolates in several countries (appendix pp 1–2), interpretations of antimicrobial resistance levels in these countries should be done with great caution. Disputed territories (Western Sahara, Jammu, and Kashmir) were not applicable and no data were available from these regions. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city, or area of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
Appropriate and timely reported data on gonococcal AMR surveillance are essential worldwide to refine international and national gonorrhoea treatment guidelines (appendix pp 4–5). Traditionally, discontinuation of first-line empirical treatment has been recommended when the level of treatment failures, AMR, or both, reach 5%. However, the evidence for this AMR threshold of 5% and above is scarce (currently reviewed and modelled by WHO), and the level and relevance of this threshold for single antimicrobials can be questioned when mostly dual therapy has been recommended during the past decade. Furthermore, the local epidemiology of gonorrhoea and AMR, aetiological diagnosis versus syndromic management, transmission frequency, sexual contact notification strategies, and treatment strategies and cost in diverse settings also affect this threshold.

Undoubtedly, the ideal information to inform treatment guidelines is the prevalence of verified treatment failures. During the past decade, sporadic failures to treat gonorrhoea with ceftriaxone (250–1000 mg) and ceftriaxone plus azithromycin or doxycycline have been confirmed and characterised in detail internationally. However, the number of gonorrhoea treatment failures is essentially unknown at the global level, and it is imperative to substantially enhance the identification, verification, and reporting of failures with recommended ceftriaxone and extended-spectrum cephalosporin plus azithromycin dual therapies.

The increasing resistance to azithromycin challenges its inclusion in recommended dual therapies. Some countries have returned to ceftriaxone monotherapy as recommended first-line therapy, such as in the UK (1 g monotherapy) and the USA (500 mg monotherapy [1 g if an individual weighs ≥150 kg]). Furthermore, the 2020 European gonorrhoea guideline recommends ceftriaxone 1 g monotherapy as an option for anorectal gonorrhoea in well controlled settings and circumstances (including absence of ceftriaxone resistance), and guidelines in Japan and China also recommend ceftriaxone 1 g monotherapy (appendix pp 4–5). The main reason to maintain azithromycin in dual therapy has been to avoid the treatment failures associated with ceftriaxone monotherapy, which have been sporadically documented and predicted to be more prevalent than reported gonorrhoea in well controlled settings and circumstances. Ceftriaxone 1 g monotherapy as an option for anorectal gonorrhoea is essentially unknown at the global level, and it is imperative to substantially enhance the identification, verification, and reporting of failures with recommended ceftriaxone and extended-spectrum cephalosporin plus azithromycin dual therapies.

To enhance WHO GASP and GLASS, political engagement and financial commitment is needed nationally and internationally. Gonococcal AMR surveillance should be considered as part of routine diagnosis and surveillance. It is crucial that clinical (e.g., collection, transportation, and storage of specimens) and laboratory (e.g., quality-assured gonococcal culture, AMR testing, and preservation of isolates) training for enhanced culture-based AMR surveillance is supported. To enhance WHO GASP and GLASS, political engagement and financial commitment is needed nationally and internationally. Gonococcal AMR surveillance should be considered as part of routine diagnosis and surveillance. It is crucial that clinical (e.g., collection, transportation, and storage of specimens) and laboratory (e.g., quality-assured gonococcal culture, AMR testing, and preservation of isolates) training for enhanced culture-based AMR surveillance is supported.

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Gonococcal Antimicrobial Susceptibility Surveillance Programme–Argentina, and the Brazilian GASP. Next-generation sequencing of gonococcal strains, from not only AMR lineages but also successful antimicrobial susceptible lineages, is revolutionising our understanding of the emergence, evolution, fitness, and geographical and temporal spread of AMR. Nevertheless, genetic AMR prediction will never completely replace culture-based AMR testing, which can detect AMR due to both known and unknown determinants and subsequently verify them.

The main limitations of WHO GASP and GLASS include the low number of participating countries in some WHO regions; the low number and representativeness of isolates (e.g., geographically, from all groups at increased risk, genders, and sites); use of disc diffusion methods in some settings, instead of recommended MIC determination; absence of implemented global external quality assessment; absence of harmonised global resistance breakpoints (although all countries reporting in 2017–18 used breakpoints from EUCAST or CLSI, which only have minor differences); and the scarce epidemiological data for patients with gonorrhoea (except for the Euro-GASP, UK Gonococcal Resistance to Antimicrobials Surveillance Programme, US Gonococcal Isolate Surveillance Project, and WHO enhanced GASP). For future WHO GASP and GLASS, the minimum number of isolates required per country for inclusion, on the basis of the number of cases in one given country, needs to be defined; details about AMR testing, including MICs of isolates, methodology, susceptibility, and resistance breakpoints and version, should be provided; and quality assurance and control measures need to be fully implemented. Accordingly, WHO and the GASP networks are continuously working on improvements through advocacy; regular training in GASP and GLASS methodologies; provision of WHO’s N. gonorrhoeae reference strains (currently under revision) for quality assurance and control of phenotypic and molecular diagnostics, genetic AMR prediction, molecular epidemiology, and as fully characterised reference genomes in next-generation sequencing analysis; and initiating WHO enhanced GASP in additional countries, which aims to collect standardised epidemiological information in combination with AMR data.

In conclusion, WHO GASP and GLASS provide imperative AMR data to inform how to refine national and international guidelines for gonorrhoea treatment and, ideally, antimicrobial stewardship, prescription policies, and drug regulations. However, WHO GASP and GLASS must continue to expand and improve, including systematic surveillance and timely reporting of ceftriaxone-resistant strains, treatment failures, and antimicrobial use or misuse, supported by molecular AMR prediction and next-generation sequencing where feasible. Culture-based testing to detect AMR due to both known and unknown determinants remains imperative. The development of new antimicrobials to treat urogenital and extragenital gonorrhoea (in conjunction with strategies to conserve these novel and current antimicrobials), gonococcal vaccines, and detection tests for diagnosis and surveillance (including rapid point-of-care tests for detecting gonococci and AMR), is crucial for future disease control.


