Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report 2022

World Health Organization

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Contents

Foreword

Antimicrobial resistance (AMR) in a wide range of infectious agents continues to be a serious threat to human, animal and environmental health, as well as the well-being of the global economy and development. Mindful of this threat, the Member States of the World Health Organization (WHO) approved the Global Action Plan on Antimicrobial Resistance at the World Health Assembly in May 2015, which was then endorsed by governments worldwide at the United Nations General Assembly in 2016. However, a critical element underpinning all effective action is the need to obtain solid data generated through robust surveillance.

The WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS) was launched in 2015 to foster AMR surveillance and inform strategies to contain AMR. The system started with surveillance of AMR in bacteria causing common human infections and has expanded its scope to include surveillance of antimicrobial consumption (AMC), invasive fungal infections, and a One Health surveillance model relevant to human health. To meet future challenges, it is in continuous evolution to enhance the quality and representativeness of data to inform the AMR burden accurately. As of today, 126 countries, territories and areas participate in GLASS.

This GLASS report, produced in collaboration with Member States, summarizes 2020 data on AMR rates in common bacteria from countries, territories, and areas. For the first time, the annual GLASS report presents data on AMC at the national level. The report brings new features, including analyses of population testing coverage, AMR trends, and a more comprehensive and user-friendly content to the WHO website.

The report discloses inequalities in testing coverage and laboratory quality assurance among countries, which may explain huge variances in AMR rates across nations. These inequalities are more prominent in low- and middle-income countries. Despite the identified gaps, the report identifies very high levels of AMR in pathogens causing bloodstream infections, regardless of the testing coverage. Especially worrisome are the high resistance rates of last-resort drugs in pathogens that are common causes of hospital-acquired infections. Carbapenems are often employed as last-resort drugs and resistant isolates are usually multidrug-resistant and often associated with treatment failure.

This report marks the end of the GLASS early implementation period. Considering the inequalities and gaps, especially in low-resource countries with weak systems, the next phase of GLASS will include regular, prospective, national AMR prevalence surveys to complement routine surveillance and achieve the collection of nationally representative AMR data and trends. WHO is also committed to reducing inequalities in laboratory capacities and a global laboratory strengthening initiative is being launched in this regard.

The COVID-19 pandemic hit the entire world in 2020, affecting several sectors, particularly public health. Efforts to improve AMR and AMC surveillance globally were no exception and several countries contributing to GLASS-AMR monitoring in previous years could not submit 2020 AMR data. Importantly, the fight against AMR is all the more critical during public health crises. Enhanced collective efforts are needed to help ensure the continuity of crucial programmes such as AMR and AMC surveillance and to seize the opportunity to develop more sustainable infection prevention and control programmes, promote integrated antibiotic stewardship guidance, and leverage increased laboratory capabilities and other system-strengthening efforts.

Throughout the GLASS journey, several partners have provided resolute support to its development and implementation, without which we could not have come so far. WHO is also grateful for the expertise provided by the WHO AMR Surveillance and Quality Assessment Collaborating Centres Network and the backing of regional AMR and AMC surveillance networks, which represent essential pillars for advancing AMR surveillance globally. Together we can turn the tide of the AMR global threat. GLASS stands ready to play its part at this pivotal moment worldwide.

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List of acronyms

AMC	antimicrobial consumption
AMR	antimicrobial resistance
AMU	antimicrobial use
AST	antimicrobial susceptibility test/testing
ATC	Anatomical Therapeutic Chemical
AWaRe	Access, Watch, Reserve (classification of antibiotics)
BCIs	bacteriologically confirmed infection/s
CAESAR	Central Asian and European Surveillance of Antimicrobial Resistance
CLSI	Clinical and Laboratory Standards Institute
CTAs	countries, territories, and areas
DDD	defined daily dose
EARS-Net	European Antimicrobial Resistance Surveillance Network
EGASP	Enhanced Gonococcal Antimicrobial Surveillance Programme
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESBL	extended spectrum beta-lactamase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GLASS	Global Antimicrobial Resistance and Use Surveillance System
GLASS-EAR	GLASS-Emerging Antimicrobial Resistance Reporting
IQR	interquartile range
LMICs	low- and middle-income countries
MRSA	methicillin-resistant *Staphylococcus aureus*
PPS-AMU	point prevalence survey of antimicrobial use
SDG	Sustainable Development Goals
WHO	World Health Organization

Summary

Antimicrobial resistance (AMR) poses a significant global threat of far-reaching economic and public health proportions. In 2015, the World Health Organization (WHO) established the Global Antimicrobial Resistance and Use Surveillance System (GLASS) to monitor AMR in common bacteria and invasive fungi, and antimicrobial consumption (AMC) in humans. GLASS aims at collecting strategic information to inform the AMR response at the national and global level. Since 2017, WHO has issued annual GLASS reports describing the expansion and gradual strengthening of the newly established global system. This edition of the GLASS report summarizes 2020 data from countries, territories, and areas (CTAs) on AMR rates and trends in common bacteria. For the first time, it also presents official data on the consumption of antimicrobial medicines at the national level. An innovative feature of the report is the contextualisation of AMR findings based on an analysis of testing coverage, which varies substantially among CTAs contributing data from all regions of the world (**Section 3.2**). Testing coverage is measured by the median number of bacteriologically confirmed infections (BCIs) with antimicrobial susceptibility test (AST) results per million population by CTA. The report shows that AMR resistance rates are lower in CTAs with a comparatively better coverage for most pathogen-drug-infection site combinations. For example, median resistance to third-generation cephalosporins in *Escherichia coli* bloodstream BCIs and methicillin resistance in *Staphylococcus* aureus bloodstream BCIs was substantially higher when considering all reporting CTAs, compared to those with a better testing coverage (above the 75th percentile). However, the higher AMR rates in CTAs with lower coverage may be due to a convenient selection of health care facilities contributing data to the surveillance system, mainly including tertiary referral or research hospitals caring for patients with complex infections, treatment failures, and hospital-acquired infections (**Section 3.3**). Of note, testing coverage in high-income countries was generally greater than in low- and middle-income countries (LMICs) (**Figs. 3.4** and **3.6a-6c** in **Section 3.2**) and lower AMR rates in these CTAs may also reflect a stronger health systems response to AMR.

The wide variation in testing coverage, and hence data representativeness, is a major limitation in interpreting AMR rates globally and nationally and the results should be interpreted with caution. Complementary AMR surveillance approaches, such as prospective AMR prevalence surveys, should be considered to achieve nationally representative AMR data and trends to evaluate and inform the AMR response, especially in low-resource countries with weak routine surveillance. In addition to the variation in testing coverage, one gap identified in this report is the low proportion of CTAs (49%) performing external quality assurance in all clinical laboratories that serve the national AMR surveillance systems (**Section 3.1**), which essentially means that not all test results are quality assured. Although current data cannot be used to calculate robust national and global resistance estimates for the combinations under surveillance, they do allow to identify combinations where resistance remains low and where high resistance is a cause for concern. This is particularly true where larger numbers of CTAs contributed data and where median global percentage resistance is consistent, regardless of coverage.

Key findings and public health implications

AMR surveillance

By the end of the 2021 data call, 109 countries plus two territories and areas were enrolled in GLASS-AMR, 99 CTAs provided information on the status of AMR surveillance implementation, and 87 CTAs on AMR rates during 2020.

The COVID-19 pandemic hit the entire world in 2020, affecting several sectors, particularly public health. Several CTAs that had been contributing to GLASS-AMR monitoring in previous years could not submit 2020 AMR data. Another observation was an increase in AMR rates by more than 15% in 2020 compared with 2017 for meropenem and third-generation cephalosporin resistance in bloodstream *E. coli* BCIs, ciprofloxacin resistance in *Salmonella* spp. bloodstream BCIs, and azithromycin resistance in gonorrhoea BCIs (**Section 3.3**). Although further studies would be needed to verify whether a real upward trend occurred for these combinations, the negative impact of the COVID-19 pandemic on both AMR surveillance activities and AMR rates has been reported previously and may have contributed, at least in part, to these findings.

The very high 2020 levels of AMR in pathogens causing bloodstream infections, regardless of testing coverage, are of major concern. Third-generation cephalosporins are recommended as a first-line empiric treatment for this type of infection. High levels of third-generation cephalosporin resistance have been reported in *Klebsiella pneumoniae*, the third most frequent pathogen causing bloodstream infections, which may drive the increase in the use of 'last resort' carbapenems. Although the reported rate of carbapenems resistance in *K. pneumoniae* was lower in CTAs with better testing coverage, the pooled rates from all reporting CTAs showed carbapenem resistance in more than 8% of bloodstream infections caused by this pathogen and may indicate the emergence of this type of resistance worldwide. The global spread of carbapenemase-producing Enterobacterales and the high rates of carbapenem and aminoglycoside resistance in *Acinetobacter* spp. (≥56% regardless of testing coverage) are of great concern. Carbapenem resistant isolates are usually multidrug-resistant and are often associated with treatment failure.

Regarding the AMR indicators monitored under the Sustainable Development Goals (SDG)[1] framework, the median rates of third-generation cephalosporin-resistant *E. coli* and methicillin-resistant *S. aureus* (MRSA) causing bloodstream infections reported by 76 CTAs are 42% and 35%, respectively. These rates are much lower in 19 CTAs with better testing coverage (11% for third-generation cephalosporin-resistant *E. coli* and 7% for MRSA). Most LMICs presented lower testing coverage compared to high-income CTAs for both SDG indicators (**Fig. 3.6a.** in **Section 3.2**).

AMC surveillance

AMC is among the main drivers of the emergence of AMR. Thirty-four CTAs provided information on the status of AMC surveillance implementation and 27 on national AMC data in 2020. The small number of reporting CTAs and different sources of AMC data collection limits the data interpretation. Nonetheless, most reporting CTAs provided AMC data from the public and private sectors with a total population coverage above 80% (**Section 4.3**). CTAs reporting on all antimicrobials show that antibacterial medicines are mainly the most consumed class of antimicrobials. This first year of GLASS-AMC reporting shows that even less-resourced CTAs can achieve the initial steps of establishing a national AMC surveillance system. At this stage, the frequency of data collection is not regular and the AMC data might be incomplete in CTAs with little experience in surveillance, thus emphasizing the need to support these CTAs in consolidating their newly established surveillance system.

Although the extent of consumption of antibacterial pharmacological subgroups varies across CTAs, the beta-lactam penicillins were often the most frequently consumed subgroup. Sixty-five per cent of CTAs reporting data met the target of at least 60% consumption of Access group antibacterials of the AWaRe (that is, Access, Watch, Reserve) classification[2], as defined by the WHO Thirteenth General Programme of Work. Oral formulations accounted for most of the antibacterials consumed in CTAs, reflecting that most antimicrobial use is in the community.

Considerations for further actions

Results and gaps documented in this report demonstrate the continuing need to build robust surveillance systems capable of producing data that can be used to inform and evaluate public health actions. Further actions are necessary to improve the representativeness and accuracy of surveillance data, which allow for robust baseline assessments, trend analysis and comparison between settings, including associations between AMR and AMC data. Key considerations include:

- The COVID-19 pandemic may have impacted on CTA reporting capacity and AMR rates in a few pathogen-drug-infection site combinations. Based on findings of increased AMR rates in an ongoing, multi-country study with a specific focus on antibiotic prescription practices and clinical outcomes in COVID-19 patients, WHO has issued evidence-based recommendations for the rational use of antibiotics in this patient population.
- The low proportion of CTAs performing external quality assurance in all clinical laboratories that serve national AMR surveillance systems calls for an urgent global effort to support the development of national clinical bacteriology networks, particularly in LMICs, and a global microbiology laboratory network to support AMR diagnosis in all regions.
- The reported AMR rates are often lower in CTAs with better testing coverage for most pathogen-drug-infection site combinations. The observed association of higher AMR rates and lower testing coverage in the population may result from patient selection bias. However, it may also reflect more advanced AMR interventions in settings with high testing coverage. Most probably, it is a mix and further studies are needed to better understand this association.

[1] The specific AMR indicator reported to the SDG monitoring framework (3.d.2) monitors the proportion of bloodstream infections due to *E. coli* resistance to third-generation cephalosporins and methicillin-resistant *S. aureus* (MRSA) among patients seeking care.

[2] The AWaRe classification is a tool to support antibiotic stewardship efforts at local, national, and global levels. Antibiotics are classified into three groups, Access, Watch, and Reserve, considering the impact of different antibiotics and antibiotic classes on AMR, to emphasize the importance of their appropriate use.

- Countries with low testing coverage and weak health systems are in great need of robust AMR baseline and trend data to guide and evaluate their AMR response. Therefore, WHO will pilot and introduce periodic nationally representative AMR surveys to overcome the paucity of crucial AMR (trend) data in selected CTAs.
- The much higher rates of the two AMR indicators monitored under the SDG[3] when considering all 76 reporting CTAs compared to the CTAs with better testing coverage require further studies, particularly as the least resourced CTAs may be the most heavily affected by higher rates.
- The very high levels of AMR in K. *pneumoniae* and *Acinetobacter* spp. causing bloodstream infections are of great concern and calls for efforts to strengthen infection prevention and control measures in hospital settings globally.
- The first year of the GLASS-AMC data call demonstrates the ability of CTAs at different levels of development to gather and report national AMC data, but also reveals the need for standardization, data validation, and improved data coverage to generate robust AMC data that are comparable over time. CTAs at a more mature stage of their national surveillance should report and use AMC data for policy and practice, link their AMC data to relevant domains (for example, AMR and access to medicines frameworks) and possibly across the human and animal sectors through a One Health approach.

This report supports the view that AMR represents a global health security threat requiring concerted cross-sectional action by governments and different stakeholders in society. Surveillance that generates reliable data is essential for sound global, regional and national strategies to contain AMR, improve the quality of patient care, and strengthen health systems.

[3] Proportions of bloodstream infections due to third-generation cephalosporins resistant to *E. coli* and MRSA.

1 Introduction

1.1 Basic facts on antimicrobial resistance (AMR)

AMR is among the top 10 global health threats *(1)*. Resistance of bacteria to antibiotics (antibiotic resistance) is an urgent global public health and socioeconomic problem. Modern medicine depends on effective antimicrobial medicines, yet high rates of resistant infections across a broad range of microorganisms have been documented in all World Health Organization (WHO) regions *(2)*. Murray et al. estimated that 4·95 million deaths were associated with bacterial antibiotic resistance, including 1·27 million deaths attributable to bacterial AMR in 2019 *(2)*. The World Bank estimated that up to 3.8% of the global gross domestic product could be lost due to AMR by 2050 *(3)*. Although the overuse or misuse of antibiotics are primary drivers of the emergence of AMR, other multiple interconnected factors contribute to its prevalence and spread. Higher AMR rates have been documented in several low- and middle-income countries (LMICs) compared to rates in high-income countries, despite a lower per-person consumption of antibiotics in the former *(4, 5)*.

Strengthening surveillance of AMR is pivotal to enhancing the scientific basis to inform risk assessments and identify opportunities for mitigation. In May 2015, the Sixty-eighth session of the World Health Assembly adopted a global action plan endorsing the urgent need for strengthening the knowledge and evidence base of AMR through surveillance and research to tackle the AMR threat *(6)*. In the same year, the Global Antimicrobial Resistance and Use Surveillance System (GLASS) was launched by WHO *(7)*. Since then, there has been a significant investment in improving AMR surveillance to generate high-quality evidence of its magnitude, distribution, and diversity globally *(7)*. Notably, GLASS is the first system that has enabled the harmonized global reporting of official national AMR and antimicrobial consumption (AMC) data *(7, 8)*. More recently, following the 2022 G7 Health Ministers' meeting in Berlin, Germany, the G7 declared its commitment to strengthening and supporting national surveillance and intelligence systems for emerging AMR threats as part of the G7 Pact for Pandemic Readiness *(9)*. Recognizing that although almost 90% of countries have developed an AMR national action plan on AMR, only 20% have identified funding for implementing and monitoring these plans, the G7 has also committed to address this main challenge at the country level and to facilitate the mobilization of domestic and external financing by supporting the development of national investment in the AMR response in LMICs *(9)*.

Despite global and regional efforts, considerable gaps remain in our understanding of the magnitude, distribution and trend of drug-resistant infections at the national and global level. Developing and sustaining robust national surveillance systems is challenging, particularly in LMICs. Robust surveillance systems require coverage of the population, access to quality assured laboratory services, adequate diagnostic stewardship, and strong reporting systems. While many high-income countries meet these requirements through systematic continuous data collection and analysis from routine clinical practice, most LMICs are not yet able to generate quality representative data that can inform national policy development, evaluate trends, or allow for country comparisons. This is of great concern as preliminary data suggest that LMICs face a significant AMR threat that requires urgent evidence-based actions. For this reason, GLASS has developed a complementary approach to collect quality representative data in LMICs. This innovative approach proposes periodic, nationally representative AMR surveys that target countries where it will take time to establish robust surveillance systems.

Knowledge of the relative contribution of different AMR drivers needs to be improved. GLASS seeks to monitor antimicrobial use (AMU) as a major driver of AMR by collating the nationally aggregated data on antimicrobial consumption (AMC), as well as promoting studies on antibiotic prescription practices. Together with national representative quality AMR data, AMC monitoring will accurately guide strategies to contain and mitigate the impact of AMR on human health.

1.2 What's new in the 2022 report?

The 2022 GLASS report is in an innovative digital format with the main findings and messages presented in a single document, which is accompanied by an expanded and more comprehensive content on the WHO website.

Previous GLASS report editions have predominantly focused on the reporting of operational activities of GLASS as part of its early implementation and development years, as well as presenting the latest year of AMR data contributed by national surveillance systems as a secondary outcome to reflect progress in the implementation of global and related regional surveillance networks *(10-13)*. The scope of the new generation of GLASS reports – of which the 2022 report is the first edition – has broadened and adds more analysis and interpretation, as well as a description of the further development of GLASS after the early implementation period. In addition to presenting data collected through the latest data call, the 2022 report contextualizes these findings by providing a summary of five years of national AMR surveillance data contributed to GLASS from its initiation. These data were collated through five data calls in 2017-2021, which invited countries enrolled in GLASS to contribute national AMR data for the previous calendar year (that is, 2016-2020).

The main objective of the 2022 report is to summarize global AMR and AMC data to date, building an evidence-based case to address ongoing limitations and gaps through strategic and concrete actions in the next phase of GLASS. AMR findings are thus presented and interpreted in the context of progress in the participation of countries in GLASS, and progress in global AMR surveillance coverage and laboratory quality assurance systems at (sub)national level.

For the first time, the report includes a description of AMC data. These data are provided by country and expressed by defined daily dose (DDD) adjusted by population to allow a comparison across countries, and in tonnes unadjusted by population to allow a comparison with other sectors, such as animal sector data reported by the World Organisation for Animal Health. To provide the broadest possible pool of data, the analysis included the latest available year of national AMC data from each country reported during the 2021 data call.

For simplicity, this document provides relevant summary statistics for AMR data at the global scale only and, where appropriate, only for some examples of combinations under surveillance[1] for illustration purposes. The user may refer to the expanded web-based content to systematically disaggregate these data by WHO region and to visualize additional data at global, regional and country levels. Comprehensive country profiles for AMR and AMC data are also only provided as part of the web-based content, with the former including a summary of frequencies of bacterial pathogens and antibiotic-resistant bacterial pathogens. AMR data presented in country profiles are further disaggregated by the age and gender of the patient population and by the infection origin, where appropriate (that is, community or hospital origin, depending on the likely onset of the identified bacteriologically confirmed infection [BCI] *(8)*).

A new and more concise terminology has been introduced in the 2022 report. GLASS-AMC and GLASS-AMR are used to refer specifically to surveillance data related to AMC or AMR. The report broadly refers to countries, territories and areas (CTAs) throughout, recognizing that not all geographical areas enrolled in GLASS correspond to countries. This report and related web-based content consider 216 CTAs according to their WHO legal status (that is, 196 countries [194 WHO Member States plus two associate members]; 20 territories and areas). This denominator is used to calculate the percentages of CTAs enrolled in GLASS where applicable.

1.3 Key findings and messages

By the end of the 2021 data call, 109 countries plus two territories and areas were enrolled in GLASS-AMR, 99 CTAs provided information on the status of AMR surveillance implementation, and 87 CTAs on AMR rates. Despite significant increases in the number of CTAs enrolled in GLASS-AMR, as well as in absolute numbers of BCIs with antimicrobial susceptibility test (AST) results reported over the years, there is no overall evidence of an increase in global testing coverage. Indeed, testing coverage measured by the median number of BCIs with AST per million population by CTA was lower or showed no net change in 2020 compared to previous years for most infectious syndromes, bacterial pathogens and antibiotic groups considered. Furthermore, the substantial variation in median BCIs with AST per million population in individual CTAs suggests major differences in diagnosis, testing, and/or reporting coverage in 2016-2020 among enrolled settings, most likely reflecting differences in clinical training and/or practice, resource availability, and capacity among others.

[1] Refers to infectious syndrome-bacterial pathogen-antimicrobial combinations.

The estimated percentage of AMR in CTAs varies substantially, depending on the testing coverage. The percentage of AMR was lower for most antimicrobial, bacterial pathogen, and infectious syndrome combinations under surveillance when considering CTAs with higher testing and/or reporting coverage.[2] These observations are consistent, at least in part, with potential biases resulting from the convenient selection of health care facilities reporting AMR data in many settings where the capacity for routine surveillance is still nascent. For instance, a convenience sample of referral hospitals and/or financial barriers to laboratory testing may result in the selection of the most severely ill patients who may have been treated previously at lower levels of the health system. Hence, the global interpretation of resistance data is limited at present due to differences in surveillance coverage and the representativeness of surveillance sites. Conclusions of any genuine differences in resistance prevalence in settings with less established surveillance networks are also hampered by these factors.

Regarding the AMR indicators monitored under the United Nations Sustainable Development Goals (SDG),3 AMR estimates were lower in CTAs where the number of BCIs with AST per million population for the relevant combination was above the 75th percentile, which is suggestive of higher surveillance coverage. For example, median resistance to third-generation cephalosporins in *Escherichia coli* bloodstream BCIs was 41.8% when considering all CTAs, but 10.6% when considering only CTAs where the number of *E. coli* BCIs with test results for this antimicrobial group per million population was above the 75th percentile. Likewise, median methicillin resistance in *Staphylococcus aureus* bloodstream BCIs was 34.7% when considering all CTAs, and 6.8% when considering CTAs above the 75th percentile.

Despite the limitations, an analysis of 2020 AMR data allows to identify combinations where resistance remains low and where high resistance is a cause for concern. Notably, high levels of resistance in pathogens frequently causing hospital-acquired bloodstream infections were reported. Examples of the latter include carbapenem and aminoglycoside resistance in *Acinetobacter* spp. (≥56% regardless of testing coverage) and third- and fourth-generation cephalosporin resistance in *Klebsiella pneumoniae* (≥57% when considering all CTAs; ≥26% when considering CTAs above the 75th percentile).

The analyses covering the 2017-2020 period of GLASS data[4] also highlight some combinations with low or high resistance, which are consistent with the analysis of 2020 data. AMR percentage estimates remained relatively stable in many CTAs during the 2017-2020 period, suggesting that annual intra-country AMR data are generally coherent each year in these CTAs. A review of longitudinal AMR data can help target surveillance quality assurance efforts by identifying CTAs where vast discrepancies over time are noted, where appropriate.

By the end of the data call, 36 CTAs were enrolled in GLASS-AMC. Of these, 34 provided information on the status of AMC surveillance implementation and 27 on annual AMC. Data reported to GLASS-AMC show a wide variation in overall antimicrobial and antibacterial consumption. This variation likely reflects actual differences in AMC, but might also be partially attributed to differences in data coverage, the choice of data sources and their inherent advantages and limitations *(14)*, as well as the maturity of the surveillance systems. Antibacterials were the most consumed class of antimicrobials by a large margin, although not all CTAs provided data for other classes of antimicrobials.

Although the extent of consumption of antibacterial pharmacological subgroups varies across CTAs, the beta-lactam penicillins were often the most frequently consumed subgroup, apart from a few CTAs. Sixty-five percent of CTAs reporting data met the target of at least 60% consumption of Access group antibacterials included in the AWaRe classification (that is, Access, Watch, Reserve) *(15)*,[5] as defined by the WHO Thirteenth General Programme of Work. Oral formulations accounted for most consumption of antibacterials in the majority of CTAs. Amoxicillin alone or in combination with beta-lactamase inhibitors was often the most consumed oral agent. It is noteworthy that ciprofloxacin and azithromycin were often among the most frequently consumed oral antibacterials among the AWaRe Watch agents, while ceftriaxone was most often the most used parenteral substance.

[2] Refers to CTAs where the number of BCIs with AST per million population for the relevant combination was above the 75th percentile.

[3] The specific AMR indicator reported to the SDG monitoring framework (3.d.2) monitors the proportion of bloodstream infections among patients seeking care due to methicillin-resistant *Staphylococcus aureus* (MRSA) and *E. col*i resistant to third-generation cephalosporins.

[4] 2016 AMR data were excluded from the time series illustrating AMR trends due to few CTAs providing data for this calendar year.

[5] The AWaRe classification is a tool to support antibiotic stewardship efforts at local, national and global levels. Antibiotics are classified into three groups, Access, Watch and Reserve, considering the impact of different antibiotics and antibiotic classes on AMR in order to emphasize the importance of their appropriate use.

2 GLASS strategy and areas of work

2.1 GLASS strategy and milestones

The AMR threat can only be addressed if strategies and interventions at different levels and by different stakeholders are informed by robust data. In 2015, WHO established GLASS to help all CTAs generate data to inform actions and monitor the effectiveness of interventions *(16)*. GLASS seeks to contribute to the global agenda by providing reliable and timely information on the magnitude and trends of AMR, including the status of a major AMR driver: AMC. The SDG have set many aspirational targets to mitigate threats to mankind. GLASS also monitors and reports on SDG progress *(13)* through the new AMR indicator 3.d.2[6] under target 3.d.[7] The new indicator is considered a building block to help catalyse the establishment of national AMR programmes for monitoring and response in CTAs *(17, 18)*.

The GLASS target by 2030 is that all CTAs will apply globally harmonized standards to capture and share information on AMR and AMC with a global surveillance system to inform local, regional and global strategies to contain AMR. Member States, the *WHO AMR Surveillance and Quality Assessment Collaborating Centres Network*, and other international partners have supported and joined forces with WHO to develop and implement GLASS *(19)*. From its outset, mindful of the cross-cutting nature of AMR, GLASS was designed to gradually incorporate key elements to compose a comprehensive understanding of the problem and its drivers. As advised by country representatives *(20)*, GLASS started with a very simple methodology based on routine clinical practices to capture AMR in clinically relevant bacteria causing common human infections. This was followed by GLASS-Emerging Antimicrobial Resistance Reporting (EAR) that was designed to collect information on novel and emerging AMR and related events to assess their importance, facilitate early information sharing, and stimulate epidemiological and microbiological discussion for coordinated actions.

The third element incorporated into GLASS in 2021 has been the monitoring of the use of antimicrobial medicines. WHO has developed standard tools to monitor AMC at national and facility levels, assisting the national monitoring and reporting of antimicrobial medicines and strengthening knowledge on the use of these medicines, depending on epidemiological, demographic and geographical patterns. The GLASS-AMC module was launched in 2020 and annual data calls on national AMC started in 2021.

By the end of 2021, 114 CTAs covering 72% of the world's population agreed to contribute data to GLASS-AMR and/or GLASS-AMC. Of the 111 CTAs in GLASS-AMR, 33 were also enrolled in GLASS-AMC (30%). Three CTAs (Montenegro, Mongolia, and South Sudan) were enrolled in GLASS-AMC only. All 36 CTAs enrolled in GLASS-AMC are WHO Member States. Global maps showing cumulative numbers of CTAs enrolled in GLASS (either GLASS-AMR, GLASS-AMC, or both) over time are shown for 2017-2021 (only alternate years are provided for space considerations) (**Fig. 2.1**).

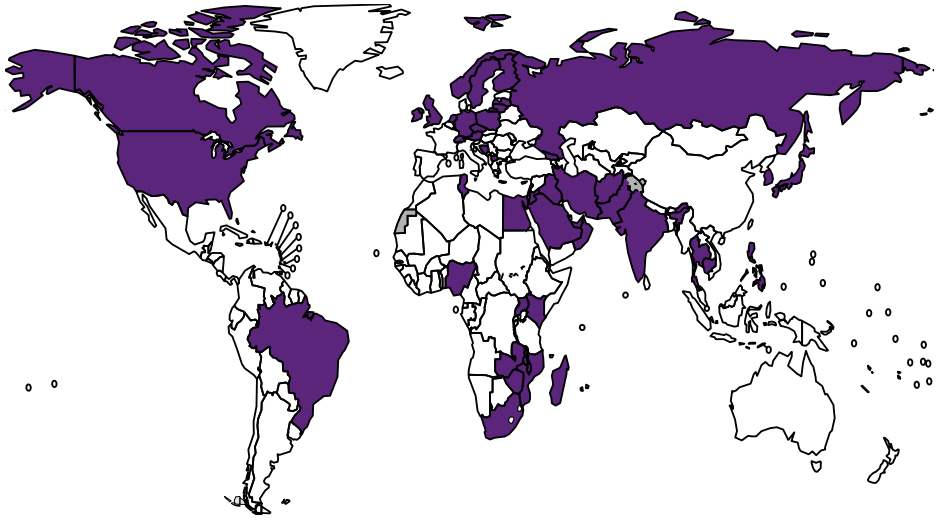
[6] SDG Indicator 3.d.2: The specific AMR indicator reported to the SDG monitoring framework monitors the proportion of bloodstream infections due to *E. coli* resistant to third-generation cephalosporins and MRSA among patients seeking care.

[7] SDG Target 3.d: Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction, and management of national and global health risks.

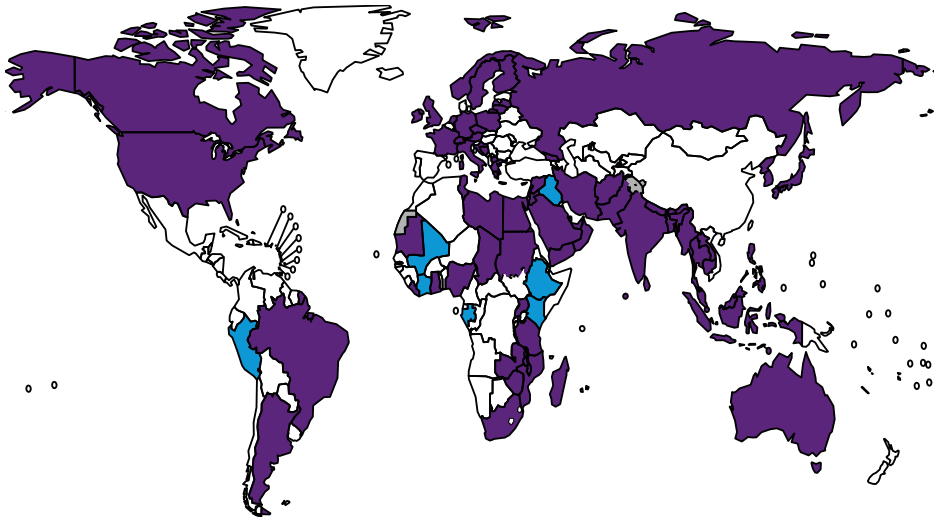
Fig. 2.1. CTAs enrolled in GLASS-AMR and/or GLASS-AMC (2017, 2019, 2021)

Enrolled in GLASS-AMR and GLASS-AMC | Enrolled in GLASS-AMR | Enrolled in GLASS-AMC | Not enrolled | Not applicable

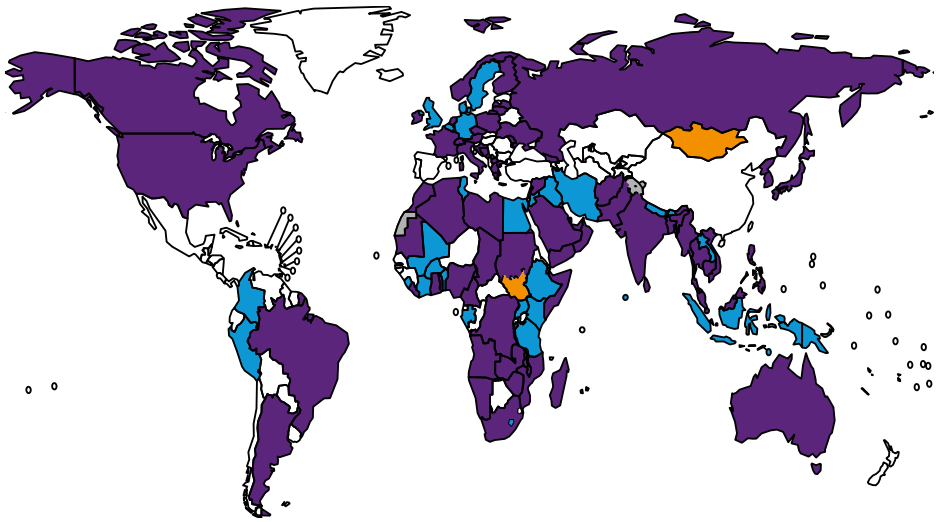
Enrolment status by end of 2017



Enrolment status by end of 2019



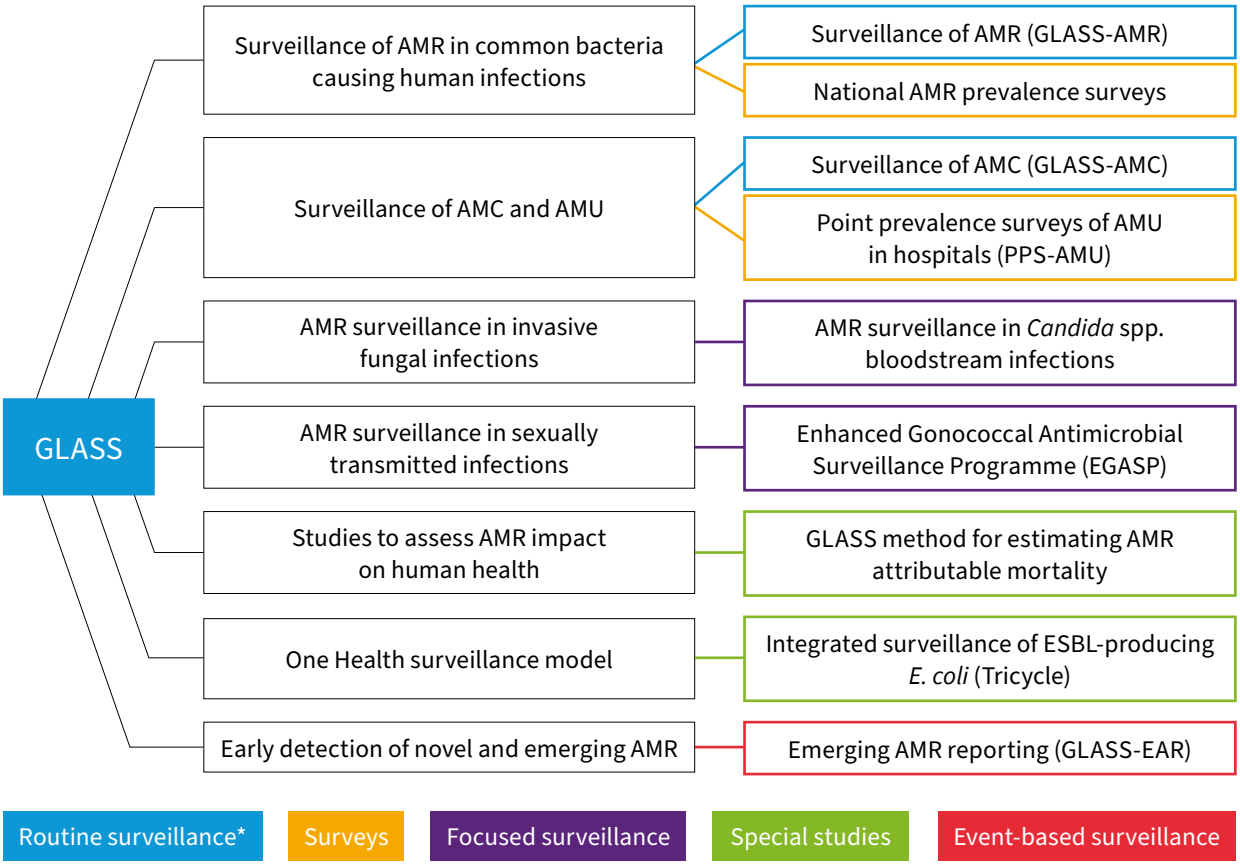
Enrolment status by end of 2021



The cross-sectoral nature of AMR requires a One Health[8] *(21, 22)* approach in every intervention aimed to tackle AMR and surveillance is no exception. The *WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance* developed the AMR surveillance model to assess the occurrence of an emerging type of AMR (extended spectrum beta-lactamase [ESBL]-producing *E. coli*) across the human, environmental and animal sectors *(23)*. This "Tricycle" model has now been implemented in several CTAs, proving its value to help understand the exchange of AMR across these sectors and it is being incorporated in GLASS.

Knowledge of the distribution of AMR in humans, across sectors and AMC patterns is not enough. Assessing the impact of AMR on human health is also fundamental to guide mitigation interventions to reduce human suffering and prioritize the ever-scarcer resources *(24)*. Application of the recently developed GLASS method for estimating attributable mortality of antimicrobial-resistant bloodstream infections *(25)* is expected to generate robust estimates of the impact of such infections on global health through a systematic, harmonized approach in all CTAs. The above-mentioned GLASS components aim at tackling the broad aspects of AMR/AMU surveillance (**Fig. 2.2**). Yet, some specific AMR issues pose pressing public health threats that require targeted surveillance approaches for rapidly informing effective interventions (**Fig. 2.2**). Examples of these include multidrug-resistant gonorrhoea and acute systemic infections due to multidrug-resistant fungi. Hence, the special project on AMR to monitor *Neisseria gonorrhoeae* (Enhanced Gonococcal Antimicrobial Surveillance Programme [EGASP]) and surveillance of AMR in bloodstream infection due to *Candida* spp. are also being incorporated in GLASS. More information on the methods of different modules can be found following the links provided in **Table 2.1**.

Fig. 2.2. GLASS technical modules



* CTAs report national data to WHO annually.

Note: AMR prevalence surveys were not implemented during the first phase of GLASS-AMR. The next phase will involve adopting this complementary approach to address knowledge gaps on the magnitude, distribution and diversity of AMR in LMICs.

[8] "One Health" is an integrated, unifying approach to sustainably balance and optimize the health of people, animals, and the environment. It recognizes that the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent. The approach mobilizes multiple sectors, disciplines and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for clean water, energy and air, safe and nutritious food, taking action on climate change, and contributing to sustainable development. One Health is particularly important to prevent, predict, detect and respond to global health threats, including combatting AMR.

Table 2.1. List of GLASS technical modules with the year of publication of related protocols and the number of CTAs implementing the modules

Technical modules	Number of CTAs where modules are implemented	Resources (web links)	Year of publication
GLASS-EAR	Voluntary participation	https://www.who.int/publications/i/item/9789241514590, accessed 3 Oct 2022	2018
AMR in *Candida* spp.	21	https://www.who.int/publications/i/item/WHO-WSI-AMR-2019.4, accessed 3 Oct 2022	2019
EGASP	5	https://www.who.int/publications/i/item/9789240021341, accessed 3 Oct 2022	2021
PPS-AMU[¥]	34	https://www.who.int/publications/i/item/9789240000421, accessed 3 Oct 2022	2020
Tricycle project	15[§]	https://www.who.int/publications/i/item/who-integrated-global-surveillance-on-esbl-producing-e.-coli-using-a-one-health-approach, accessed 3 Oct 2022	2021
AMR attributable mortality	9	https://www.who.int/publications/i/item/9789240000650, accessed 3 Oct 2022	2019

[¥] Point prevalence survey of antimicrobial use (PPS-AMU) in hospitals.

[§] The project was pilot tested in some of these CTAs before the formal launch of the protocol in 2021.

In the short period of its existence, GLASS has already gathered an unprecedented mass of information on the frequency of AMR in human health, proving to be an essential link for the global public health good. Five annual GLASS reports have been published, accumulating AMR data from 10.9 million BCIs from all WHO regions and, as of May 2022, 124 CTAs have enrolled in GLASS.[9] However, many gaps remain, despite the achievements in the early implementation phase of GLASS. Much improvement is needed in methodological and technological approaches and the use of surveillance data for policy making purposes. GLASS data collection faces significant challenges related to the lack of representativeness in settings with low testing coverage among patients presenting with signs and symptoms consistent with the studied conditions, especially in LMICs. The next phase of GLASS will prioritize the efforts to address the limitations of the system.

2.2 Enhancing quality and coverage of surveillance to estimate the magnitude of AMR

Global surveillance of AMR must necessarily build upon nationally representative AMR prevalence estimates obtained following standardized methods for data to be interpretable. Only such data can be used to characterize and track the global scale and trend of AMR, help identify emerging and spreading threats, evaluate the impact of interventions to prevent and/or mitigate AMR, and evaluate whether global targets for reductions in AMR and related disease and mortality are achieved. For example, in cases where not all health care facilities in a CTA can contribute data to GLASS, statistically meaningful probability sampling methods must be followed for the selection of sites to ensure that the resultant data are representative at the national level, comparable between and within CTAs and over time, and fit to inform national and global policies.

[9] This report considers only CTAs enrolled in GLASS up to 31 December, 2021. These correspond to CTAs that could have contributed AMR and/or AMC 2020 data to GLASS for this 2022 edition.

Multiple undocumented sources of variance may limit the interpretation of AMR data from routine surveillance, thus making it impossible to differentiate between genuine changes in AMR prevalence within and between CTAs over time and operational changes. For example, undocumented sources include the quality of laboratory services, differences in the make-up of health care facilities contributing data, numbers of facilities not reporting data (that is, surveillance coverage), numbers of eligible patients not being tested (that is, underdiagnosis), or numbers of patients tested for whom results are not reported (that is, underreporting). These factors are closely related to diagnostic access and affordability, as well as clinical and diagnostic practices specific to each setting.

In its next phase, GLASS will focus on strengthening global surveillance to ultimately measure progress towards defined milestones and targets for reductions in AMR prevalence. To this end, WHO plans to institute a "two-pronged" approach that involves both continuing to strengthen data collection based on the routine clinical sampling of patients seeking health care, and the application of complementary strategies, such as national prevalence surveys, to improve quality, completeness and representativeness of data. National surveys involving intermittent, strategic sampling of a population subset can provide a reliable direct measurement of the prevalence of AMR. In addition, they can overcome the paucity of interpretable AMR data from human infections where health system infrastructures are too weak to support a robust surveillance system with adequate coverage and representativeness. Such surveys may also give an indication of whether sources of bias apply to AMR surveillance data from routine clinical diagnostics in CTAs with weaker health systems and the nature of these sources. As such, periodic surveys have the potential to strengthen national technical capacity to improve patient care and ultimately strengthen surveillance based on routine clinical sampling.

As part of this process, WHO is defining high-level criteria to identify CTAs that may benefit from survey-based surveillance, in addition to developing a framework and a global roadmap to scale up these activities both systematically and strategically. Between surveys, the survey platform can serve to conduct specialized studies to fill CTA-specific evidence gaps. The proposed survey approach builds on the experiences of other disease programmes that date back to the 1990s and which have been instrumental to estimate and monitor the national and global prevalence of drug resistance in malaria, tuberculosis, and HIV *(26-31)*.

The next phase of GLASS will also involve the formulation of simple quantitative indicators that can be used to measure surveillance coverage in four dimensions, that is, at the population level, health systems level, clinical diagnostic stewardship level *(32)*, and laboratory diagnostics level. Such indicators can be used to tailor meaningful uses and applications of AMR surveillance data at national and global levels and to better target and inform CTA-specific interventions, such as epidemiological reviews, to help strengthen national AMR surveillance systems, based on the routine clinical sampling of patients seeking health care. The latter is the long-term goal of GLASS.

2.3 Enhancing quality and coverage of surveillance to estimate the magnitude of AMC and use

In 2020, GLASS incorporated the monitoring of AMC at the national level through the GLASS-AMC module. To ensure data quality and coverage, GLASS-AMC methodology has recently been developed *(14, 33, 34)*. This methodology defines all required data elements and sets the standards so that national AMC data are correctly quantified, validated, and adjusted for the population to which the data apply, and results are adequately interpreted. During the annual data submission to GLASS-AMC, CTAs are asked to provide the list of registered antimicrobial medicines and their consumed quantities, package data for each product, used data sources, Anatomical Therapeutic Chemical (ATC) classes, including the population and health sectors to which these data apply. These detailed instructions not only clarify data requirements for newcomers, but also help CTAs assess and enhance the quality and coverage of their data consistently over time. Moreover, the GLASS-AMC data collection template includes built-in information on the standardized ATC/DDD index codes to assist CTAs with data entry (by minimizing the risk of codification errors) and allows for an accurate and harmonized monitoring of AMC trends globally.

In terms of data sources, national AMC surveillance is based on existing databases with aggregated data on medicines, which are often established by (or in collaboration with) the national medicines regulatory agencies *(35)*. The use of existing databases facilitates the data collection process and contributes to the quality and coverage of AMC data reported to GLASS-AMC in the first place. However, the flexibility of GLASS-AMC methodology allows for AMC data to be retrieved at different levels of the value chain of medicines *(14)*, depending on sources of data available in each CTA. As a result, the data sources and consequently the coverage across CTAs can vary to a certain extent.

To improve coverage over time, CTAs must understand all the actors and their roles along the medicines value chains and adjust their data sources in a stepwise manner. Ideally, if quality macro-level data sources are used (that is, import and local manufacturing), the data are most likely to be representative as this type of data reporting to the government is mostly mandatory. In addition, if the parallel (non-official) markets are non-existent or negligible, then the population coverage is close to the national population census. Next, the coverage at mid-level data sources (that is, distribution and sales) can be lower compared to the macro-level due to the fragmented medicines' market and the lack of regulations for mandatory reporting of medicine turnover by wholesalers. To improve data representativeness at this level, it is key to map the supply chain of medicines and ensure that the wholesalers who cover most of the market are included in the surveillance system. Yet, there is still a risk that by leaving out the smaller wholesalers, the niche market for some specific medicines (including Reserve antibiotics, etc.) and certain patient groups will be missed. Finally, data representativeness is lowest for data sources at the micro-level (that is, prescriptions, dispensing, and insurance records), but it can be improved by introducing electronic data capture systems and triangulating the data from different data sources.

2.4 Mortality due to AMR

Recent studies position AMR as one of the leading causes of death worldwide, with the highest mortality in low-resource settings *(2)*. However, the exact morbidity and mortality associated with AMR is very difficult to establish and in many settings no reliable estimates are available, particularly in LMICs *(24, 36, 37)*. These knowledge gaps emphasize the need to foster studies on AMR attributable mortality and morbidity using standardized methods *(24, 38)*. To this end, GLASS has developed a protocol to specifically assess attributable mortality due to AMR in target settings *(25)*. However, as previously mentioned, attributable mortality studies must necessarily build upon improved estimates of the prevalence of AMR in the first place in order to accurately assess the impact of AMR on human health (see **Section 2.2**).

The GLASS protocol to assess attributable mortality due to AMR (*25)* has so far been implemented in selected CTAs and health care facilities in Africa and South-East Asia through the Oxford University ACORN ("A Clinically-Oriented Antimicrobial Resistance Surveillance Network") network *(39)*. In addition, the WHO Regional Office for the Americas/Pan American Health Organization and the Regional Office for the Eastern Mediterranean are working directly with CTAs in their regions to begin pilot implementation of the protocol in 2022/2023.

3 Progress in the development of national surveillance systems reporting data to GLASS-AMR

From its outset, GLASS-AMR has focused on the surveillance of AMR in four infectious syndromes (bloodstream [1], gastrointestinal [2], gonorrhoea [3], and urinary tract [4]); eight bacterial pathogens isolated from patients with clinical signs and symptoms compatible with these infectious syndromes (*Acinetobacter* spp. [in 1], *E. coli* [in 1, 4], *K. pneumoniae* [in 1, 4], *Salmonella* spp. [in 1, 2], *S. aureus* [in 1], *Streptococcus pneumoniae* [in 1], *Shigella* spp. [in 2], *N. gonorrhoeae* [in 3]); and 11 antibacterial classes comprising 23 individual antibiotics (Annex 1). The main unit of observation for AMR data described in this report are BCIs for bacterial pathogens and syndromes under surveillance for which interpretable AST results are available for any of these 23 antibacterials.

The reader is referred to previous report editions *(10-13)* and the manual for early implementation *(8)* for a detailed description of GLASS methods, as well as an in-depth description of global and regional activities and technical modules linked to GLASS. A new edition of the manual, expanding on the number of infectious syndrome-pathogen-antibacterial combinations under surveillance and updating AMR surveillance standards for the next phase of GLASS is expected to be published in early 2023.

This section first describes the implementation status, quality assurance, and standards of national AMR surveillance systems at the time of the latest data call (2021) (**Section 3.1**), followed by a description of the participation and coverage of national surveillance systems reporting to GLASS-AMR (**Section 3.2**), and global AMR data (**Section 3.3**).

Section 3.2 uses four broad summary statistics over time to illustrate progress in GLASS-AMR surveillance participation and coverage: numbers of CTAs enrolled in GLASS-AMR; numbers of CTAs reporting AST results for ≥ 80% of identified BCIs; absolute numbers of reported BCIs and BCIs with AST results; and the median (IQR) number of BCIs with AST results per million population, with the latter based on per million population data from individual CTAs *(40, 41)*.[10] Data calls collating BCI and AST data for the previous calendar years (that is, 2016-2020) involved the participation of pools of CTAs that were so far enrolled on the year submitting the data (that is, 2017-2021). Global maps showing median numbers of BCIs with AST results per million population in each CTA each year are shown to illustrate progress and geographical variations in GLASS-AMR surveillance coverage. Maps are consistently shown for alternate years (that is, 2016, 2018, and 2020), but users of this report are referred to the web-based content to visualise global maps for all years.

To help interpret longitudinal data describing summary statistics related to surveillance coverage (**Section 3.2**) or percentage resistance in combinations under surveillance (**Section 3.3**), percentage change[11] has been calculated in selected cases. These summary statistics provide a quantitative measure of the magnitude of change and hence a means to compare progress for the various key indicators presented in this report from the latest available year compared to in the early years of GLASS-AMR. However, presented values are solely for comparison and illustration purposes, applicable only to the data considered in each analysis, and should not be considered as representative of global trends at this stage.

[10] January 2022 Eurostat population estimates were used for countries of the European Economic Area. World Population Prospects 2019 from the United Nations Population Division, Department of Economic and Social Affairs, were used for all other CTAs.

[11] Percentage change is calculated as: ([final value – initial value]/initial value) * 100, considering non-rounded values.

3.1 Implementation indicators

Implementation data collected by GLASS allow for a better understanding of the level of development of national AMR surveillance based on routine patient sampling in reporting CTAs. National plans for AMR surveillance are available in most (75.7%) CTAs enrolled in GLASS-AMR (**Fig. 3.1**), which highlights the importance of AMR as a public health priority and well demonstrates the formal commitment to control it by CTAs. Likewise, the components needed to build effective surveillance systems, specifically the national coordinating centre and the national reference laboratory/ies, are planned or in place in most (60.4% and 77.5%, respectively) CTAs (**Fig. 3.1**). These are crucial elements to support data management and diagnostic capacities at the national level and for reporting activities to GLASS. It is also reassuring to see that national reference laboratories are participating in an external quality assurance scheme in most enrolled CTAs (70.3%), and that laboratories perform AST according to internationally recognized standards, that is, those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and/or the Clinical and Laboratory Standards Institute (CLSI) (80.2% of CTAs) (**Fig. 3.1**). Only five of 89 CTAs performing AST according to EUCAST and/or CLSI standards reported also using other undefined AST methods. However, one gap identified is still the low proportion of CTAs (48.6%) performing external quality assessment in all clinical laboratories that serve national AMR surveillance programmes (**Fig. 3.1**), which can affect quality management, a crucial element to ensure that test results are reliable.

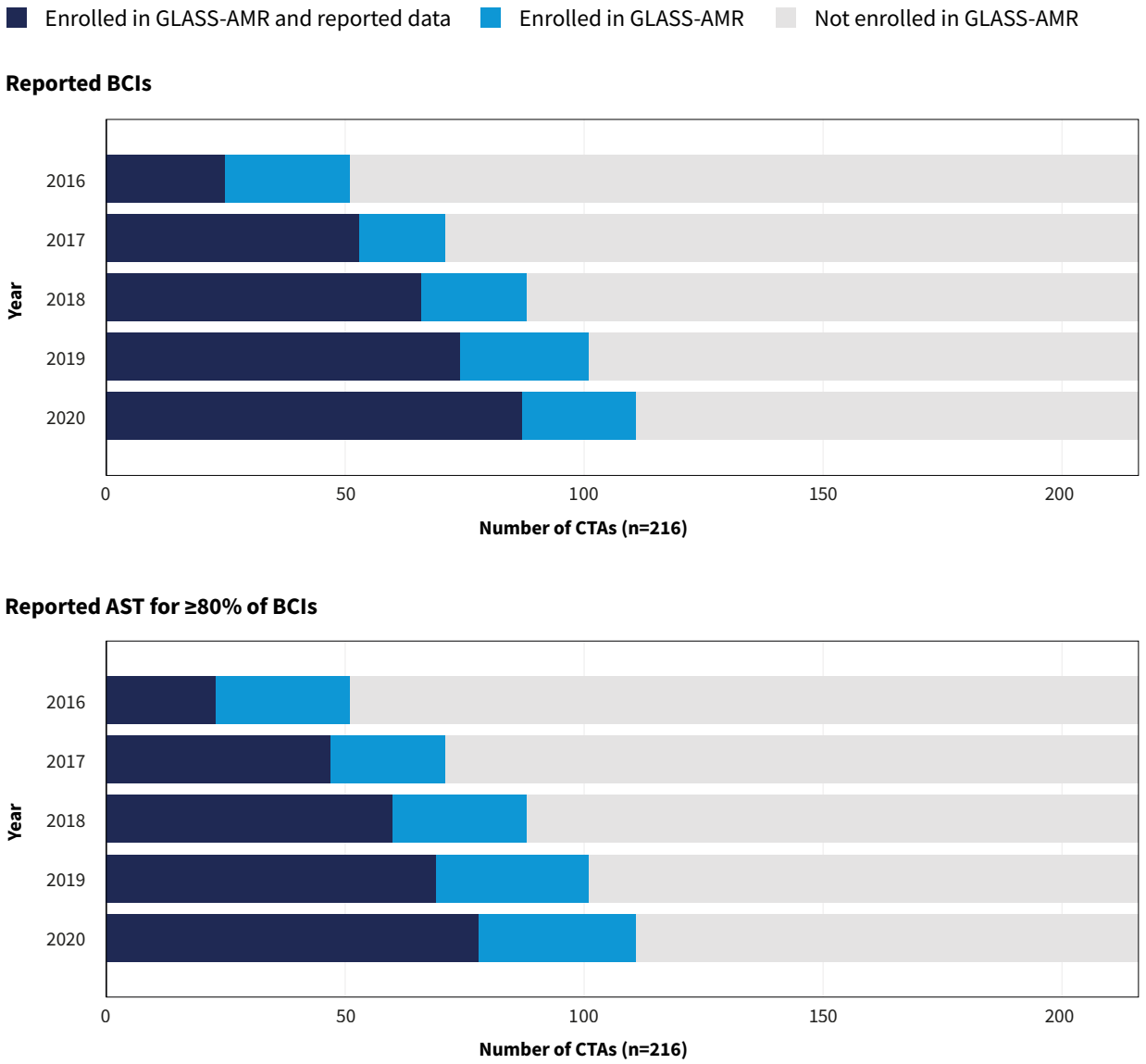
Fig. 3.1. Implementation status, quality assurance, and standards of national AMR surveillance systems at the time of the 2021 data call for CTAs reporting to GLASS-AMR

Note: Percentages were calculated using the total number of CTAs enrolled in GLASS-AMR as the denominator (n=111). In each plot, scales correspond to percentages; numbers and percentages of CTAs shown next to each lane (bar) add up to 111 and 100%, respectively.

3.2 Participation and coverage

By 31 December 2021, 111 out of 216 CTAs were enrolled in GLASS-AMR (n=109 Member States plus two territories or areas). CTAs enrolled during the early implementation years (2016-2017) were mainly from the European region (39% [20/51]), while those enrolled in recent years (2020-2021) were mainly from the African Region (48% [11/23]) (Fig. 2.1). The percentage of enrolled CTAs that also provided bacterial identification results has increased by 59% in 2016-2020 (2016: 49% [25/51]; 2020: 78% [87/111]), while the number providing AST results for at least one antimicrobial for ≥80% of BCIs of any infectious syndrome type has increased by 56% (2016: 45% [23/51]; 2020: 70% [78/111]) (Fig. 3.2).

Fig. 3.2. CTAs enrolled in GLASS-AMR that reported 2016-2020 bacterial identification results and/or AST results for bacteriologically confirmed infectious syndromes under surveillance in 2017-2021 data calls



Note: CTAs reported BCIs and AST results for the previous calendar year (that is, 2016-2020) during five data calls in 2017-2021.

A larger number of CTAs reported bloodstream BCIs[12] in 2016-2020 compared to other infectious syndromes (**Fig. 3.3**). However, consistent with the high frequency of urinary tract infections in the population also reported in the literature *(42)*, the average annual number of urinary tract BCIs reported to GLASS-AMR in 2016-2020 was four-fold that of bloodstream BCIs (**Fig. 3.3**).

A high percentage of AST performance in BCIs is important for identifying the AMR profile and informing (sub)national actions such as empiric treatment. Most CTAs that reported BCIs of any infectious syndrome also reported AST results for any antimicrobial for ≥80% of BCIs in 2016-2020. However, a drop in the number of CTAs meeting this benchmark was observed in 2020 for all combinations under surveillance (**Fig. 3.3**, **3.5a-5d**), except for gonorrhoea BCIs. Less than 80% of CTAs reported AST in 2020 for ≥80% of bloodstream BCIs for assessing methicillin resistance in *S. aureus*, penicillin resistance in *S. pneumoniae*, and fluoroquinolone resistance in *Salmonella* spp. (**Fig. 3.5a**). Less than 70% met the benchmark for key antimicrobials in gastrointestinal and urinary tract BCIs and macrolides in gonorrhoea BCIs, and only about 50% reported sulfonamides and trimethoprim AST for ≥80% of *E. coli* or *K. pneumoniae* urinary tract BCIs (**Fig. 3.5b-5d**). The negative impact of the COVID-19 pandemic on AMR surveillance activities has been reported previously *(43)* and may at least in part explain these findings.

In 2016-2020, the median number of BCIs with AST per million population increased by 58% for bloodstream infections (50.5 [2016] – 79.9 [2020]), but dropped by 43% (7.7 [2016] – 4.4 [2020]) and 88% (445.4 [2016] – 55.7 [2020]) for gastrointestinal and urinary tract infections, respectively, with no net change observed for gonorrhoea BCIs (**Fig. 3.3**). These observations are consistent with similar changes in underlying diagnostic and reporting coverage for specific infections described in this report (**Fig. 3.5a-5d**).

A net increase in the median number of bloodstream BCIs with AST per million population was driven by an increase in *K. pneumoniae* with AST results for third-generation cephalosporins (+111%: 10.6 [2016] – 22.4 [2020]) and an increase in *K. pneumoniae* (+57%: 11.5 [2016] – 18.2 [2020]) and *Acinetobacter* spp. (+32%: 6.3 [2016] – 8.4 [2020]) with AST results for carbapenems. These observations are consistent with similar trends being observed, regardless of the availability of AST results (data not shown), thus suggesting that changes were at least in part due to changes in the initial identification and/or reporting of bloodstream BCIs.

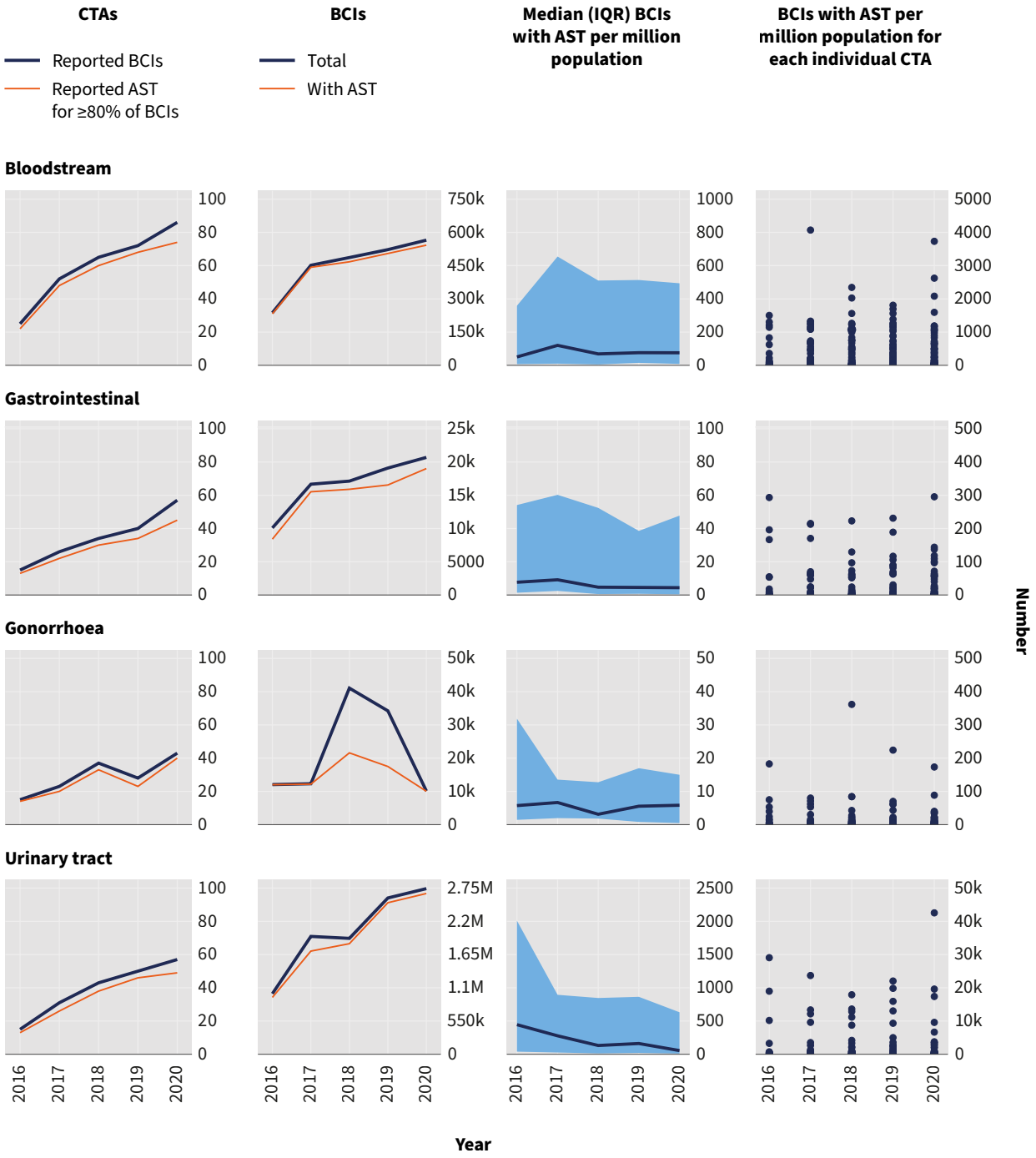
These increases may also reflect enhanced surveillance awareness of the emergence of resistance in these bacterial pathogens. A moderate downward trend or no net change was observed for all other bloodstream pathogen-antibiotic combinations, as measured by the median BCIs with AST per million population (**Fig. 3.5a**). The most notable drop (-46%) was for *S. aureus* BCIs with AST per million population (median: 27.1 [2016] – 14.6 [2020]).

Changes in the median number of BCIs with AST per million population are influenced by both intra-CTA testing coverage over time and changes in the make-up and number of CTAs contributing data each year. For example, Brazil, Canada, and the United States of America among others reported bloodstream BCIs in earlier years, but not in 2020 (**Fig. 3.4**), and relatively more CTAs from the African region were enrolled in GLASS-AMR in 2020-2021. Lower median values for BCIs with AST per million population in 2020 for most combinations considered may at least in part result from the enrolment of CTAs where testing coverage is still low. Testing coverage within each CTA over time is summarized in global maps in **Figs. 3.4** and **3.6**. Assessing intra-CTA testing coverage trends can help identify gaps in CTA surveillance systems and inform further improvement.

A major feature of the data is the wide interquartile range (IQR) envelopes around median BCIs with AST per million population, reflecting variations in individual CTA values for most infectious syndromes, bacterial pathogens and antibiotic groups considered (**Figs. 3.3** and **3.5a-5d**). These findings suggest substantial differences in diagnosis, testing and/or reporting coverage between CTAs in 2016-2020, which are evident across all regions of the world (**Figs. 3.4** and **3.6a-6c**).

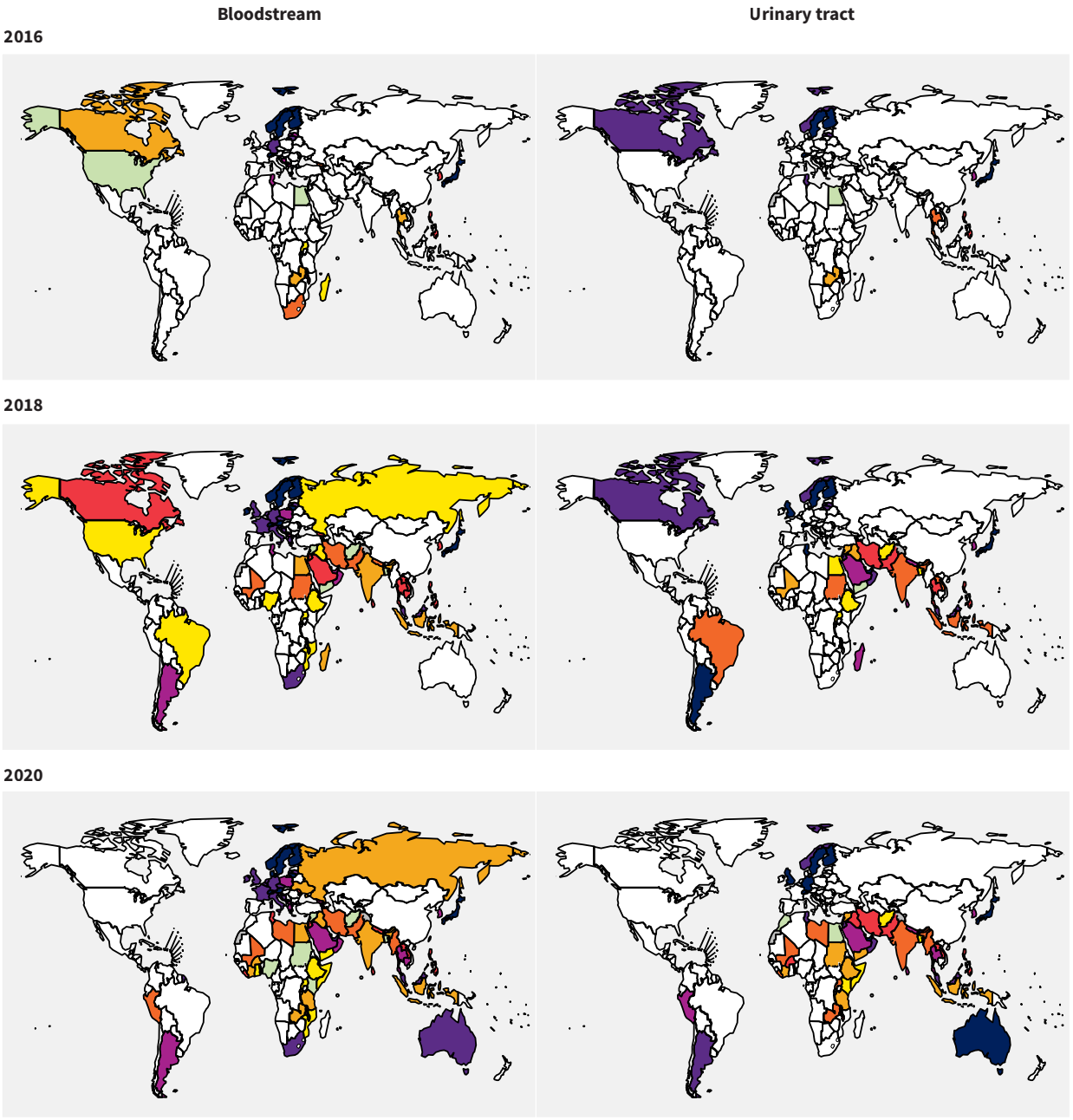
[12] The European Antimicrobial Resistance Surveillance Network (EARS-Net) and the European arm of the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) networks collate only national bloodstream BCI data. In consequence, 9/29 CTAs in the European region reporting BCIs in 2020 reported only bloodstream BCIs. In addition, 3/15 CTAs in the African Region and 2/9 CTAs in the Western Pacific Region reported only bloodstream BCIs.

Fig. 3.3. Progress in reporting of BCIs and AST test results to GLASS-AMR for infectious syndromes under surveillance (2016-2020)



Note: Almost double the number of CTAs reported bloodstream BCIs compared to other infectious syndromes in 2020 (bloodstream: 86 CTAs; gastrointestinal and urinary tract: 57 CTAs; gonorrhoea: 43 CTAs). The average number of urinary tract BCIs reported annually to GLASS-AMR in 2016-2020 was four-fold that of bloodstream BCIs and more than 90-fold that of gonorrhoea or gastrointestinal BCIs.

Fig. 3.4. BCIs with AST results reported to GLASS-AMR per one million population for selected infectious syndromes under surveillance (2016, 2018, 2020)



Note: In 2020, 16 CTAs reported bloodstream BCIs and 14 reported urinary tract BCIs with AST results for the first time. Five CTAs reported bloodstream BCIs in earlier years, but not in 2020, including Brazil, Canada and the United States of America, and nine reported urinary tract BCIs in earlier years, but not in 2020, including Brazil and Canada. Most CTAs reporting higher numbers of bloodstream BCIs with AST results per million population in 2020 (that is, ≥ 70.2) were from the European region (56%), whereas most CTAs reporting higher numbers of urinary tract BCIs with AST results were from the Eastern Mediterranean region (36%). Maps for gastrointestinal and gonorrhoea infectious syndromes are available as part of the web-based expanded content.

Fig. 3.5a. Progress in reporting AST results to GLASS-AMR for selected antimicrobial groups in bloodstream BCIs, by bacterial pathogens under surveillance (2016-2020)

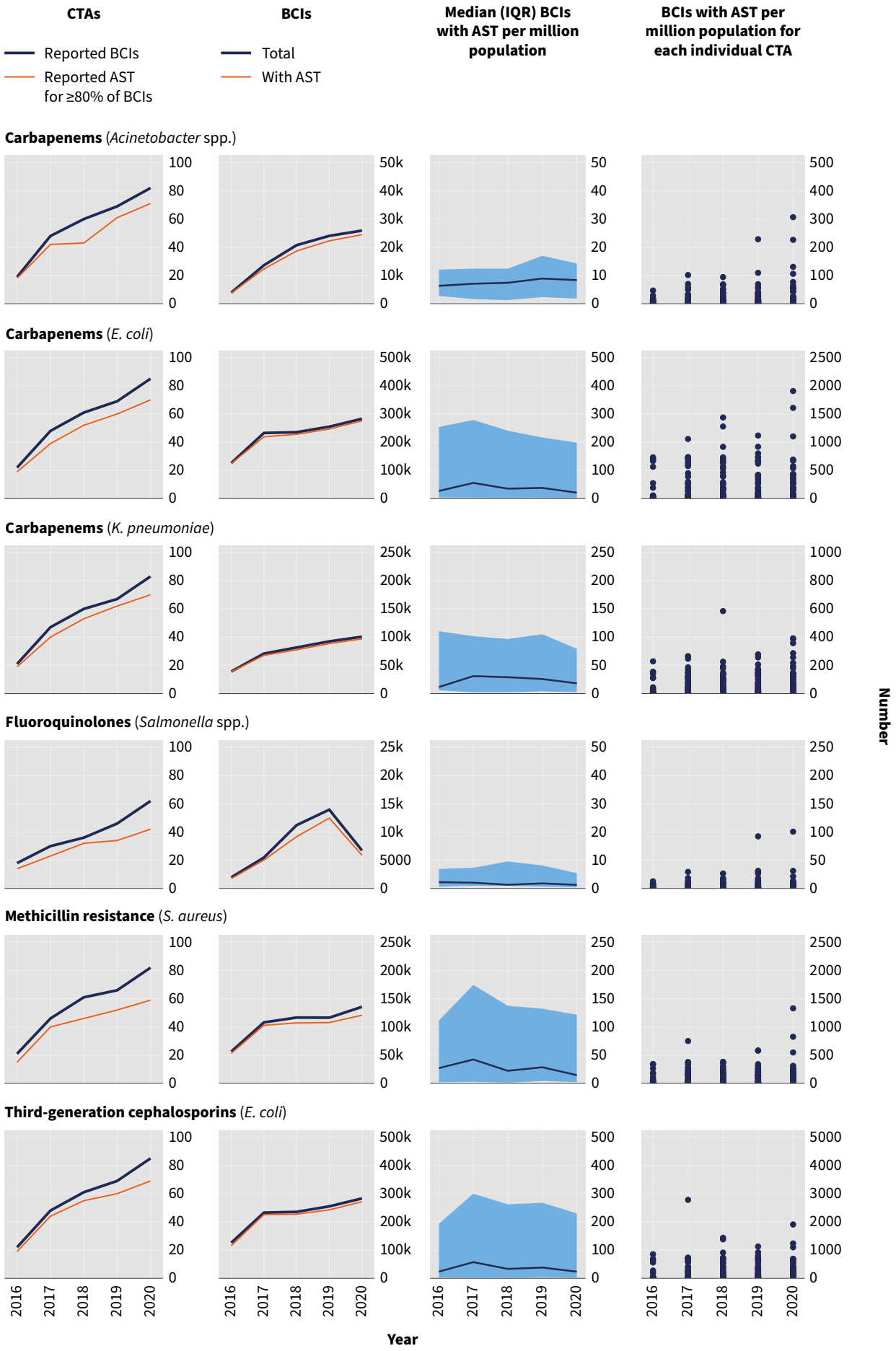
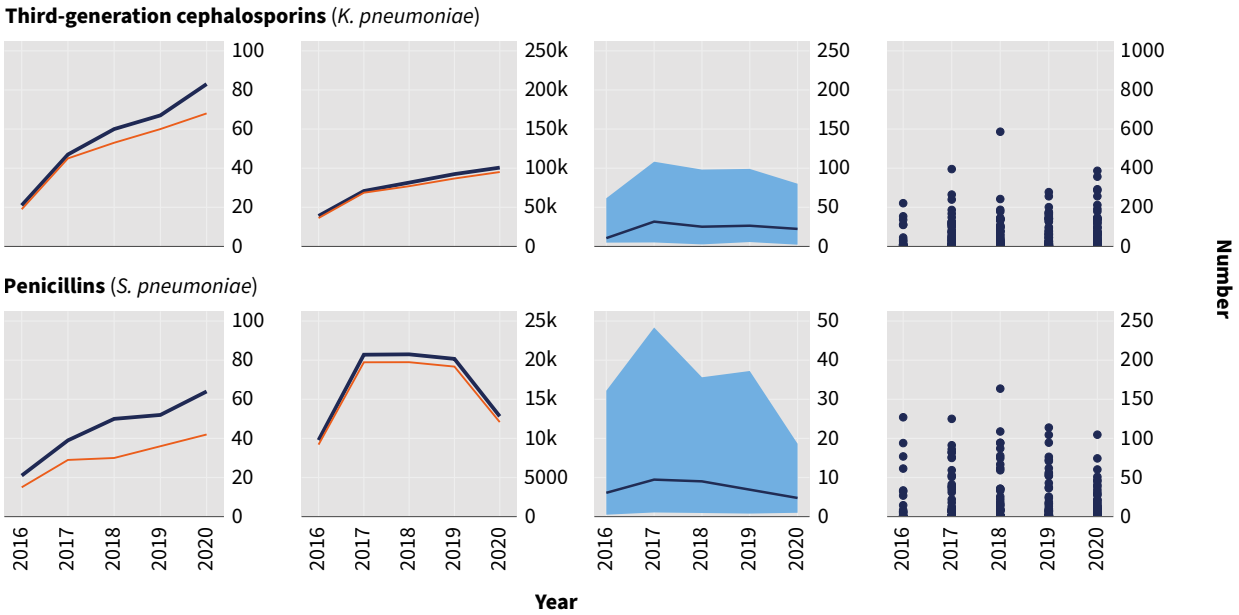
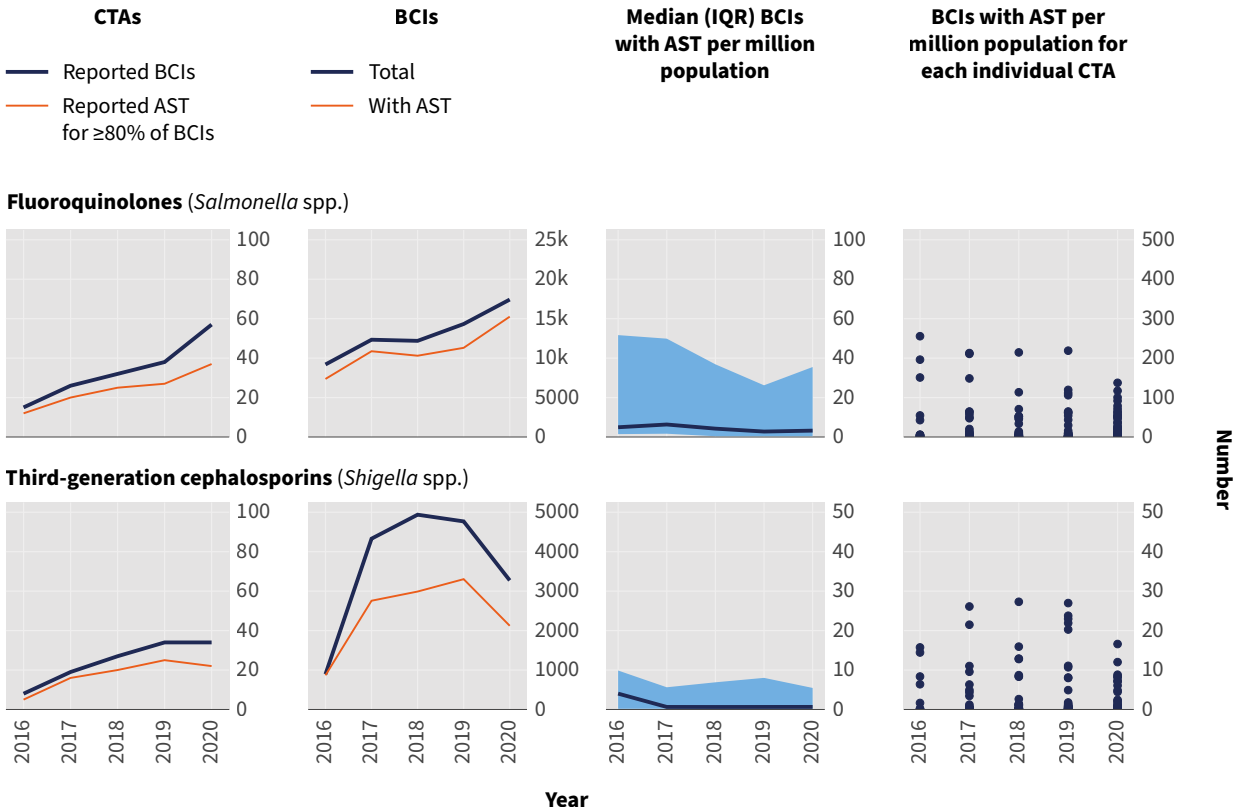


Fig. 3.5a (Continued). Progress in reporting AST results to GLASS-AMR for selected antimicrobial groups in bloodstream BCIs, by bacterial pathogens under surveillance (2016-2020)



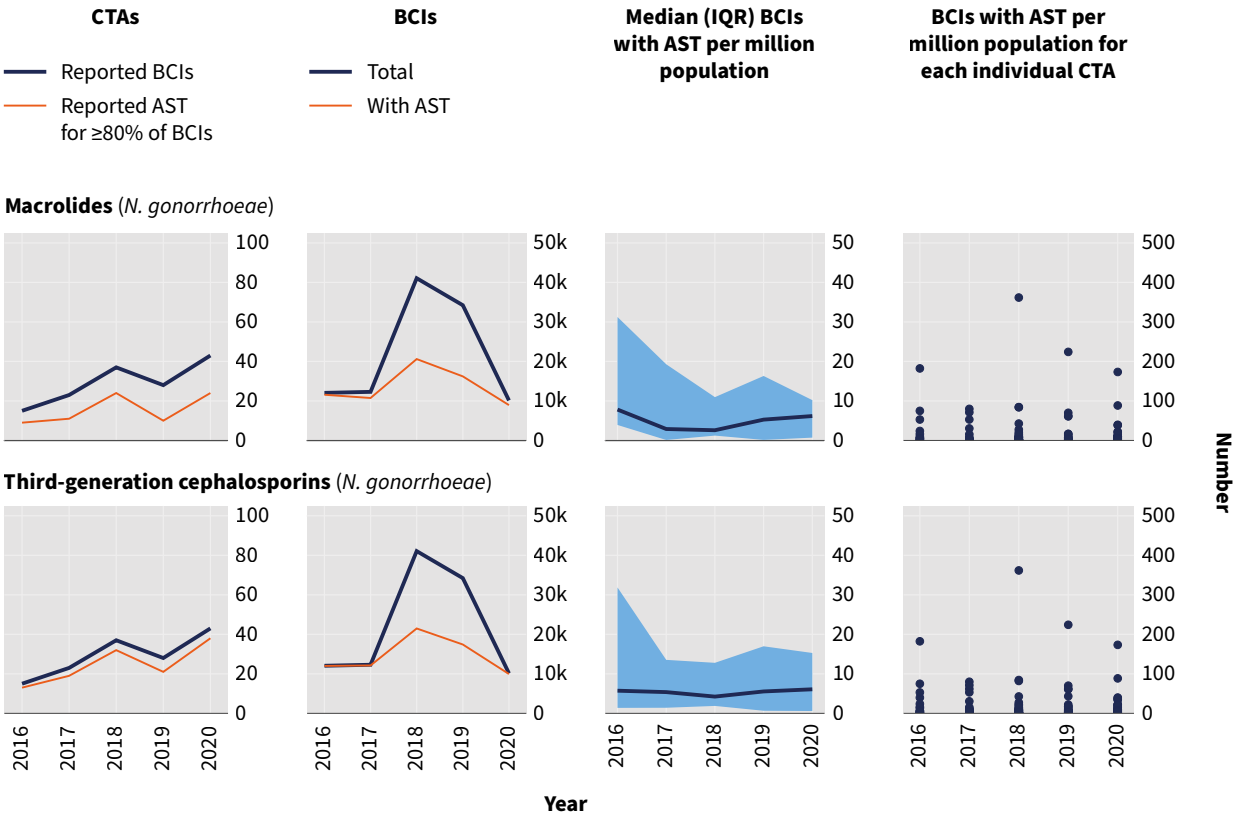
Note: Bloodstream BCIs in 2016-2020 were predominantly due to *E. coli*, with the average annual number being double that of S. aureus, three-fold that of *K. pneumoniae*, and more than 10-fold that of other bacterial species. A net increase in the median number of bloodstream BCIs with AST per million population in 2016-2020 was due to an increase in *K. pneumoniae* with AST results for third-generation cephalosporins and an increase in *K. pneumoniae* and *Acinetobacter* spp. with AST results for carbapenems.

Fig. 3.5b. Progress in reporting AST results to GLASS-AMR for selected antimicrobial groups in bacteriologically confirmed gastrointestinal BCIs, by bacterial pathogens under surveillance (2016-2020)



Note: *Salmonella* spp. BCIs were almost four-fold the average annual number of *Shigella* spp. BCIs in 2016-2020. The lower median number of gastrointestinal BCIs with AST per million population in 2020 compared to in 2016 was consistent with similar changes in the coverage of *Salmonella* spp. with AST results for fluoroquinolones (4.9 (2016) to 3.2 (2020)), and of *Shigella* spp. with AST results for third-generation cephalosporins (4.0 (2016) to <1 (2020)) per million population.

Fig. 3.5c. Progress in reporting AST results to GLASS-AMR for selected antimicrobial groups in bacteriologically confirmed gonorrhoea BCIs (2016-2020)



Note: The median number of *N. gonorrhoeae* BCIs with AST results per million population ranged from 5.7 (2016) to 6.1 (2020) for third-generation cephalosporins, and from 7.8 (2016) to 6.2 (2020) for macrolides.

Fig. 3.5d. Progress in reporting antimicrobial susceptibility test results to GLASS-AMR for selected antimicrobial groups in bacteriologically confirmed urinary tract BCIs, by bacterial pathogens under surveillance (2016-2020)

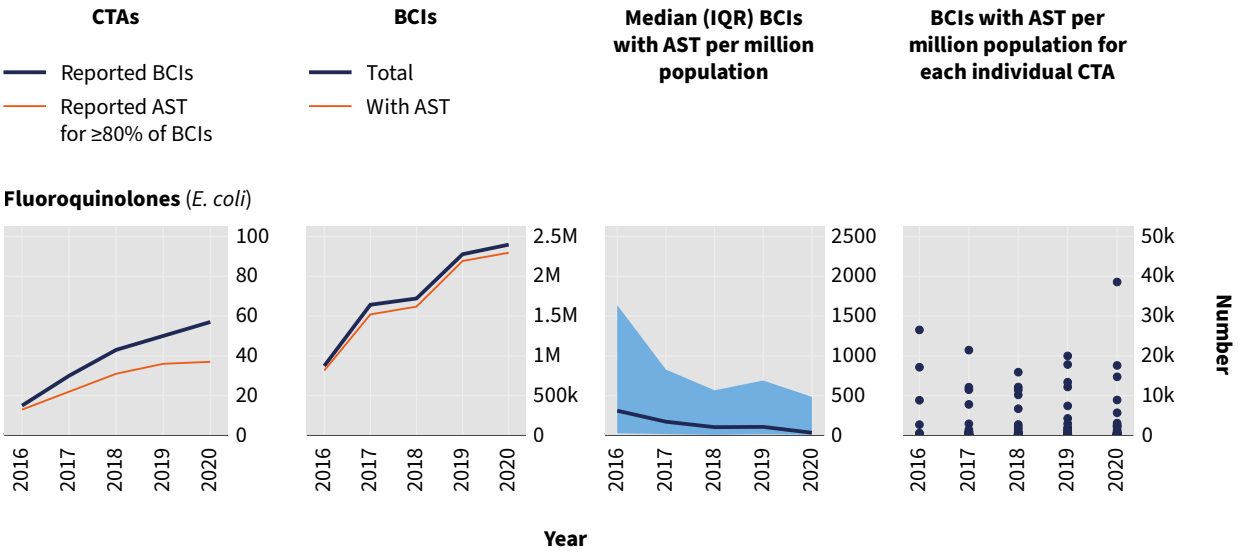
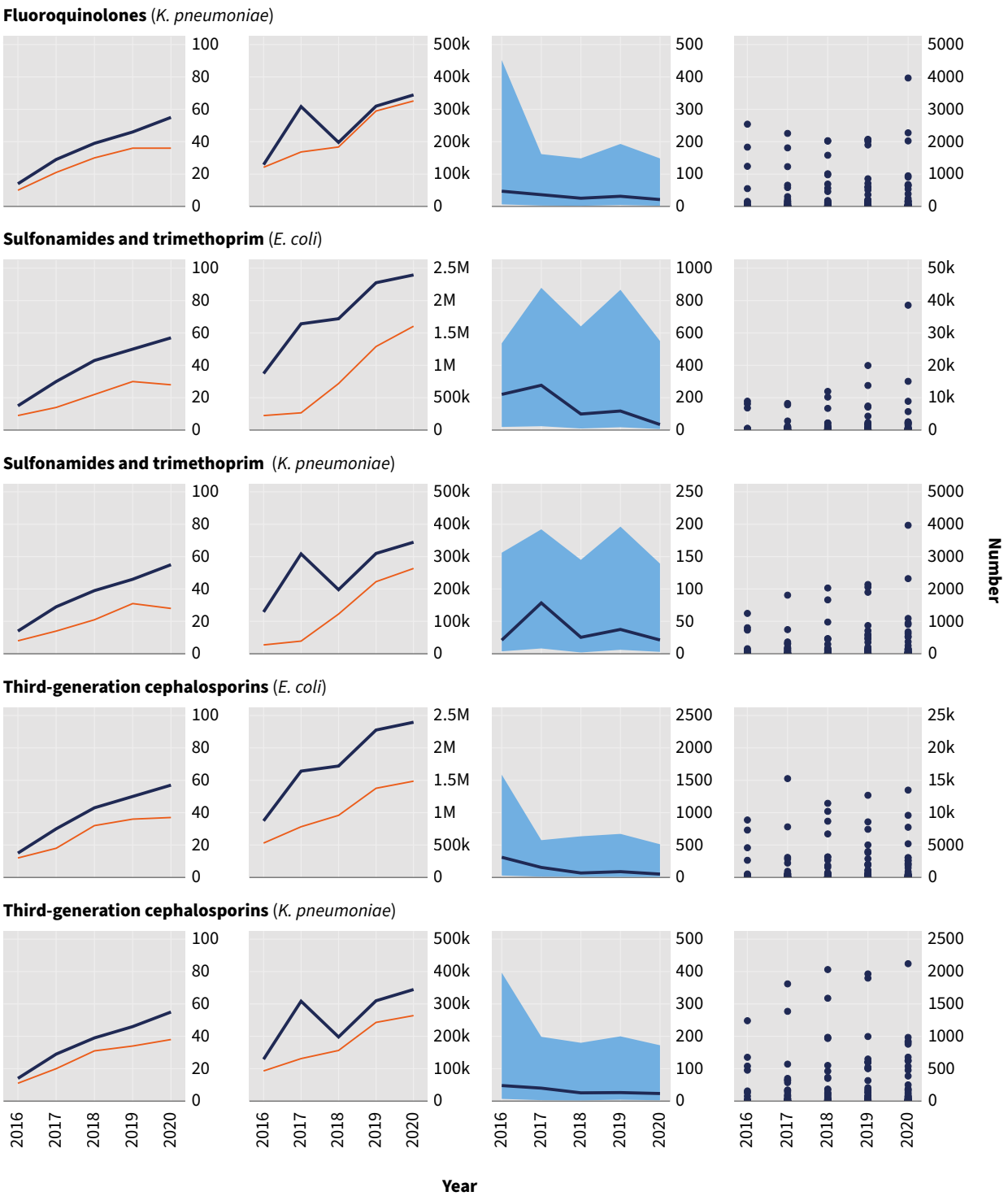
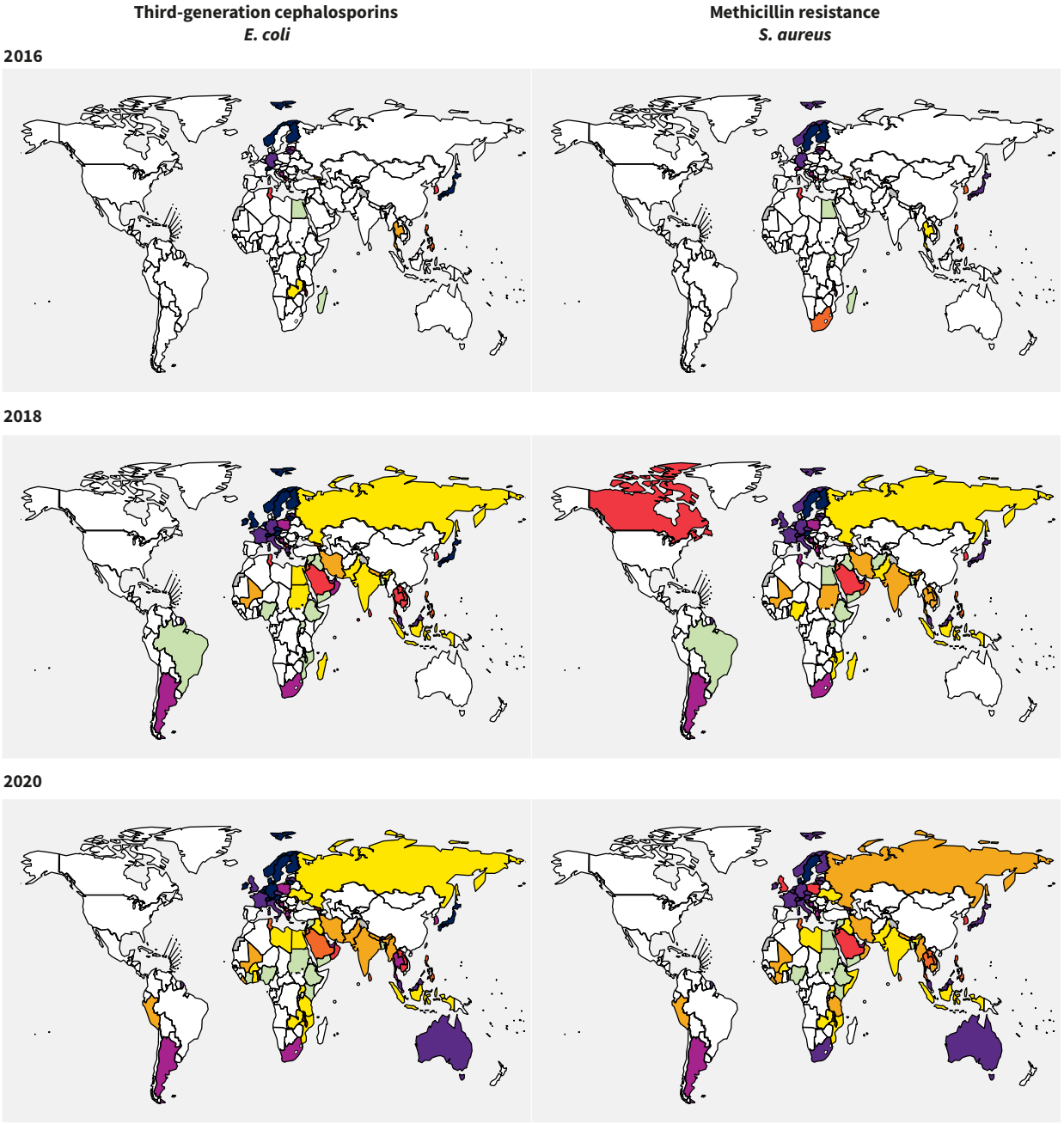


Fig. 3.5d (Continued). Progress in reporting antimicrobial susceptibility test results to GLASS-AMR for selected antimicrobial groups in bacteriologically confirmed urinary tract BCIs, by bacterial pathogens under surveillance (2016-2020)



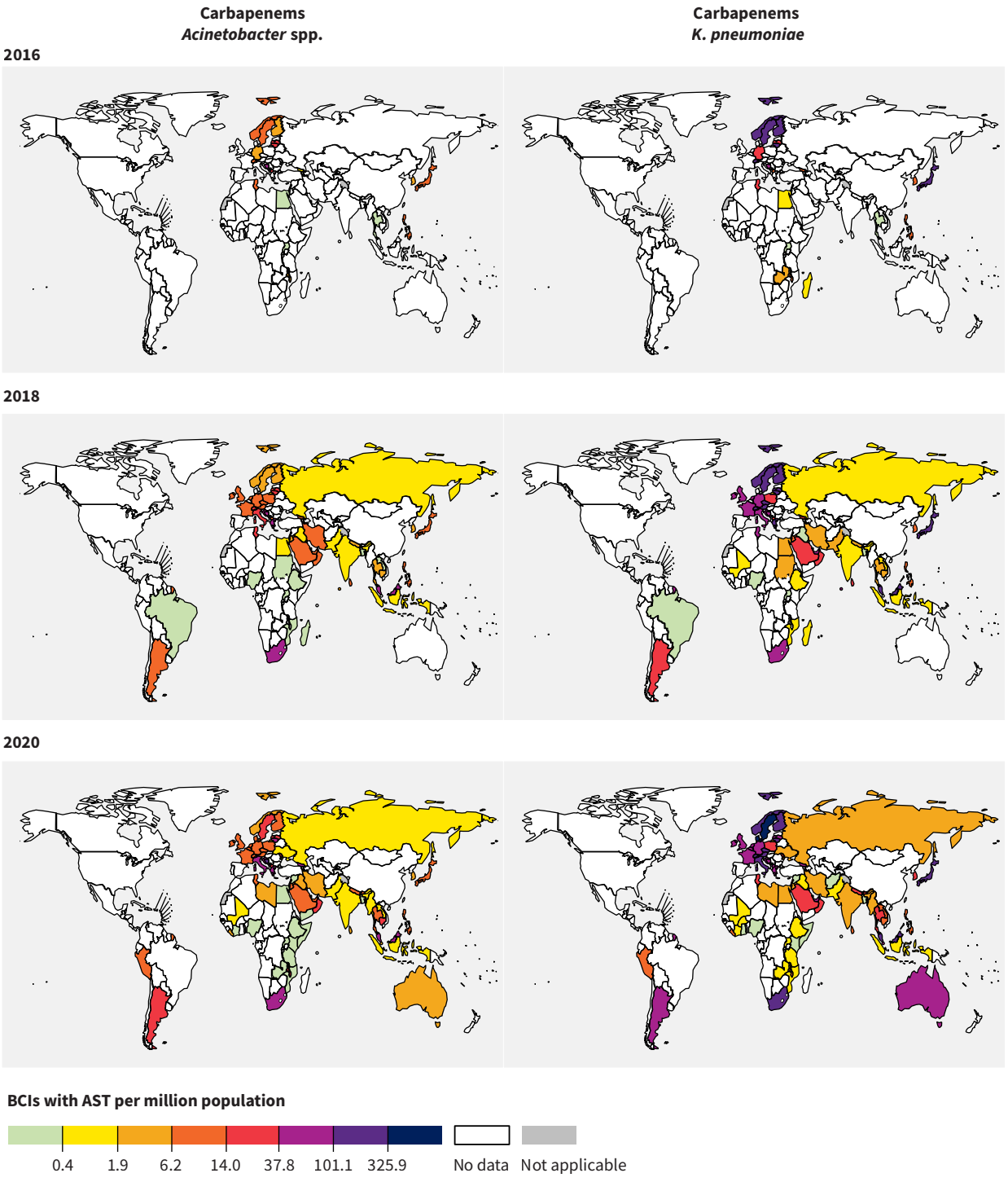
Note: Urinary tract *E. coli* BCIs were almost seven-fold the average annual number of *K. pneumoniae* BCIs in 2016-2020. The lower median number of urinary tract BCIs with AST per million population in 2020 compared to in 2016 was consistent with similar changes in the coverage of *E. coli* and *K. pneumoniae* urinary tract BCIs with AST results for fluoroquinolones, sulfonamides and trimethoprim, and third-generation cephalosporins.

Fig. 3.6a. Bloodstream infections with third-generation cephalosporins (*E. coli*) or methicillin resistance (*S. aureus*) susceptibility test results reported to GLASS-AMR, per one million population (2016, 2018, 2020)



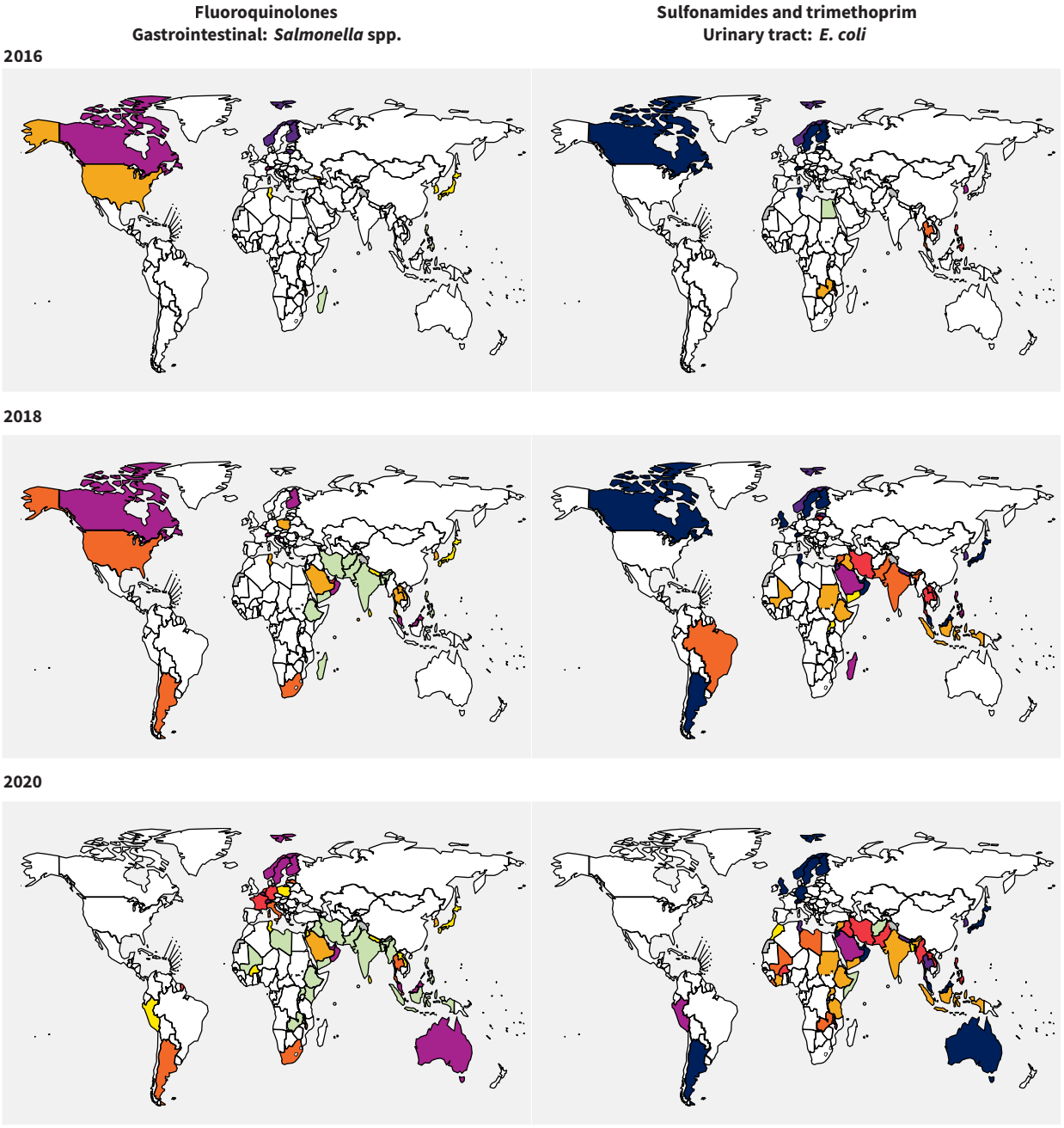
Note: Most CTAs reporting higher coverage for these infection-antibacterial combinations per million population in 2020 (that is, ≥ 37.8), were from the European region (*E. coli* with AST results for third-generation cephalosporins: 61% [23/38]; *S. aureus* with AST results for methicillin resistance: 66% [23/35]).

Fig. 3.6b. *Acinetobacter* spp. and *K. pneumoniae* bloodstream infections with susceptibility results reported to GLASS-AMR, per one million population (2016, 2018, 2020)



Note: Most CTAs reporting higher coverage for these infection-antibacterial combinations per million population in 2020 (that is, ≥37.8) were from the European region (*Acinetobacter* spp. with AST results for carbapenems: 58% [7/12]; *K. pneumoniae* with AST results for carbapenems: 69% [24/35]).

Fig. 3.6c. *Salmonella* spp. gastrointestinal infections with fluoroquinolone susceptibility test results, and *K. pneumoniae* urinary tract infections with sulfonamides and trimethoprim AST results reported to GLASS-AMR, per one million population (2016, 2018, 2020)



Note: Most CTAs reporting higher coverage for these infection-antibacterial combinations per million population in 2020 (that is, ≥ 37.8), were from the European region (gastrointestinal *Salmonella* spp. BCIs with AST results for fluoroquinolones: 57% [8/14]) or the Eastern Mediterranean region (urinary tract *E. coli* with AST results for sulfonamides and trimethoprim: 38% [10/26]).

3.3 Global AMR data

Percentage resistance to individual antibiotics within each bacterial pathogen and infectious syndrome under surveillance in the latest AMR data call (that is, 2020 AMR data) has been calculated for each combination as the number of BCIs with resistant or non-susceptible AST results (excluding intermediate observations) out of the total BCIs with interpretable AST results in each CTA. Global percentage resistance for each combination is measured by the median (IQR) of the 2020 percentages reported by individual CTAs, considering either all CTAs reporting ≥10 BCIs with AST, or only the pool of CTAs where the number of BCIs with AST per million population for the relevant combination was above the 75th percentile (**Section 3.3.1**). The latter is taken to represent the pool where testing and/or reporting coverage of BCIs and AST is likely higher and where routine surveillance may be more widely implemented and consolidated, thus potentially reducing bias due to convenience sampling and/or reporting only from selected health care facilities. In such cases, data are often limited to tertiary referral hospitals, private hospitals or research facilities and are likely to be biased towards complex infections, treatment failures, and hospital-acquired infection, and/or are too sparse to be confident of generalizability *(44, 45)*. Median resistance considering CTAs above the 75th percentile is only shown if ≥ 4 CTAs reported ≥ 10 BCIs with AST in 2020.

Time series illustrating AMR trends for selected bacterial pathogen and antimicrobial combinations from four infectious syndromes under surveillance have been summarized for CTAs that have provided ≥10 BCIs with AST results for the past four consecutive years without interruption (2017–2020 AMR data). Percentage resistance for each combination under surveillance is shown for each CTA individually and summarized by the median and IQR of these individual observations over time. Time series are only shown for combinations where continuous 2017-2020 data were available from at least five CTAs. Of note, 2016 AMR data were excluded due to few CTAs providing data for this calendar year (**Section 3.3.2**). Time series for additional combinations are available as part of the web-based expanded content.

3.3.1 Resistance to antibacterials under surveillance in 2020

As in previous years, the two most reported infectious syndromes among the four monitored by GLASS were bloodstream (n=564 854; 17% of total BCIs) and urinary tract infections (2 750 846, 82% of total BCIs) (**Table 3.1**), with *E. coli* as the most frequent pathogen. The number of surveillance sites collecting these data varies among CTAs, but coverage and representativeness are expected to improve as surveillance systems mature. Most surveillance sites were outpatient clinics (62 823), compared to sites offering only inpatient services (7 138). In addition, many sites were hospitals with both inpatient services and outpatient clinics (8 938). This is paramount for CTAs to also monitor AMR in the community. The interpretation of AMR in pathogens causing the infectious syndromes needs to take into consideration the testing coverage, defined as median BCIs with AST per million population in this report.

Table 3.1. Numbers of BCIs, BCIs with AST results for any antibacterial, and CTAs reporting BCIs in 2020

Infectious syndrome	Bacterial pathogen	Number of CTAs reporting BCIs	Total BCIs	BCIs with AST for any antibacterial
Bloodstream				
	Acinetobacter spp.	82	25 913	24 574
	E. coli	85	283 030	280 010
	K. pneumoniae	83	100 716	98 354
	Salmonella spp.	62	6 738	6 176
	S. aureus	82	135 631	120 802
	S. pneumoniae	64	12 826	12 276
	Total	**86**	**564 854**	**542 192**
Gastrointestinal				
	Salmonella spp.	57	17 420	15 904
	Shigella spp.	34	3 273	3 109
	Total	**57**	**20 693**	**19 013**
Gonorrhoea				
	N. gonorrhoeae	43	10 130	10 036
Urinary tract				
	E. coli	57	2 396 191	2 327 636
	K. pneumoniae	55	344 525	332 414
	Total	**57**	**2 750 846**	**2 670 086**
	Grand Total	**87**	**3 346 523**	**3 241 327**

Out of 94 antimicrobial, bacterial pathogen, and infectious syndrome combinations under surveillance (**Figs. 3.7a-7k**), the median percentage of resistance was calculated for all CTAs and for those above the 75th percentile in 91 combinations.[13] In 74.7% of these combinations (68/91), the median percentage resistance was lower when considering CTAs above the 75th percentile. Some examples of this observation are further detailed below.

The median resistance to third-generation cephalosporins in *E. coli* bloodstream BCIs was 41.8% when considering all CTAs. However, it decreased to 10.6% when considering only CTAs where the number of *E. coli* BCIs with AST results for this antimicrobial group per million population was above the 75th percentile. Of note, the higher resistance rates to cefotaxime and ceftriaxone in *E. coli* bloodstream BCIs compared to ceftazidime are compatible with the broader distribution of CTX-M type ESBLs worldwide compared to other ESBLs *(46)* and alternative resistance mechanisms to third-generation cephalosporins in this pathogen. These data suggest that cefotaxime and ceftriaxone are the most appropriate choice for the surveillance of third-generation cephalosporin resistance in *E. coli*. Similarly, the median methicillin resistance in *S. aureus* bloodstream BCIs was 34.7% when considering all CTAs, and 6.8% when considering CTAs above the 75th percentile.

These observations are at least in part consistent with bias resulting from the convenient selection of health care facilities for surveillance of AMR in many settings. Considering all CTAs, 18.1% of combinations under surveillance (17/94) showed ≥50% percentage resistance in tested BCIs compared to only 8.8% of combinations (8/91) when CTAs above the 75th percentile were considered. Of note, only 57.4% of combinations (54/94) had data contributed from ≥30 CTAs. Global interpretation of resistance data is therefore limited at present due to differences in surveillance coverage and the representativeness of surveillance sites across the

[13] That is, those with ≥4 CTAs reporting ≥10 BCIs with AST in 2020.

globe. Although lower resistance in settings with high coverage could be due to potentially better diagnostic practices, stronger health systems to combat AMR, and fewer testing biases, firm conclusions of any genuine differences in resistance prevalence would require further investigation.

Even though current data cannot be used to calculate a global resistance estimate for the combinations under surveillance, these data allow to identify combinations where resistance remains low and where high resistance is a cause for concern. This is particularly true where larger numbers of CTAs contributed data and where the median global percentage resistance is consistent, regardless of whether all CTAs or only those above the 75th percentile are considered. For example, in 35 antimicrobial, bacterial pathogen, and infectious syndrome combinations under surveillance, despite median resistance values differing between CTA pools, median resistance was consistently ≥50% (n=8) or ≤5% (n=27), irrespective of whether data from all CTAs or only from those above the 75th percentile were considered. However, it should be noted that wide IQRs were observed for most combinations under surveillance (**Figs. 3.7a-7k**).

It is a matter of concern that very high levels of resistance in pathogens causing bloodstream infections have been reported in 2020, regardless of testing coverage. Third-generation cephalosporins are recommended as first-line empiric treatment for this type of infection *(47, 48)*. Considering all CTAs, high levels of third-generation (median: 59.0-64.7%, depending on the individual antibiotic) and fourth-generation (57.4%) cephalosporin resistance were reported in *K. pneumoniae*, the third most frequent pathogen in bloodstream BCIs, which could be attributed in part to the presence of ESBLs (**Fig. 3.7c**). Severe infections, such as bloodstream infections resistant to third- and fourth-generation cephalosporins, pushes the use of carbapenems, named 'last resort' drugs, for effective treatment. As a result, carbapenem resistance may occur; these resistant isolates are usually multidrug-resistant and often associated with treatment failure. *K. pneumoniae* resistance to co-trimoxazole was also high (61.3% considering all CTAs; 34.3% considering CTAs above the 75th percentile). This observation is relevant since cotrimoxazole resistance genes in Enterobacterales are frequently associated with mobile genetic elements that increase the likelihood of pan-drug-resistant and extreme-drug-resistant isolates *(49)*.

When considering all CTAs, high levels of resistance to carbapenems (median: 69.0-73.4%, depending on the individual antibiotic) and aminoglycosides (median: 56.0-56.3%) in *Acinetobacter* spp. causing bloodstream infections in hospitals were also reported; these rates were broadly consistent regardless of testing coverage (**Fig. 3.7a**).

The data on *Salmonella* spp. and *Shigella* spp. resistance causing gastrointestinal infections must be interpreted with caution due to the small number of CTAs providing data. *Salmonella* spp. and *Shigella* spp. may cause bloody diarrhoea and some patients may require antibiotic treatment with ciprofloxacin, the first-line antimicrobial *(47, 48)*. Low rates of resistance to both third-generation cephalosporins and carbapenems (≤5%) have been reported in *Salmonella* spp. causing gastrointestinal infections (**Fig. 3.7g**). However, the resistance rates for ciprofloxacin >10% for both *Salmonella* spp. and *Shigella* spp. reported by several CTAs are of concern (**Figs. 3.7g-7h**).

Resistance rates in *E. coli*, the most common pathogen in urinary tract infections, to first-line antibiotics such as ampicillin and co-trimoxazole, and second-line drugs such as fluoroquinolones were >20%, regardless of testing coverage (**Fig. 3.7j**). These antibiotics are frequently used for oral treatment of these infections and such high rates in a very common type of infection are of great concern. Equally concerning is the high ciprofloxacin resistance reported in *N. gonorrhoeae*, which was above 60%, regardless of testing coverage (**Fig. 3.7i**).

Fig. 3.7a. Percentage resistance to antimicrobials under surveillance in *Acinetobacter* spp. in all CTAs reporting ≥10 *Acinetobacter* spp. bloodstream infections with AST results compared to CTAs where the reported number per million population was above the 75th percentile in 2020

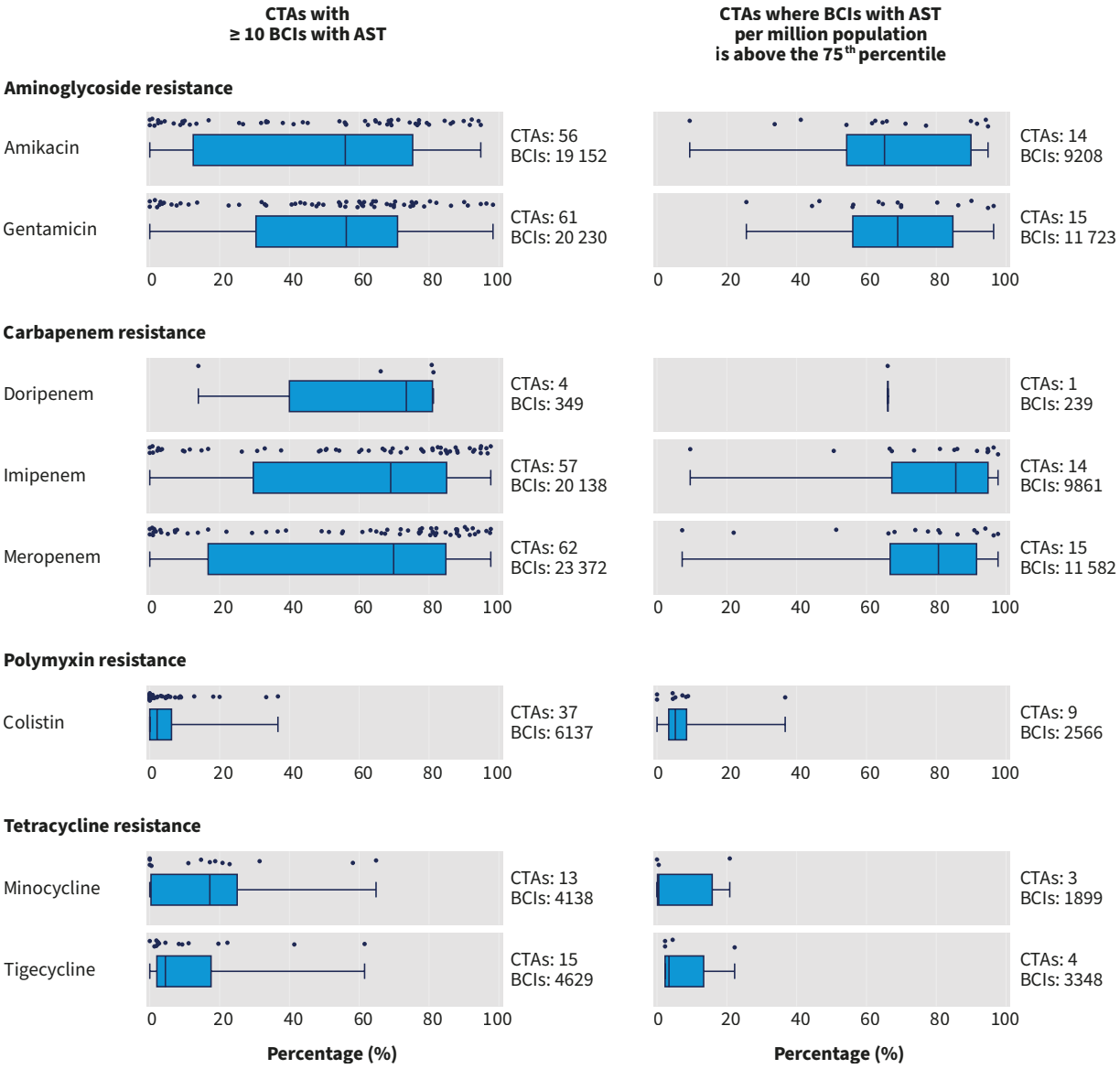


Fig. 3.7b. Percentage resistance to antimicrobials under surveillance in *E. coli* in all CTAs reporting ≥10 *E. coli* bloodstream infections with AST results compared to CTAs where the reported number per million population was above the 75th percentile in 2020

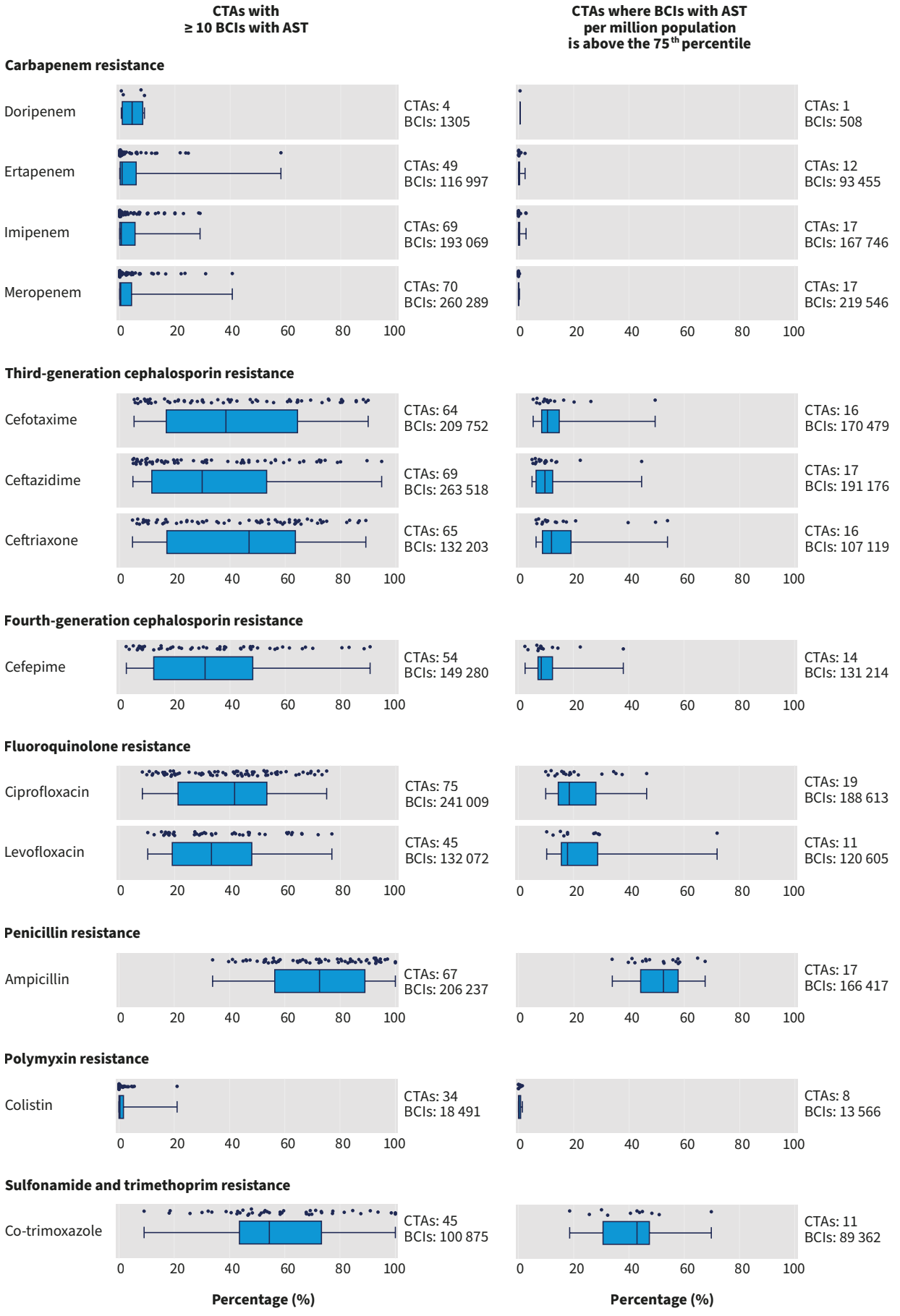


Fig. 3.7c. Percentage resistance to antimicrobials under surveillance in *K. pneumoniae* in all CTAs reporting ≥ 10 *K. pneumoniae* bloodstream infections with AST results compared to CTAs where the reported number per million population was above the 75th percentile in 2020

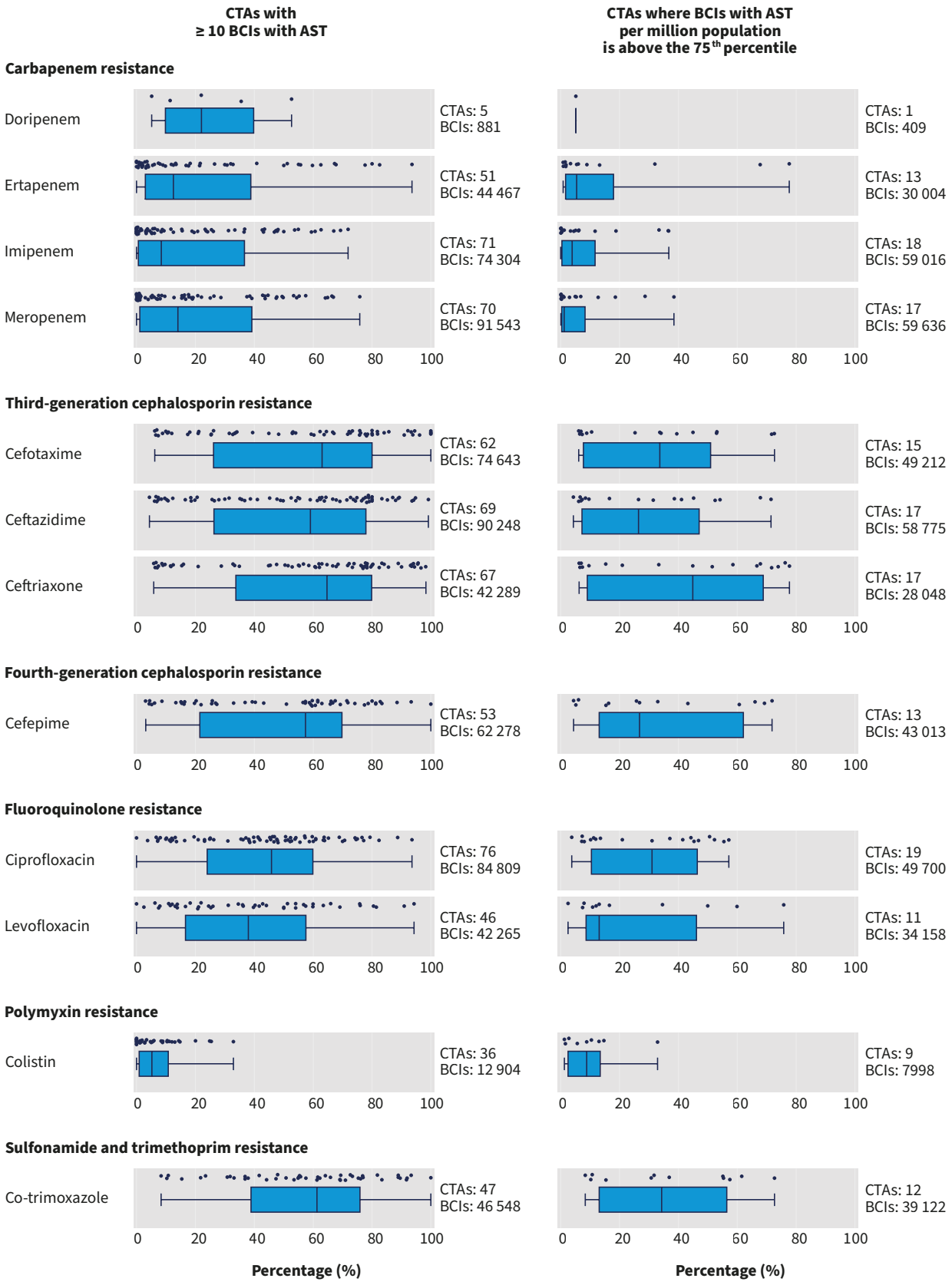


Fig. 3.7d. Percentage resistance to antimicrobials under surveillance in *Salmonella* spp. in all CTAs reporting ≥10 *Salmonella* spp. bloodstream infections with AST results compared to CTAs where the reported number per million population was above the 75th percentile in 2020

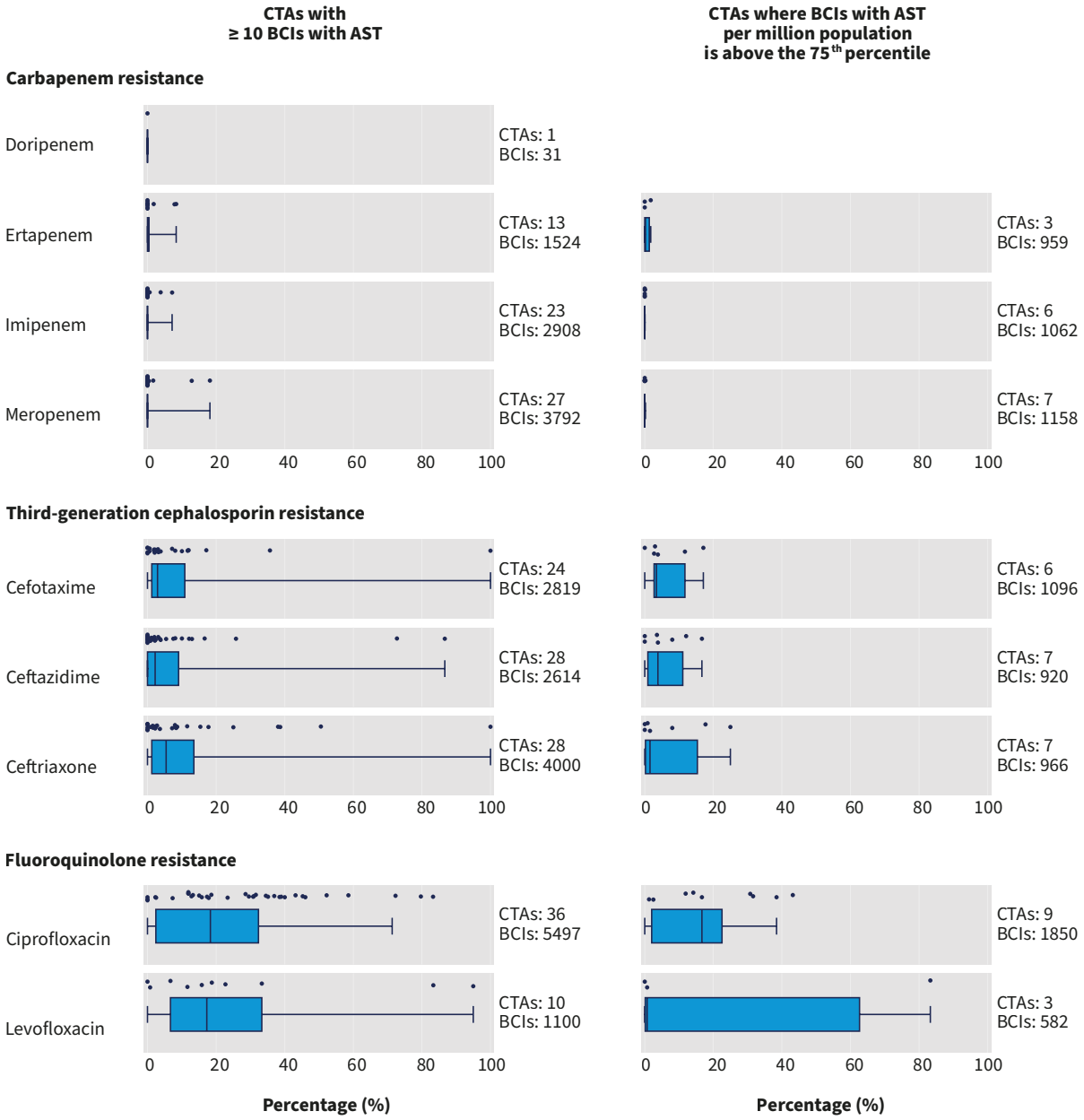


Fig. 3.7e. Percentage resistance to antimicrobials under surveillance in *S. pneumoniae* in all CTAs reporting ≥10 *S. pneumoniae* bloodstream infections with AST results compared to CTAs where the reported number per million population was above the 75th percentile in 2020

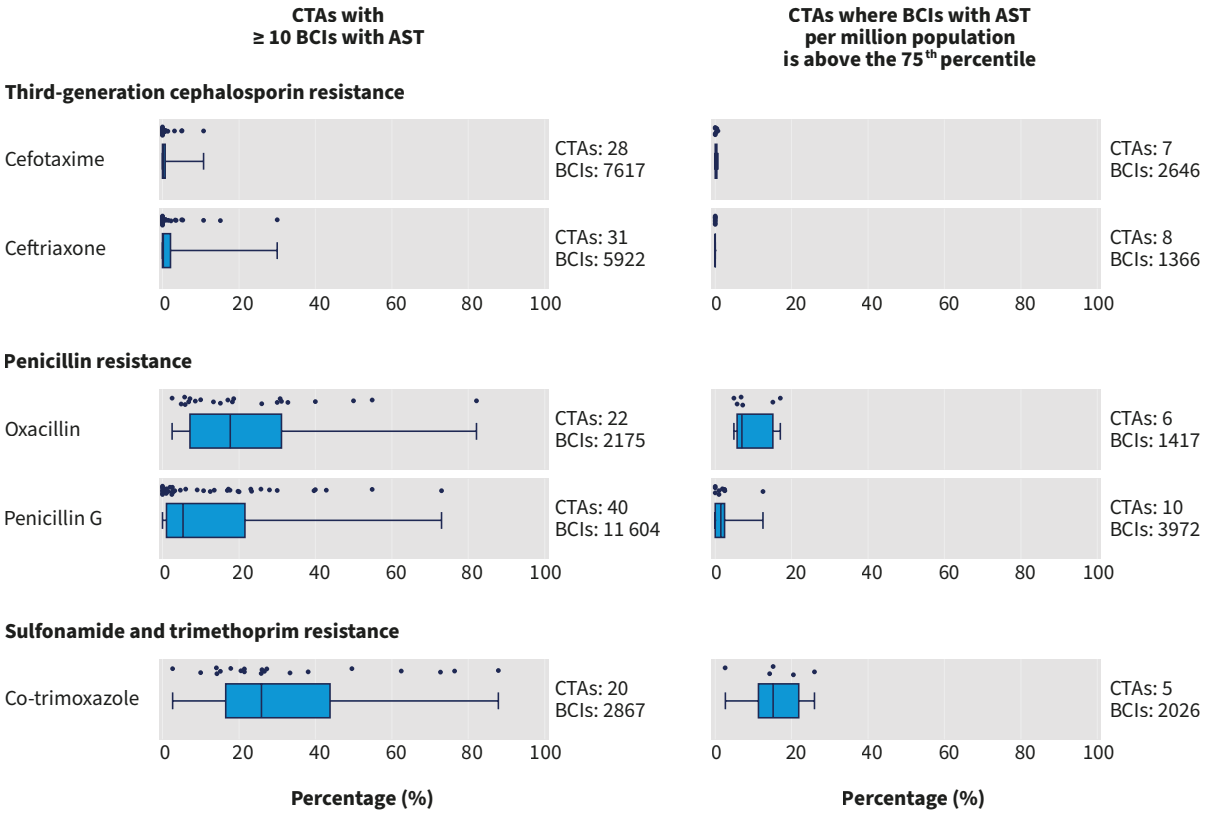
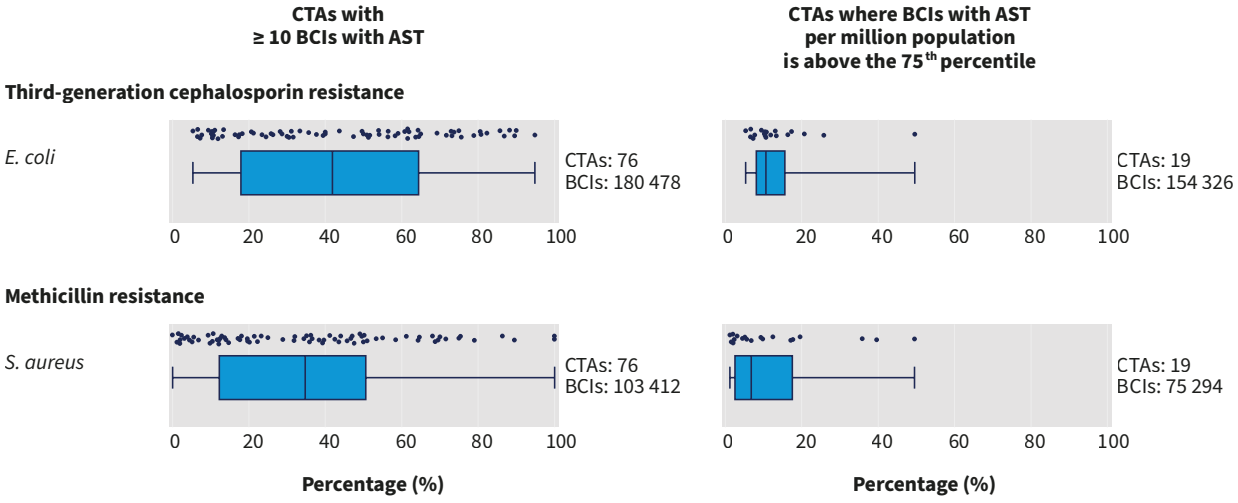


Fig. 3.7f. Percentage resistance to third-generation cephalosporins in *E. coli*, and percentage methicillin resistance in *S. aureus* in CTAs reporting ≥10 bloodstream BCIs with AST results compared to CTAs where the reported numbers per million population were above the 75th percentile in 2020



Note: The specific AMR indicator reported to the SDG monitoring framework (3.d.2) monitors the proportion of bloodstream infections among patients seeking care due to MRSA and *E. coli* resistant to third-generation cephalosporins.

Fig. 3.7g. Percentage resistance to antimicrobials under surveillance in *Salmonella* spp. in all CTAs reporting ≥10 *Salmonella* spp. gastrointestinal infections with AST results compared to CTAs where the reported number per million population was above the 75th percentile in 2020

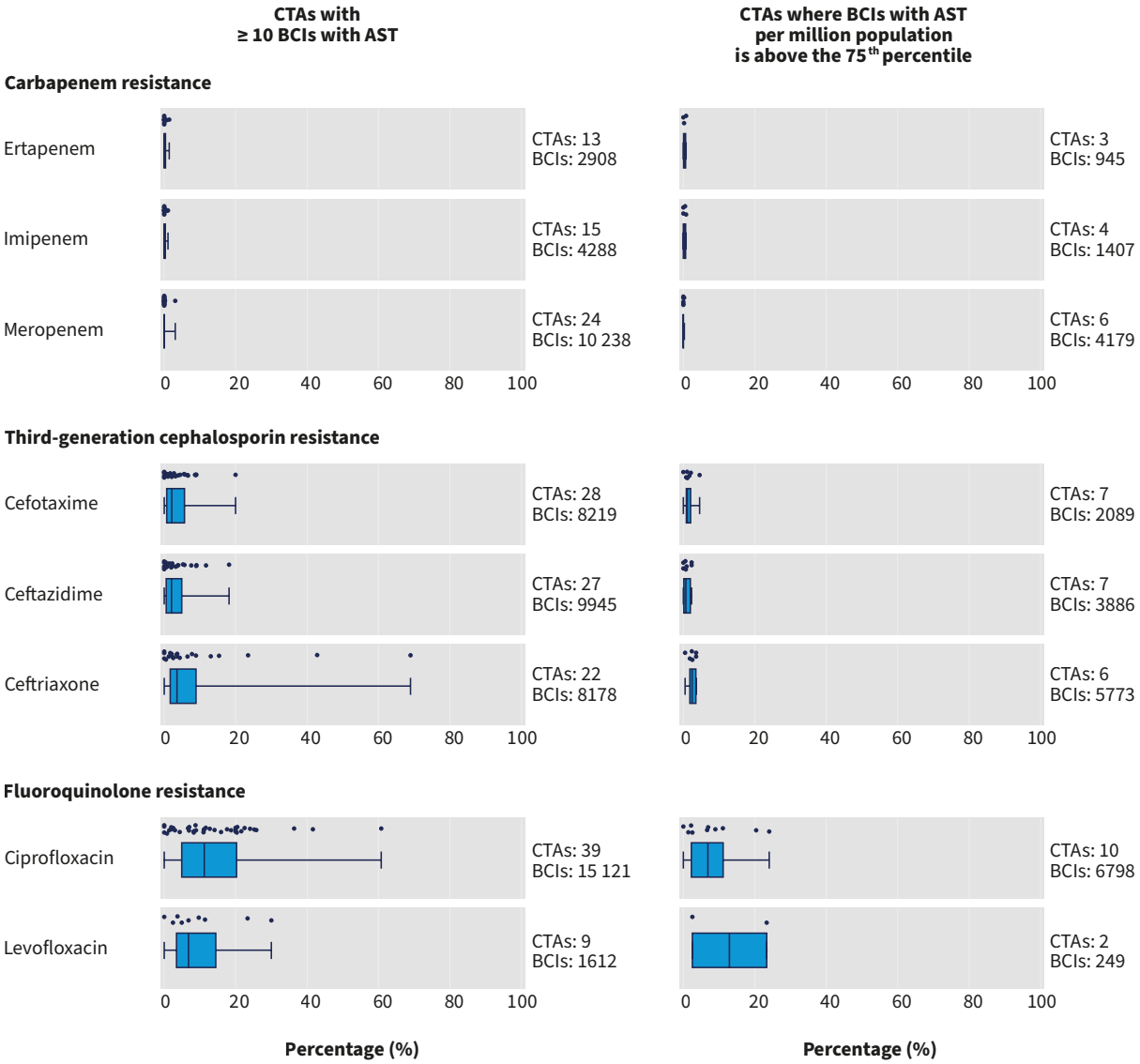


Fig. 3.7h. Percentage resistance to antimicrobials under surveillance in *Shigella* spp. in all CTAs reporting ≥10 *Shigella* spp. gastrointestinal infections with AST results compared to CTAs where the reported number per million population was above the 75th percentile in 2020

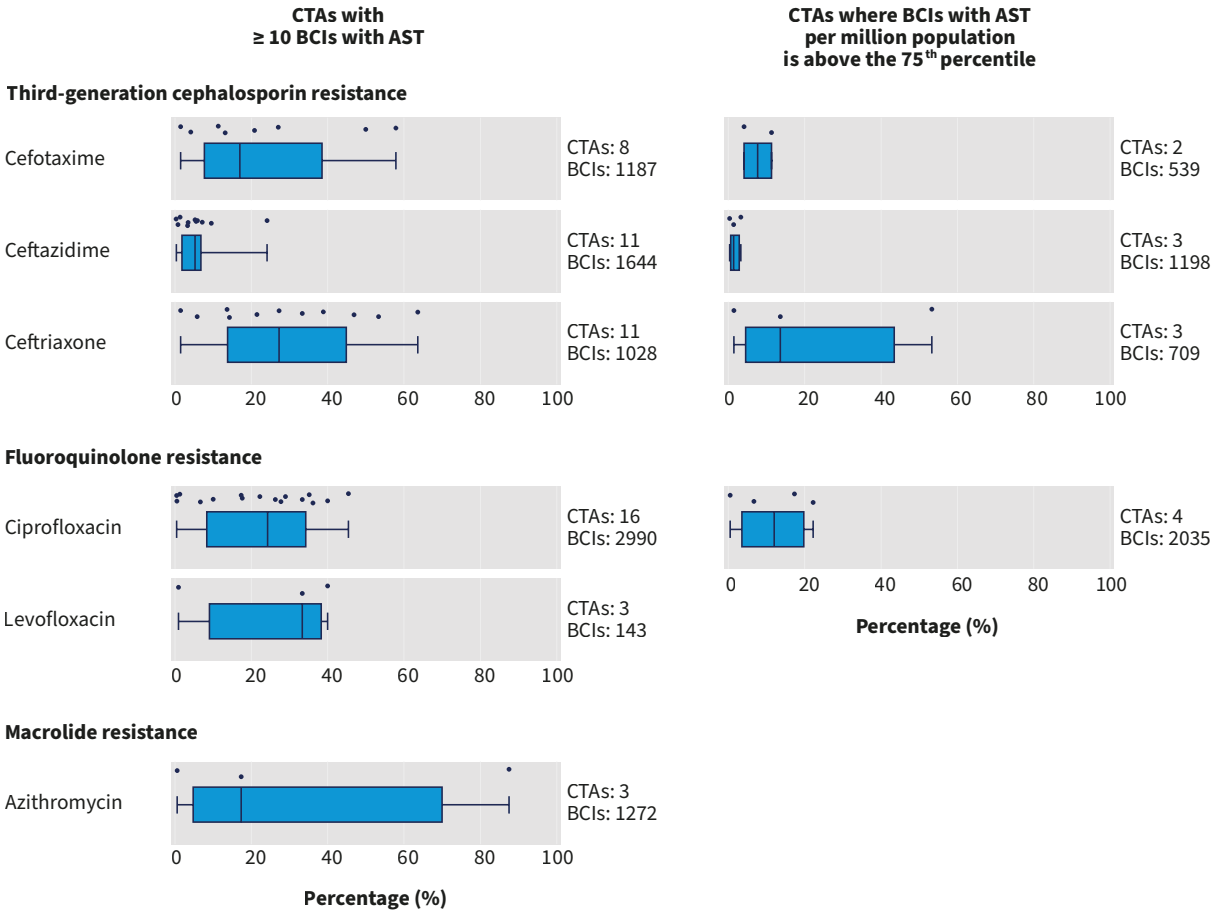


Fig. 3.7i. Percentage resistance to antimicrobials under surveillance in *N. gonorrhoeae* in all CTAs reporting ≥10 gonorrhoea BCIs with AST results compared to CTAs where the reported number per million population was above the 75th percentile in 2020

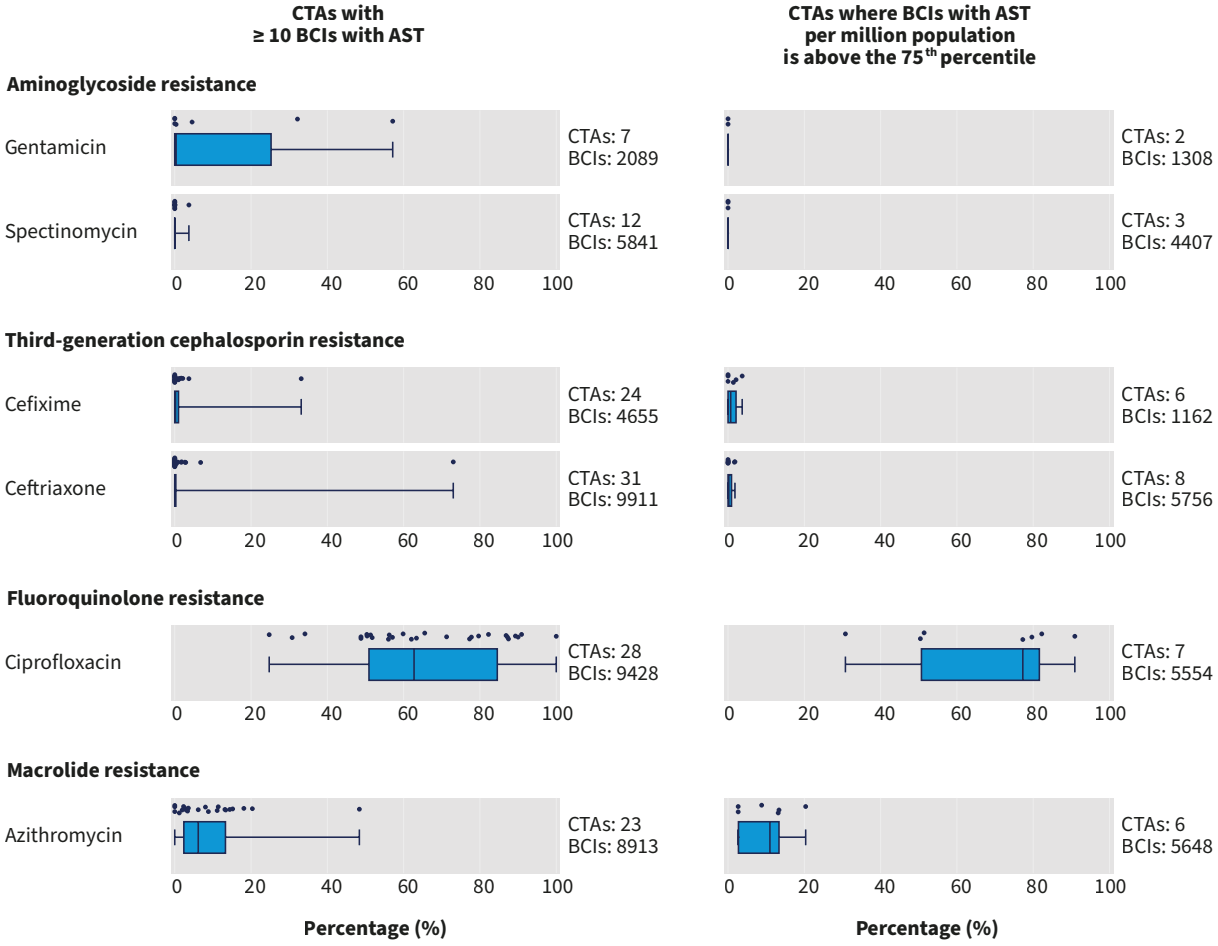


Fig. 3.7j. Percentage resistance to antimicrobials under surveillance in *E. coli* in all CTAs reporting ≥10 *E. coli* urinary tract infections with AST results compared to CTAs where the reported number per million population was above the 75th percentile in 2020

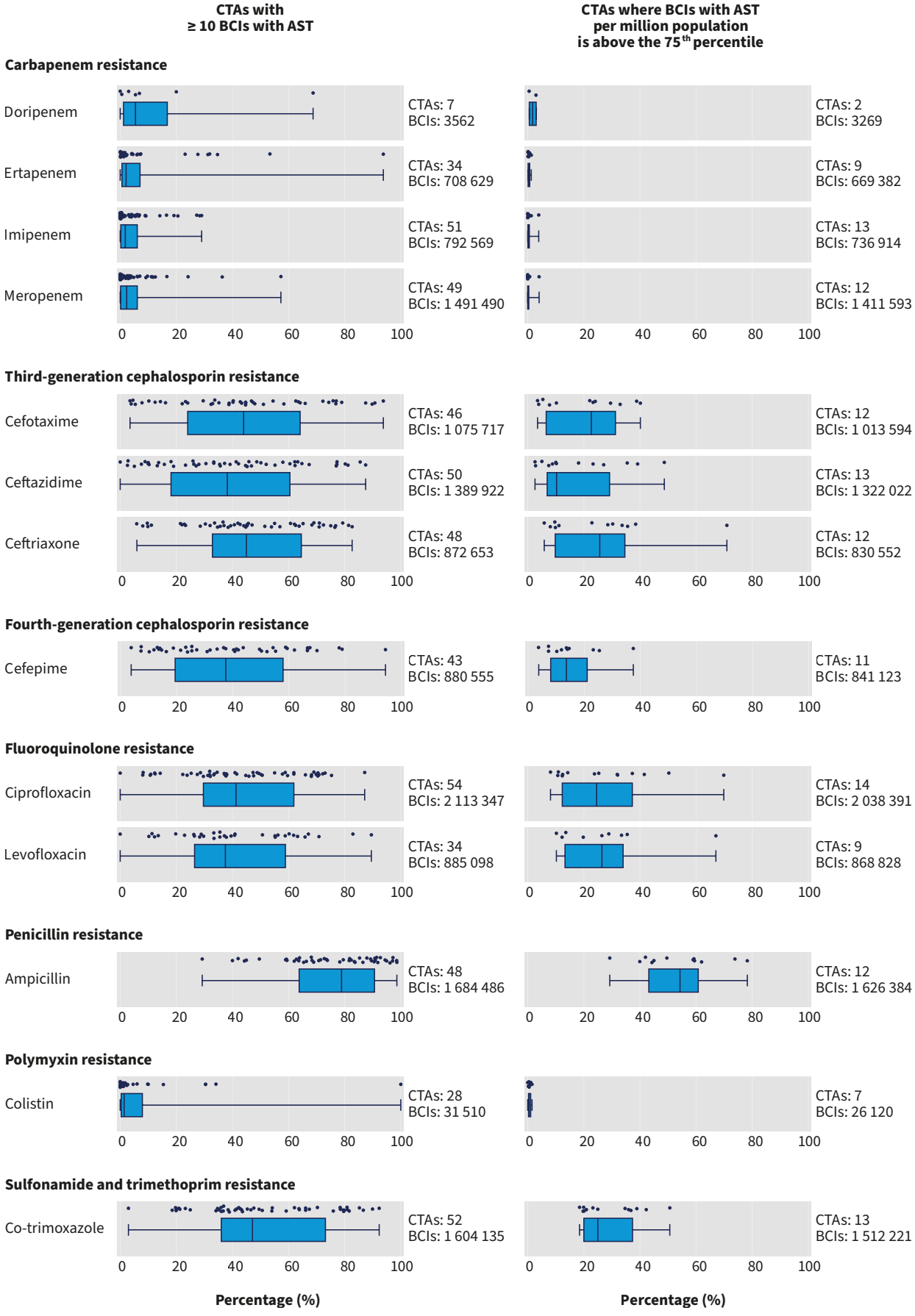
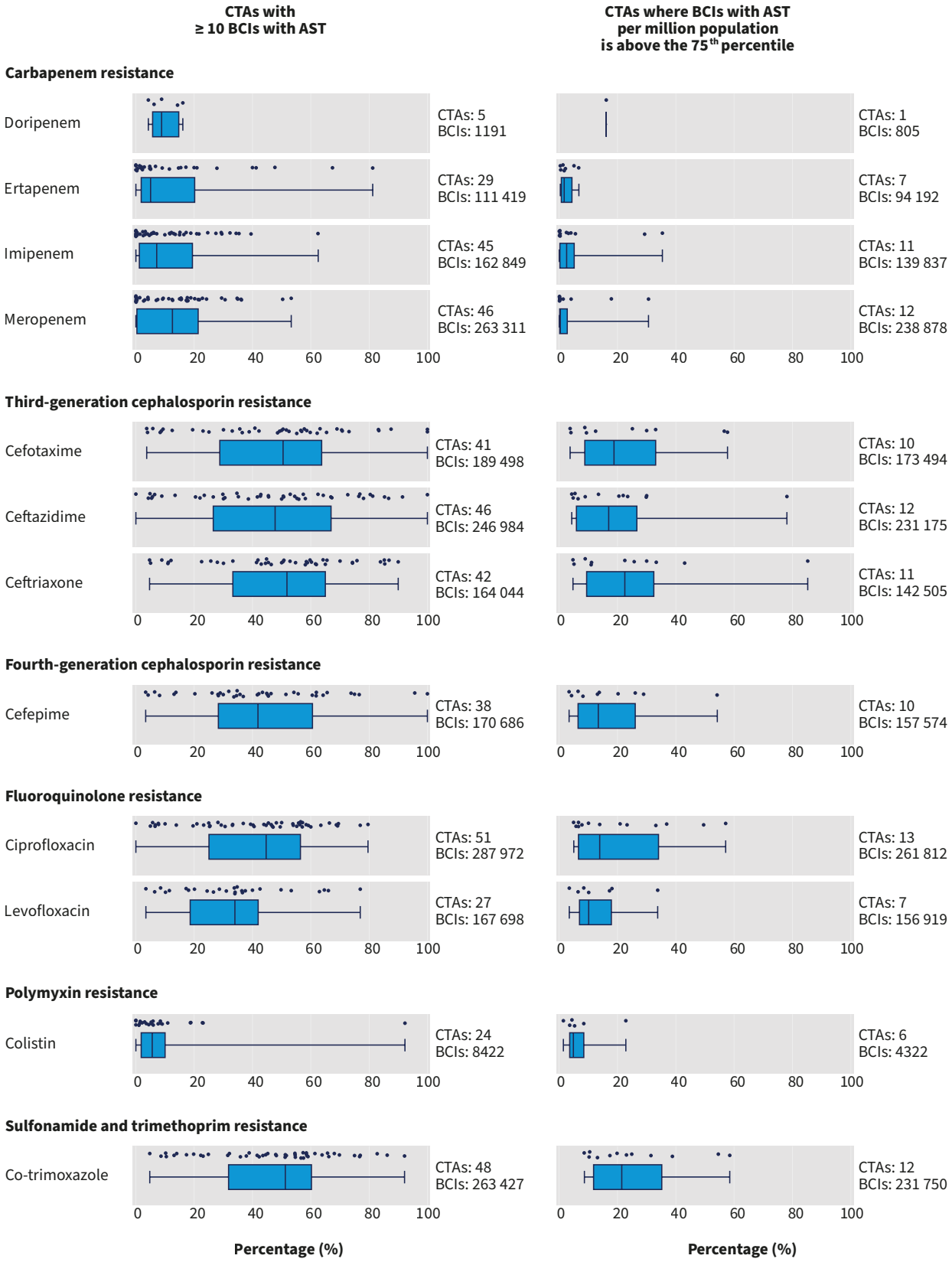


Fig. 3.7k. Percentage resistance to antimicrobials under surveillance in *K. pneumoniae* in all CTAs reporting ≥10 K. pneumoniae urinary tract infections with AST results compared to CTAs where the reported number per million population was above the 75th percentile in 2020



3.3.2 Time series of resistance to selected antibacterials, 2017-2020

The AMR trends for selected bacterial pathogen and antimicrobial combinations from four infectious syndromes under surveillance are summarized in **Figs. 3.8a-8e.** In each panel, left-hand side plots show the percentage resistance for the combination of interest for each CTA individually. The user can refer to the web-expanded content to display information specific to each of the individual CTA time series. The right-hand side plot provides the median percentage resistance and IQR for the pool of CTAs shown on the left-hand side.

A major feature of these data is the consistency of median resistance percentage estimates over time and the consistency of many, but not all, individual CTA time series in the 2017-2020 period. Only 4/17 combinations (**Figs. 3.8a-8e**) showed >15% change in median resistance in 2020 compared to 2017, with small inter-annual variations each year, thus reflecting broadly stable median resistance estimates in each cohort of CTAs. More than 15% change was only observed for meropenem resistance (0.5% [2017] – 0.9% [2020]) and third-generation cephalosporin resistance (20.2% [2017] – 24.0 [2020]) in bloodstream *E. coli* BCIs, ciprofloxacin resistance in *Salmonella* spp. bloodstream BCIs (12.0% [2017] – 19.7% [2020]), and azithromycin resistance in gonorrhoea BCIs (7.2% [2017] – 8.8% [2020]). Although further studies would be needed to verify whether a real upward trend occurred for these combinations, an increase in AMR rates during the COVID-19 pandemic has been reported in the literature *(50)*.[14] All other time series showed ≤15% change over time, including methicillin resistance in *S. aureus*, where median percentage resistance increased from 16.6% in 2017 to 18.3% in 2020, representing a 10.7% change. These findings suggest that annual intra-CTA percentage resistance data are generally coherent with previous years of data reported within the 2017-2020 period.

Time series findings also suggest that a review of longitudinal percentage resistance data can help target quality assurance efforts by identifying CTAs with vast discrepancies over time. In these instances, an epidemiological review may be triggered to investigate the causes of these undocumented sources of time variance, which may range from changes in composition, patient case mix, and numbers of health care facilities reporting data to GLASS, to changes in clinical diagnosis and laboratory practice, data recording and reporting errors, or genuine changes in percentage resistance due to changes in the epidemiology of the drug-susceptible and drug-resistant bacterial pathogens under surveillance (for example, outbreaks). Of note, where nationwide surveillance systems are not yet established, changes are bound to reflect, at least partially, modifications in surveillance sites collecting and reporting data – a fact that limits data interpretation. Relatively stable, median percentage resistance estimates reflecting broadly stable intra-CTA estimates contrast with a significant variation in resistance percentage estimates between CTAs for reasons discussed earlier (**Section 3.3.1**).

It should be noted that median percentage resistances shown in **Figs. 3.8a-8e** are only applicable to the pool of CTAs considered in each time series and cannot be taken to be representative of global trends or trends for CTAs enrolled in GLASS-AMR. For example, due to the inclusion of a different set of CTAs in each time series considered in **Figs. 3.8a-8e**, median 2020 percentage resistance estimates for the same combinations may differ from those given in **Figs. 3.7a-7k**. Nonetheless, the time series shown here highlight some types of AMR of concern, consistent with the analysis of 2020 data, which considered all CTAs with ≥10 BCIs with AST in 2020 and thus based on a broader pool of CTAs (**Figs. 3.7a-7k**). For example, time series also showed high percentage resistance (>50%) to carbapenems in *Acinetobacter* spp. (median: 73.1% [2017] – 72.9% [2020]) and to third-generation cephalosporins in *K. pneumoniae* (median: 61.5% [2017] – 63.7% [2020]) bloodstream BCIs. The emergence and spread of AMR in both of these bacterial pathogens has been a major concern in hospital settings *(51-53)*.

[14] WHO has issued evidence-based recommendations for the rational use of antibiotics in COVID-19 patients, based on similar findings from an ongoing multi-country study with a specific focus on antibiotic prescription practices and clinical outcomes in these patients.

Fig. 3.8a. Percentage resistance to selected antimicrobials in CTAs reporting ≥10 bloodstream BCIs with AST results annually (2017-2020)

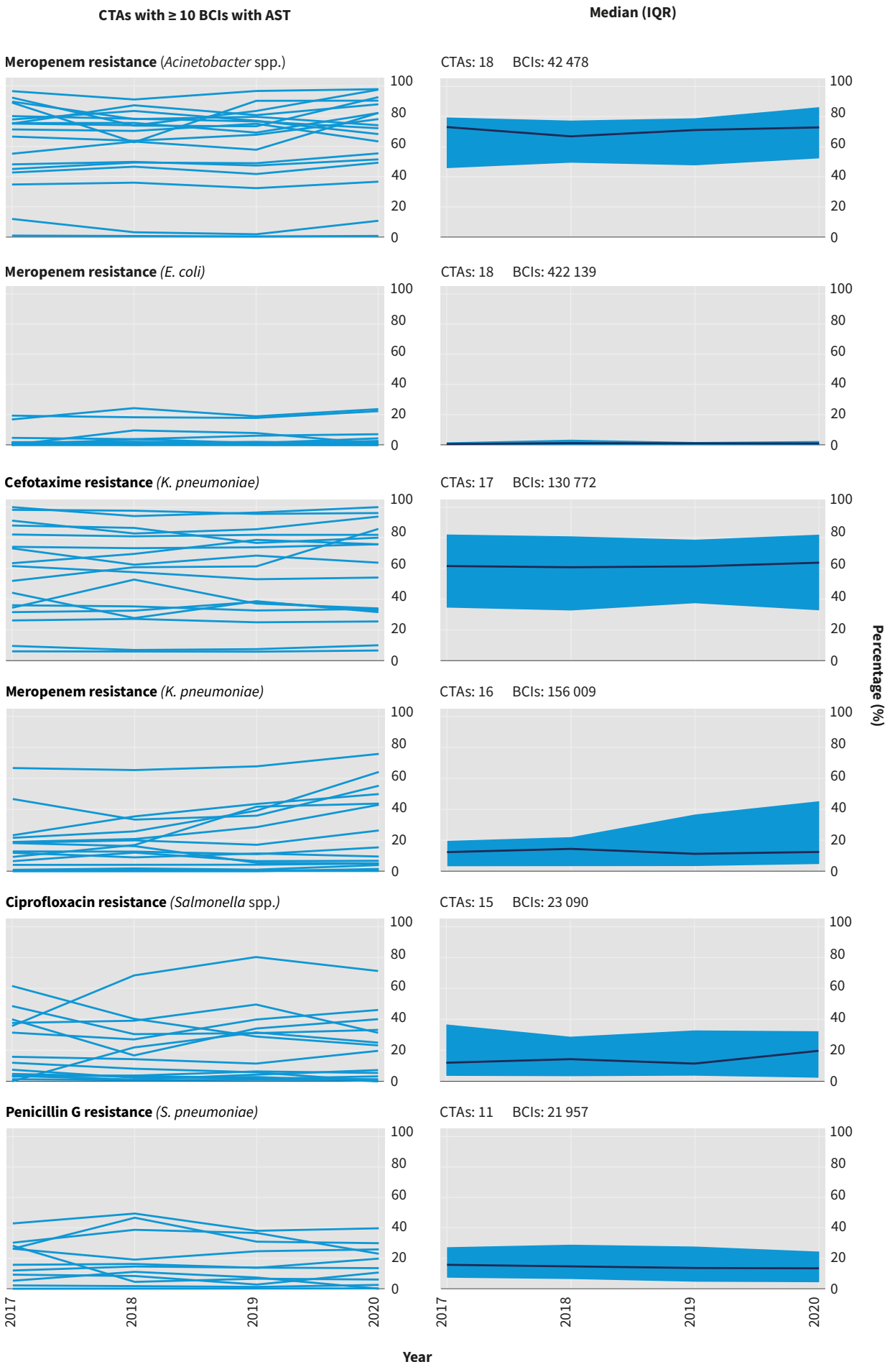
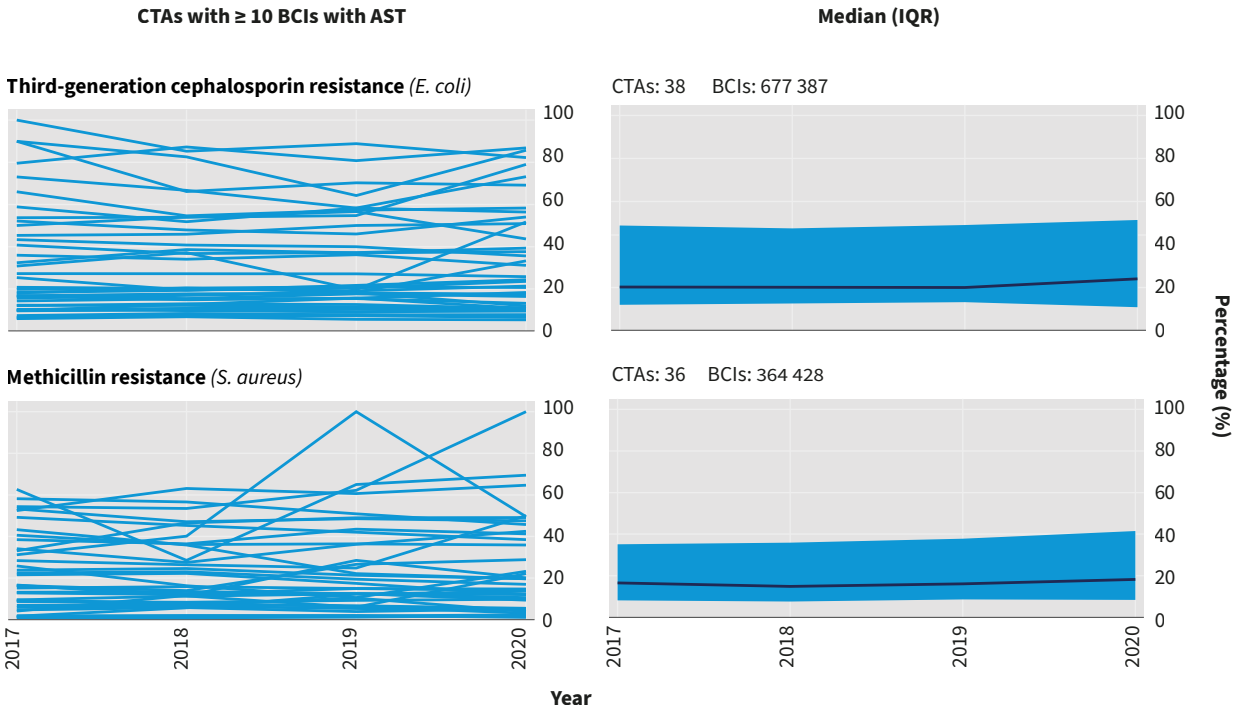
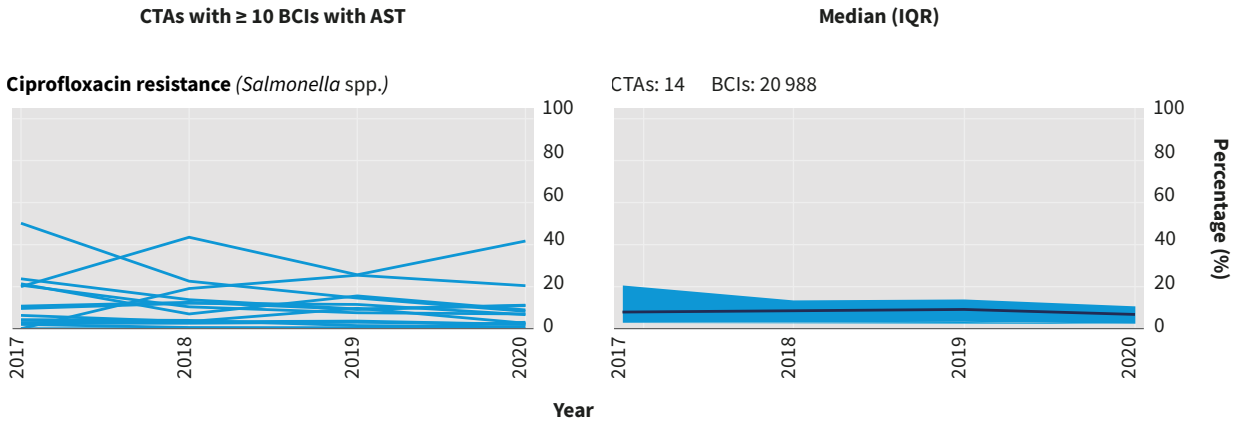


Fig. 3.8b. Percentage resistance to third-generation cephalosporins in *E. coli* and percentage methicillin resistance in *S, aureus* in CTAs reporting ≥10 bloodstream BCIs with AST results annually (2017-2020)



Note: The specific AMR indicator reported to the SDG monitoring framework (3.d.2) monitors the proportion of bloodstream infections among patients seeking care due to MRSA and *E. coli* resistant to third-generation cephalosporins.

Fig. 3.8c. Percentage resistance to ciprofloxacin in *Salmonella* spp., in CTAs reporting ≥10 gastrointestinal BCIs with AST results annually (2017-2020)



Note: Less than five CTAs reported continuous 2017-2020 AST data for key antibacterials in the case of *Shigella* spp. Consequently, no time series data are shown for this gastrointestinal bacterial pathogen.

Fig. 3.8d. Percentage resistance to selected antimicrobials in CTAs reporting ≥10 gonorrhoea BCIs with AST results annually (2017-2020)

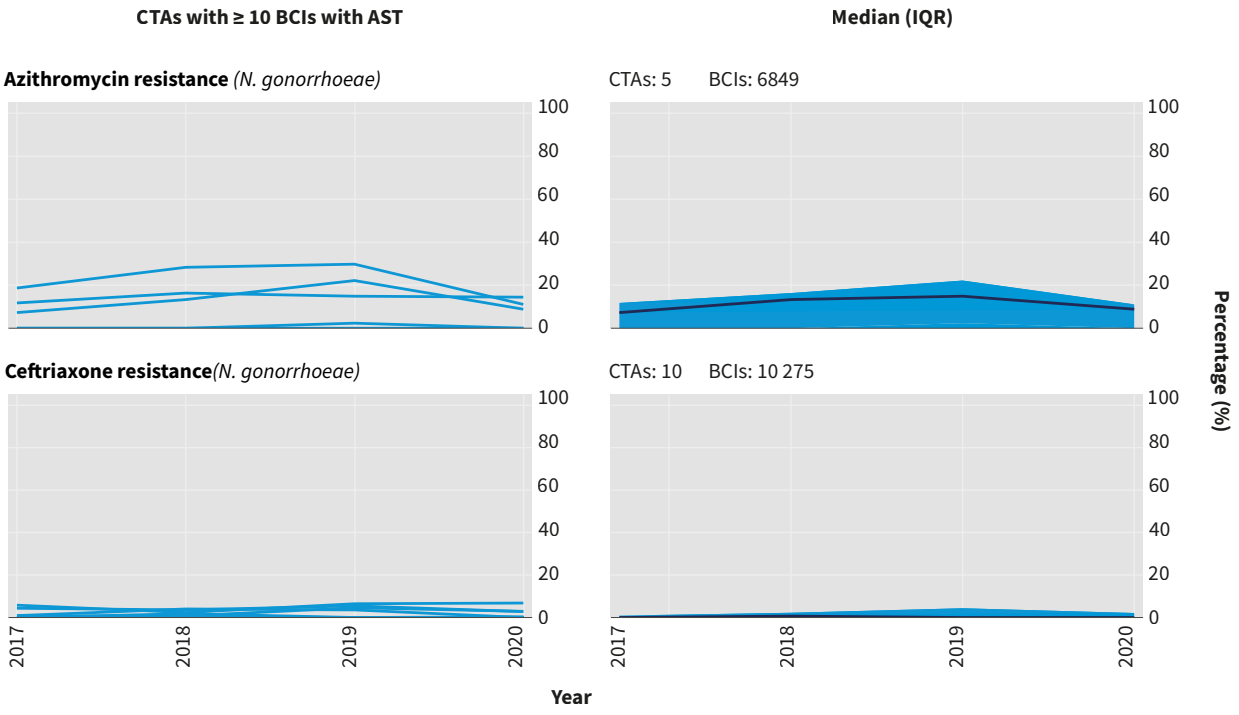
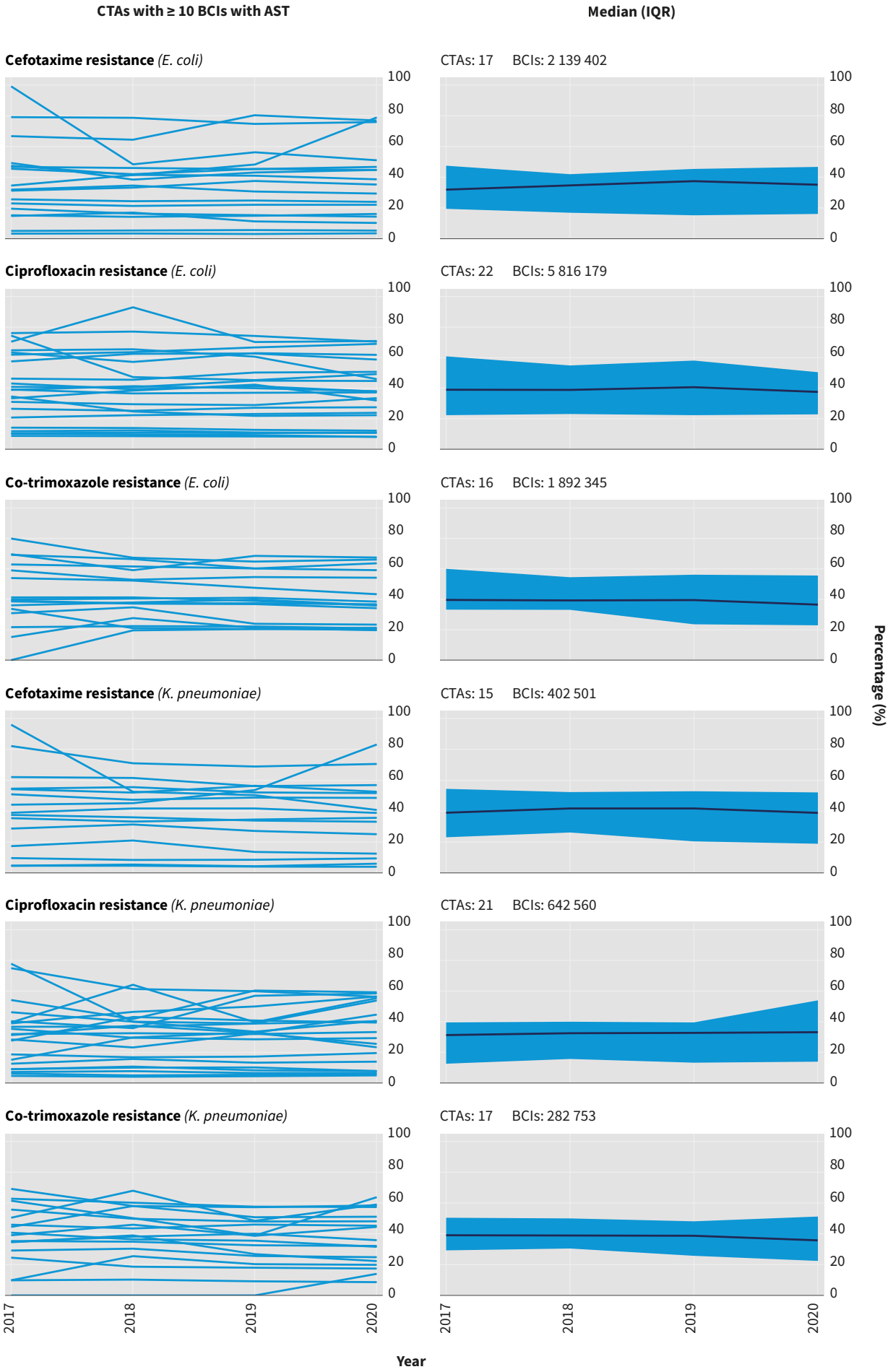


Fig. 3.8e. Percentage resistance to selected antimicrobials in CTAs reporting ≥10 urinary tract BCIs infections with AST results annually (2017-2020)



4 Progress in the development of national surveillance systems reporting data to GLASS-AMC

Following the pilot phase and the first WHO-AMC 2018 report *(54)*, WHO surveillance of AMC became mainstream within GLASS in 2020. The "GLASS methodology for surveillance of national antimicrobial consumption" published in 2020 *(14)*, hereafter referred to as the "GLASS-AMC methodology", is the national AMC surveillance framework. It describes the components of and the steps for setting up national AMC surveillance systems, provides methods for AMC surveillance at the national and global level, and streamlines the reporting process to GLASS-AMC. GLASS-AMC methodology is built on and collaborates with existing international AMC monitoring systems such as the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) *(55)*, the Antimicrobial Medicines Consumption Network of the WHO Regional Offices for Europe *(56)*; and the Western Pacific Regional Antimicrobial Consumption Surveillance System *(57)*.

GLASS-AMC monitors annual aggregated data on AMC, which are usually collected for administrative purposes from a variety of data sources along the medicine value chains and can serve as a proxy for the actual use of antimicrobials. The methodology for AMC surveillance is based on the ATC classification system and the DDD methodology, the WHO reference for drug utilization monitoring and research to improve the quality of drug use since 1981. GLASS-AMC aims to collect consumption data for all health care sectors (that is, private and public) at all health care levels (that is, community and hospital). CTAs can provide either aggregated or disaggregated data from different health care sectors and levels. The latter facilitates the monitoring of consumption data in different sectors and can guide targeted stewardship activities. CTAs are expected to report AMC data for consumed antibacterials for systemic use (J01, P01AB, and A07AA) and are also invited to report AMC data for consumed antimycotics and antifungals for systemic use (ATC classes J02, D01B), antivirals for systemic use (ATC class J05), drugs for the treatment of tuberculosis (ATC class J04A), and antimalarials (ATC class P01B). CTAs can retrieve consumption data at different levels of the medicine value chain from one or more data sources. Importantly, GLASS-AMC only considers official data sources.

GLASS-AMC also collects information on the implementation status of the national AMC surveillance system in order to monitor the progress of AMC surveillance and to identify any technical support that CTAs may need. CTAs can enrol in GLASS-AMC at any stage of development of their surveillance system and can start reporting AMC data at later stages. They can register in GLASS directly, with official communication to GLASS, or through government-based regional networks. The collection and submission process for AMC data is described in the GLASS-AMC methodology and related technical manuals and tools *(33)*.

In 2021, GLASS-AMC opened its first call for data. CTAs enrolled in GLASS-AMC up to December 2021 were invited to report on the implementation status of their national AMC surveillance system in 2021. They were also invited to report 2020 national AMC data and/or retrospective annual data up to 2014, where available. This report describes the 2021 implementation status of national AMC surveillance systems in **Section 4.1** before moving on to describe the participation of CTAs and the global coverage of GLASS-AMC in **Section 4.2.** Given that most CTAs did not report disaggregated data by health care sectors or levels (public or private; community or hospital), consumption data is shown for all sectors combined.

Section 4.3 presents the total consumption of antimicrobials in 2020 by CTAs. In the absence of 2020 data, the latest available year of data is presented instead. The volume of consumed antimicrobials is calculated in DDD and the weight of the antimicrobial substances in metric tonnes (t) using the 2021 ATC/DDD index version.

To adjust for population size and allow a comparison of AMC data across CTAs, consumption is presented as the number of DDDs per 1000 inhabitants per day, which can be roughly interpreted as the average number of individuals per 1000 inhabitants on antimicrobial treatment each day. Some CTAs may have submitted data that represent only one health care sector or one health care level. Any deviation from 2020 total data is provided in footnotes. After presenting the total consumption by antimicrobial classes in DDD per 1000 inhabitants per day, the report focuses on the consumption of antibacterials (A07AA, J01, P01AB) expressed in DDD and metric tonnes (t). Details on the indicators presented in the report and on how metrics and indicators are calculated are provided in **Annex 2**.

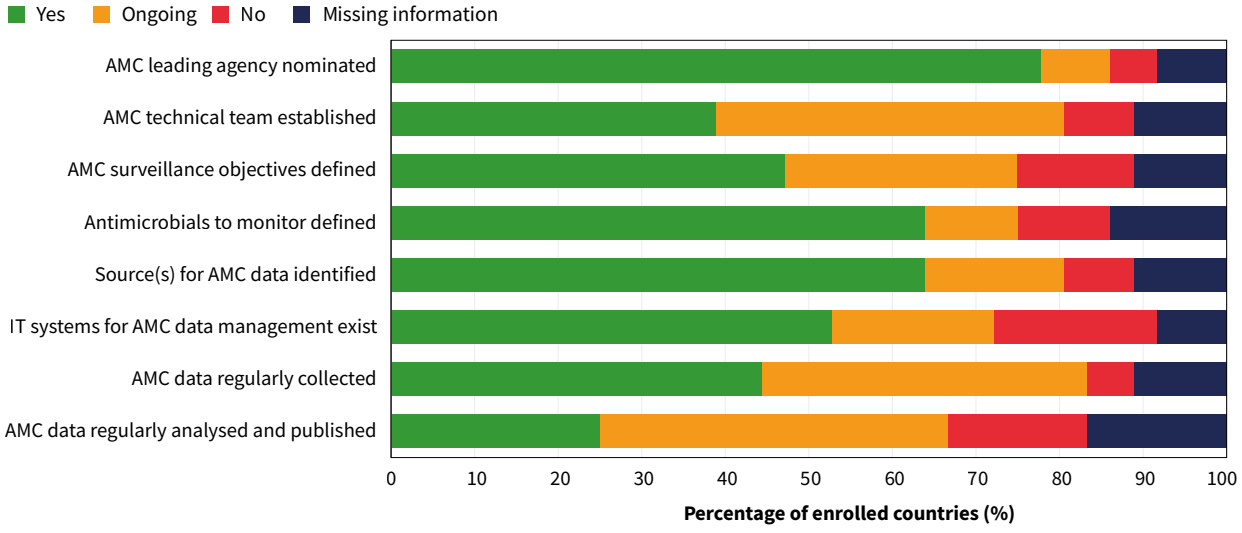
4.1 Implementation indicators

The 2021 status of the implementation of national AMC surveillance of 36 CTAs enrolled in GLASS-AMC by December 2021 is shown in **Fig. 4.1.** Results are reported as percentages using the total number of enrolled CTAs as the denominator. The implementation is evaluated over eight indicators with the implementation level classified as fully established (yes), ongoing establishment (ongoing), and establishment not started (no), or missing information (missing information).

The nomination of the body to lead the surveillance of AMC is often the first step in establishing a surveillance system and this has been fully accomplished by 78% of the reporting CTAs. A multidisciplinary AMC national technical team with clear terms of reference and skills in pharmaceutical supply chain systems and data management is also fully established in 39% of the CTAs.

A functional AMC surveillance system needs a defined methodology with clear objectives, antimicrobial classes to target, and identified data source(s) to capture the most accurate, granular and representative data. Almost one-half of the reporting CTAs have set surveillance objectives. More than 60% have specified the target antimicrobials and identified the sources for AMC data. Information technology systems to facilitate data collection and extraction need to be set up to reduce manual work as much as possible so as to decrease the risk of data errors and ensure sustainability. Almost one-half of the CTAs have such systems in place. CTAs are expected to collect, analyse and publish AMC data regularly, at least annually. Data collection is performed yearly in 44%, but only one-quarter publish the data every year.

Fig.4.1. Status of implementation of national AMC surveillance systems in 36 CTAs enrolled in GLASS-AMC as of December 2021



4.2 Participation and coverage

Of the 36 CTAs enrolled by the end of 2021, 27 (75%) reported antibacterial consumption data: eight from the African Region; two from the Region of the Americas; five from the Eastern Mediterranean Region; six from the European Region; three from the South-East Asia Region; and three from the Western Pacific Region. The consumption of antimycotics and antifungals for systemic use (J02, D01B) and antivirals (ATC J05) were reported by 12 CTAs each. Fifteen CTAs reported AMC for drugs for the treatment of tuberculosis (ATC J04A). Consumption of antimalarials (ATC P01B) was reported by three CTAs.

Table 4.1 summarizes the latest available year of data by CTA, the system's coverage, data sources used to retrieve the data, health care sectors covered, and antimicrobial classes reported. All the 27 CTAs reported data for 2020, except for Mali, the United Republic of Tanzania, Tunisia, and the Maldives, which reported data for 2019, and Burkina Faso and Nepal, which reported data from 2018.

As mentioned in **Section 2.3**, flexibility in GLASS-AMC methodology for the surveillance of national AMC allows for different options on where to capture these data along the medicine value chain. Our results show that data collected by CTAs come from different data source levels. Twenty-two CTAs combined different data sources to report AMC. Import records were the most common data sources (13 CTAs). These records were combined with production data for the domestic market in eight CTAs with a substantial local manufacturing of medicines. Eight CTAs used wholesalers' data as the sole data source or combined with sales from the public sector's central drug store or other data sources. Five CTAs reported sales data from pharmacies (community and hospitals), and two European CTAs reported insurance reimbursement data. It is important to note that most LMICs have chosen the import/production level as these data sources are more accessible and less resource-demanding. High-income countries often use the other data sources closer to actual consumption that provide more accurate information on AMC, but many LMICs lack the structures and processes to collect data at these levels and require support for adapting their national health and pharmaceutical systems.

In 20 CTAs, the reported data cover 100% of the population, whereas data cover between 80% and 91% in six CTAs. For the latter CTAs, the population was adjusted to ensure comparability with the others. In Iraq, where the data covered 25% of the population, data were considered not representative and excluded from the analysis. Twenty-one CTAs reported total consumption data of antibiotics at the national level; of these, four – all European – reported data disaggregated for the hospital and community health care levels. Four CTAs provided only public data; one CTA provided only data from the community, and another only data from the hospital sector.

Depending on the source(s) selected, data may have different level of health care sectors and/or level completeness and disaggregation, and/or the population coverage may be incomplete. It is important to take this into consideration when interpreting the results and making cross CTA comparisons. Moreover, the data on AMC should be interpreted within the context of the specific CTA, considering other aspects such as the burden of infectious diseases, national or local treatment guidelines, and broader health system issues.

Table 4.1. Coverage of the surveillance systems, data sources, levels of stratification by health care sectors and levels and antimicrobial classes reported from 27 CTAs that submitted data on national consumption of antimicrobials to GLASS-AMC in 2021

CTAs	Year[a]	Population coverage (%)	Data sources	Health care sector[b]	Health care level[c]	AB[d]	AFM[e]	AV[f]	AT[g]	AM[e]
African region										
Benin	2020	100	Wholesalers	Pub+Priv	Com+Hos	Y	Y	Y	Y	Y
Burkina Faso	2018	100	Central drug store	Pub+Priv	Com+Hos					
Côte d'Ivoire	2020	100	Wholesalers	Pub+Priv	Com+Hos					
Ethiopia	2019	80	Production for the domestic market, Import	Pub+Priv	Com+Hos	Y	Y	Y	Y	Y
Gabon	2020	90	Import	Pub+Priv	Com+Hos	Y		Y	Y	
Mali	2019	100	Wholesalers, central drug store	Pub+Priv	Com+Hos	Y			Y	
Uganda	2020	100	Import	Pub	Com+Hos	Y			Y	
United Republic of Tanzania	2019	100	Production for the domestic market, import	Pub+Priv	Com+Hos	Y			Y	
REGION OF THE AMERICAS										
Colombia	2020	100	Production for the domestic market, Import	Pub+Priv	Com+Hos	Y				
Peru	2020	100	Hospitals, pharmacies	Pub	Com+Hos	Y				
Eastern Mediterranean region										
Egypt	2020	90	Import, wholesalers	Pub+Priv	Com+Hos	Y	Y	Y	Y	
Iran (Islamic Republic of)	2020	100	Wholesalers	Pub+Priv	Com+Hos	Y	Y	Y	Y	Y
Iraq	2020	25	Wholesalers	Pub	Com+Hos	Y				
Jordan	2020	100	Production for the domestic market, import	Pub+Priv	Com+Hos	Y	Y	Y	Y	
Tunisia	2019	100	Production for the domestic market, import	Pub+Priv	Com+Hos	Y				
European region										
Belgium	2020	100	Insurance data	Pub+Priv	Com, Hos	Y	Y	Y	Y	
Cyprus	2020	100	Wholesalers, central drug store	Pub+Priv	Com, Hos	Y	Y	Y	Y	
Denmark	2020	100	Hospitals, pharmacies	Pub+Priv	Com, Hos	Y	Y	Y	Y	

CTAs	Year[a]	Population coverage (%)	Data sources	Health care sector[b]	Health care level[c]	AB[d]	AFM[e]	AV[f]	AT[g]	AM[e]
Germany	2020	88	Insurance data	Pub+Priv	Com	Y	Y	Y	Y	
Sweden	2020	100	Hospitals, pharmacies	Pub+Priv	Com, Hos	Y	Y	Y	Y	
United Kingdom of Great Britain and Northern Ireland	2020	91	Hospitals, non-governmental organizations, pharmacies, wholesalers	Pub	Com, Hos	Y				
South-east Asia region										
Bhutan	2020	100	Central drug store	Pub+Priv	Hos	Y				
Maldives	2019	100	Import	Pub+Priv	Com+Hos	Y	Y	Y		
Nepal	2018	85	Production for the domestic market, Import, non-governmental organizations	Pub+Priv	Com+Hos	Y	Y		Y	
Western Pacific region										
Brunei Darussalam	2020	100	Import	Pub+Priv	Com+Hos	Y				
Lao People's Democratic Republic	2020	100	Production for the domestic market, import	Pub+Priv	Com+Hos	Y				
Mongolia	2020	100	Production for the domestic market, import	Pub+Priv	Com+Hos	Y				

[a] **Year:** year of the most recent data reported to GLASS-AMC.
[b] **Health care sector:** Pub=public; Priv=private; Pub+Priv=public and private aggregated.
[c] **Health care level:** Com=Community; Hos=Hospital; Com+Hos=community and hospital aggregated; Com,Hos=community and hospital disaggregated.
[d] **AB:** antibacterial (ATC J01, A07AA, P01AB) data reported.
[e] **AFM:** data on antimycotics and antifungals for systemic use (J02, D01B) reported.
[f] **AV:** data on antivirals for systemic use (ATC J05) reported.
[g] **AT:** data on drugs for the treatment of tuberculosis (ATC J04A) reported.
[h] **AM:** data on antimalarials (ATC P01B) reported.

4.3 Global AMC data

AMC data from 26 CTAs have been included in the analysis of the report. When available, data are presented here for the total consumption (private and public sectors, community and hospital levels aggregated together) of antimicrobials at the national level for 2020. All figures and tables present data by CTAs, ordered alphabetically by region. The consumption of total antimicrobials expressed in DDD per 1000 inhabitants by antimicrobial classes is presented in **Fig. 4.2**.

All CTAs provided antibacterial consumption data (J01, A07AA, P01AB). The median value of the overall consumption of antibacterials is 16.6 (range, 12.3-31.2) DDD per 1000 inhabitants per day. A higher fluctuation among CTAs can be observed in the WHO African (median, 15.3 [range, 3.6-58.2]), South-East Asian and West Pacific Regions (median 15.3 [range, 9.5-57.4]). All CTAs in the WHO Eastern Mediterranean Region reported a consumption >29 DDD per 1000 inhabitants (median, 31.8 [range, 29.4-53.6]). The median value for the six European CTAs is 15.3 (range, 9.2-30).

Consumption of antimycotics and antifungals for systemic use (J02, D01B) and antivirals (ATC J05) was reported by 12 CTAs, resulting in a median value of 0.9 (range, 0.03-3.35) and 1.7 (range, 0.8-3.36) DDD per 1000 inhabitants per day, respectively. Fifteen CTAs reported AMC for tuberculosis treatment drugs (ATC J04A), with a median value of 0.2 (range, 0.01-4.9) DDD per 1000 inhabitants per day. Consumption of antimalarials (ATC P01B) was reported only by Benin, Ethiopia and Iran (Islamic Republic of) (median, 1.5 per 1000 inhabitants per day (range, 0.01-4.3)).

The consumption of antibacterials by pharmacological subgroups is presented as DDD per 1000 inhabitants in **Fig. 4.3**. Beta-lactam penicillins (J01C) were the most frequently consumed antibacterial subgroup in 22 out of 26 CTAs. Median consumption was 7.1 (range, 1.0-24.2) DDD per 1000 inhabitants per day, representing 34% of total antibacterial consumption, ranging from 4% in the United Republic of Tanzania to 72% in Gabon. Median consumption of macrolides/lincosamides/streptogramins (J01F) was 2.2 (range, 0.2-15.8) DDD per 1000 inhabitants per day, with other beta-lactam antibacterials (J01D) (1.4 DDD per 1000 inhabitants per day; range, 0.1–19.3) in a similar range, with the subgroups accounting for 16% and 15% of total antibacterial consumption, respectively. The consumption of macrolides/lincosamides/streptogramins (J01F) was proportionally the highest in Ethiopia (38%), Iran (Islamic Republic of) (26%), and Nepal (27%). Other beta-lactam antibacterials (J01D) were the most frequent antibacterial subgroup in the Maldives (53%) and Mongolia (48%). The consumption of quinolones (J01M) and tetracyclines (J01A) were similar with a median consumption of 1.6 (range, 0.4-13.2) DDD per 1000 inhabitants per day and 1.7 (range, 0.1-12.1) DDD per 1000 inhabitants per day, corresponding to a proportional use of 11% and 9%, respectively. The consumption of agents against amoebiasis and other protozoal diseases (P01A) and sulfonamides and trimethoprim (J01E) were similar with a median consumption of 0.7 (range, 0.0-8.4) DDD per 1000 inhabitants per day and 0.7 (range, 0.0-7.8) DDD per 1000 inhabitants per day, corresponding to a proportional use of 6% and 5%, respectively. The consumption of P01A was relatively high in Tanzania (16%) and Uganda (14%). The consumption of sulfonamides and trimethoprim (J01E) was relatively high in Burkina Faso (34%) and Uganda (13%).

Concerning the routes of administration, the median percentage of oral forms in the different CTAs was 95% (range, 44-100%). The oral form was the lowest in Mongolia (44%) and nearly 100% in Germany, which provided only community data (**Fig. 4.4**). Oral formulations corresponds mainly to the community use of antibiotics. For CTAs with lower oral consumption, it might be important to understand the reasons for the higher proportional use of parenteral medicines, which could be related to health and pharmaceutical system peculiarities or prescribers' behaviour.

Classification according to the WHO AWaRe categories showed that the Access group antibacterials accounted for >60% of the total consumption in 17 out of the 26 CTAs. The median proportional consumption of the Access group was 67%, with values ranging from 26% in Nepal to 88% in Bhutan. The median proportion of Watch group antibiotics related to total consumption was 31%, with values ranging from <12% in Bhutan to 74% in Nepal. Reserve group antibiotics were rarely used in most CTAs with a median proportional use of 0.1% (range, 0-3%). Not classified/not recommended antibiotics had a median proportional consumption of 2% (range, 0–9%) (**Fig. 4.5**).

The oral and parenteral antibacterial medicines that comprise 75% of the total consumption of antibacterials (DU75) in each of the participating CTAs are shown in **Tables 4.2** and **4.3**, respectively. The number of medicines constituting the DU75 for oral substances ranged from 3-9 (median, 5.5). There were substantial variations in the distribution of antibiotics (26 substances). Amoxicillin alone (J01CA04) was the most consumed oral substance (median relative consumption, 19%) and ranked number one in 12 (46%) of the 26 CTAs reporting data and was in the DU75 of 24 CTAs. Amoxicillin and a beta-lactamase inhibitor (J01CR02) ranked number one in six CTAs and were part of the oral DU75 in 15 CTAs. Other substances included in the oral DU75 in over 40% of CTAs were doxycycline (J01AA02), ciprofloxacin (J01MA02), azithromycin (J01FA10) and metronidazole (P01AB01). Notably, AWaRe Watch group medicines were included in the DU75 for all CTAs, except for Gabon and Denmark.

The median relative consumption of parenteral substances was 5% (range, 0-56%). The number of medicines constituting the CTAs' DU75 for parenteral substances ranged from 1-10 (median, 5), with even more variations observed across CTAs (a total of 36 different substances) than for the oral DU75. Ceftriaxone (J01DD04), a Watch group substance, ranked as the most often consumed parenteral substance in 12 CTAs (median relative parenteral consumption, 23%) and was in the DU75 of 20 CTAs.

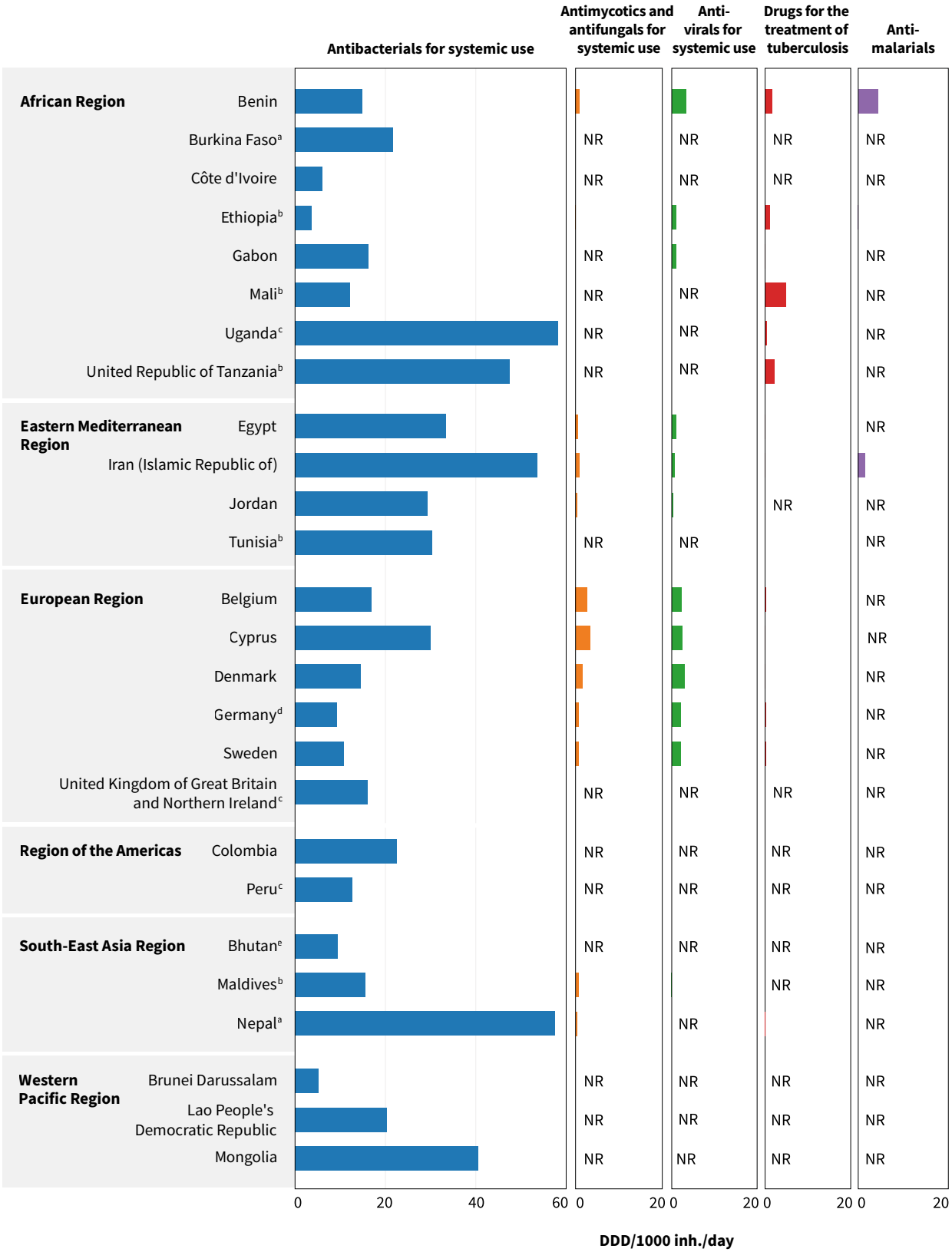
The relative consumption of penicillins by chemical subgroups is given in **Fig. 4.6.** Extended-spectrum penicillins (J01CA) were the most frequently prescribed chemical subgroups among all penicillins in 17 CTAs (median relative consumption, 54% [range, 12-94%]). Combinations of penicillins, including beta-lactamase inhibitors (J01CR), ranked first in eight CTAs (median relative consumption, 21% [range, 1-85%]). Beta-lactamase-sensitive penicillins (J01CE) had a median relative consumption of 3% (range, 0-42%). Of note, Sweden was the only country where beta-lactamase-sensitive penicillins (J01CE) were the most consumed penicillins, representing 42%. The median consumption of beta-lactamase-resistant penicillins (J01CF) was 5% (range, 0-32%).

Among cephalosporins (J01DB, J01DC, J01DD, J01DE, and J01DI) (**Fig. 4.7**), third-generation cephalosporins (J01DD) were the most frequently prescribed chemical subgroups within cephalosporins in 12 CTAs, with a median relative consumption of 43% (range, 9-99%). First-generation cephalosporins ranked first in eight CTAs (median relative consumption, 28% [1-91%]). Second-generation cephalosporins ranked first in the remaining 6 CTAs (median relative consumption, 11% [range, 0-87%]). Relative consumption of fourth-generation cephalosporins (J01DE) was below 1% in 24 CTAs (median value, 0% [range, 0-3%]).

Table 4.4 presents the consumption of antibacterials (J01, A07AA, P01AB) expressed in tonnes. Expressing consumption in tonnes and not in DDD is important for the One Health approach as it allows direct comparisons with consumption in other sectors, such as the animal and agricultural sectors. The figures provided in this report in tonnes have not been adjusted by population and benchmarking between CTAs should be done with caution.

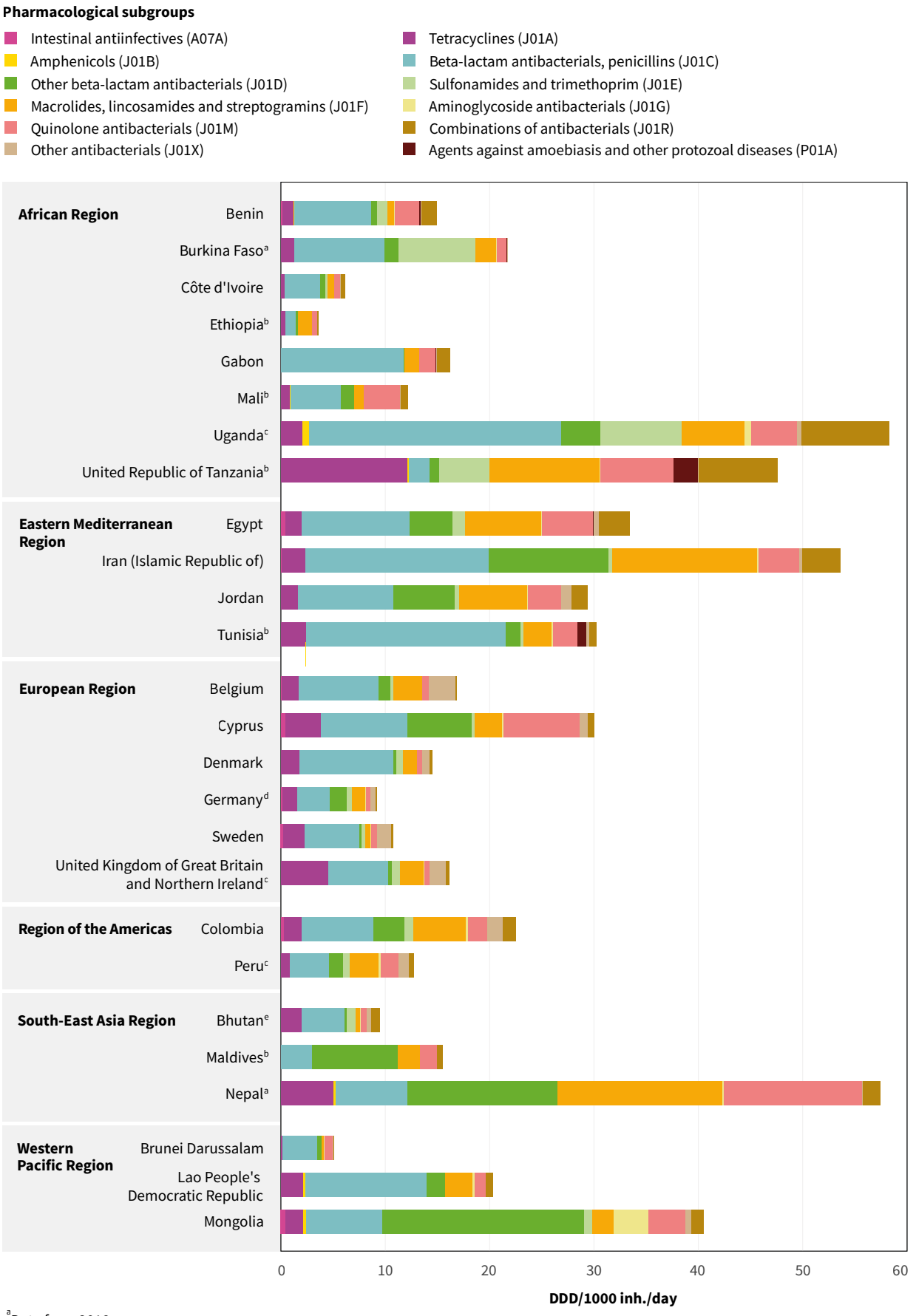
AMC data provide very useful information for policy makers and health care professionals. Although not always complete, national AMC data may signal misuse or poor access to medicines issues. National authorities may then conduct more focused surveys to investigate such signals and develop corrective measures at all levels of the medicine value chain.

Fig. 4.2. Total consumption by antimicrobial classes in 26 CTAs in 2020, expressed as DDD per 1000 inhabitants per day



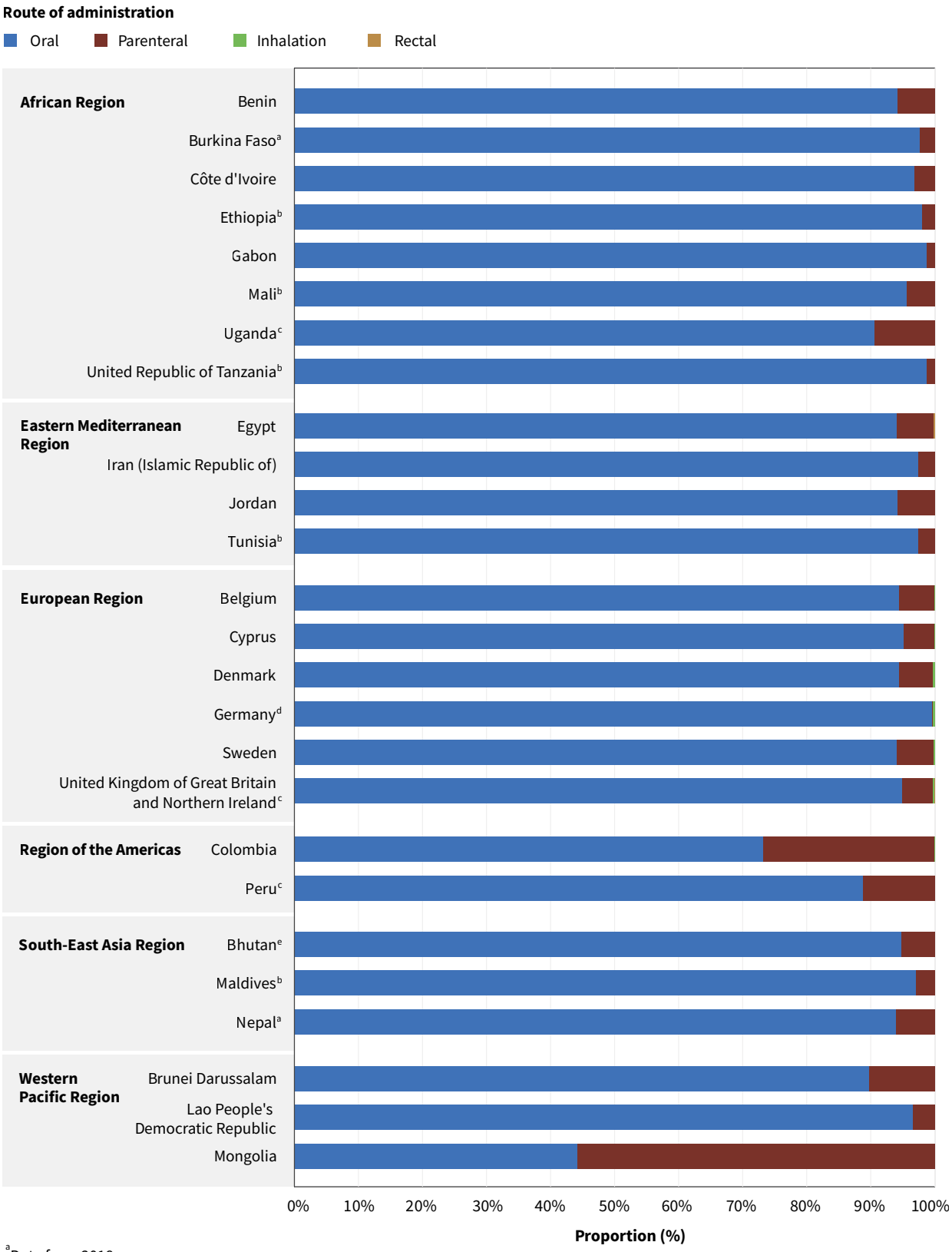
[a] Data from 2018
[b] Data from 2019
[c] Only public sector reported
[d] Only community consumption reported
[e] Only hospital consumption reported
NR: Not reported

Fig. 4.3. Total consumption of antibacterials (ATC J01, A07AA, P01A) by pharmacological subgroup (ATC3) in 26 CTAs in 2020, expressed as DDD per 1000 inhabitants per day



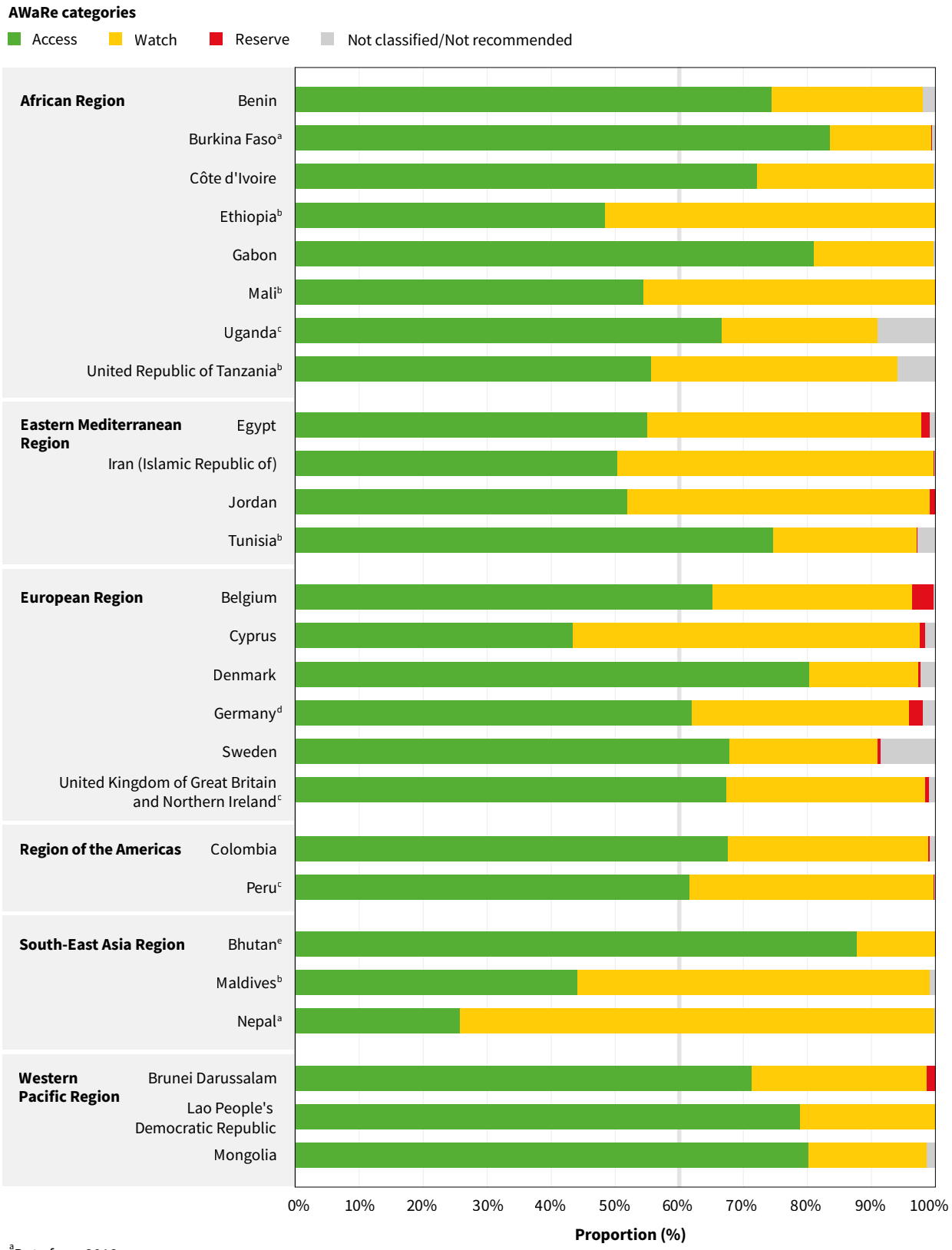
[a] Data from 2018
[b] Data from 2019
[c] Only public sector reported
[d] Only community consumption reported
[e] Only hospital consumption reported

Fig. 4.4. Relative consumption of antibacterials (ATC J01, A07AA, P01AB) by route of administration in 26 CTAs in 2020



[a] Data from 2018
[b] Data from 2019
[c] Only public sector reported
[d] Only community consumption reported
[e] Only hospital consumption reported

Fig. 4.5. Relative consumption of antibacterials (ATC J01, A07AA, P01AB) by AWaRe classification in 26 CTAs in 2020



[a] Data from 2018
[b] Data from 2019
[c] Only public sector reported
[d] Only community consumption reported
[e] Only hospital consumption reported

Table 4.2. Antibacterial substances that made up 75% (DU75) of oral consumption in 26 CTAs in 2020

	Benin	Burkina Faso	Côte d'Ivoire	Ethiopia	Gabon	Mali	Uganda	United Republic of Tanzania	Colombia	Peru	Egypt	Iran (Islamic Republic of)	Jordan	Tunisia	Belgium	Cyprus	Denmark	Germany	Sweden	United Kingdom of Great Britain and Northern Ireland	Bhutan	Maldives	Nepal	Brunei Darussalam	Lao People's Democratic Republic	Mongolia	Median relative consumption (% (range))	Percentage of CTAs (%)
Number of DTU75 substances	5	4	5	4	4	5	6	5	7	8	7	4	8	4	6	7	8	9	8	8	4	5	5	3	6	7		
Amoxicillin	1	2	1	2	2	1	1		1	1	6	1	2	1	2	6	5	1	8	2	1		5	3	1	1	19 (1-42)	92
Doxycycline	4	4	5	3		3		1	3	5	7			3		4	4	2	4	1	2		4			3	8 (1-23)	69
Amoxicillin and beta-lactamase inhibitor			2		1	4				6	1		1	2	1	1	6	4		7		3		1		6	7 (0-56)	58
Ciprofloxacin	2		4	4		2		3	4	3	5		6	4		5			7			5	2	2		2	6 (0-26)	62
Azithromycin			3	1					2	2	2	2	3		4			9				4	1		6		6 (1-38)	46
Metronidazole	3				4	5	2	2	6		3	4	8								4					5	4 (0-16)	42
Sulfamethoxazole and trimethoprim	5	1					3	5		7								8			3						4 (1-35)	27
Dicloxacillin										8							3										4 (0-12)	8
Lymecycline															6				3	3							3 (0-12)	12
Methenamine																			5								2 (0-8)	4
Erythromycin		3					6	4																	3		1 (0-14)	15
Flucloxacillin					3														2	4							1 (0-15)	12
Phenoxymethylpenicillin							4										1	6	1	8							1 (0-21)	19

Table 4.2 (Continued). Antibacterial substances that made up 75% (DU75) of oral consumption in 26 CTAs in 2020

Cefalexin						5																					4	4	1 (0-7)	12
Nitrofurantoin							4							3				7				6							1 (0-15)	15
Levofloxacin								4							2														1 (0-17)	8
Cefixime									3	7														2	3				1 (0-21)	15
Clarithromycin										5					7							5					7		1 (0-9)	15
Pivmecillinam																2				6									1 (0-20)	8
Trimethoprim																8													1 (0-4)	4
Combinations of penicillins					5																								0 (0-10)	4
Ampicillin							7																				2		0 (0-20)	8
Cefuroxime										4				5	3			3											0 (0-15)	15
Tetracycline																7											5		0 (0-6)	8
Clindamycin																		5											0 (0-6)	4
Cefadroxil																								1					0 (0-22)	4

Note: Substances are sorted according to the median relative consumption calculated in all CTAs with substance consumption greater than 0. Panels are coloured according to the AWaRe classification: Access (green), Watch (yellow), Reserved (red), and Not classified/not recommended (grey) *(15)*. The numbers shown in the table next to the antibiotics refer to the rank of use, for example, 1 equals the most often consumed antimicrobial. Please note that for Burkina Faso and Nepal, the table displays 2018 data; for Ethiopia, Mali, United Republic of Tanzania, Tunisia and the Maldives, data are from 2019; Uganda and the United Kingdom of Great Britain and Northern Ireland data are only from the public sector; Germany data are only from the community level; and Bhutan data are only from the hospital level.

Table 4.3. Antibacterial substances that made up 75% (DU75) of parenteral consumption in 26 CTAs in 2020

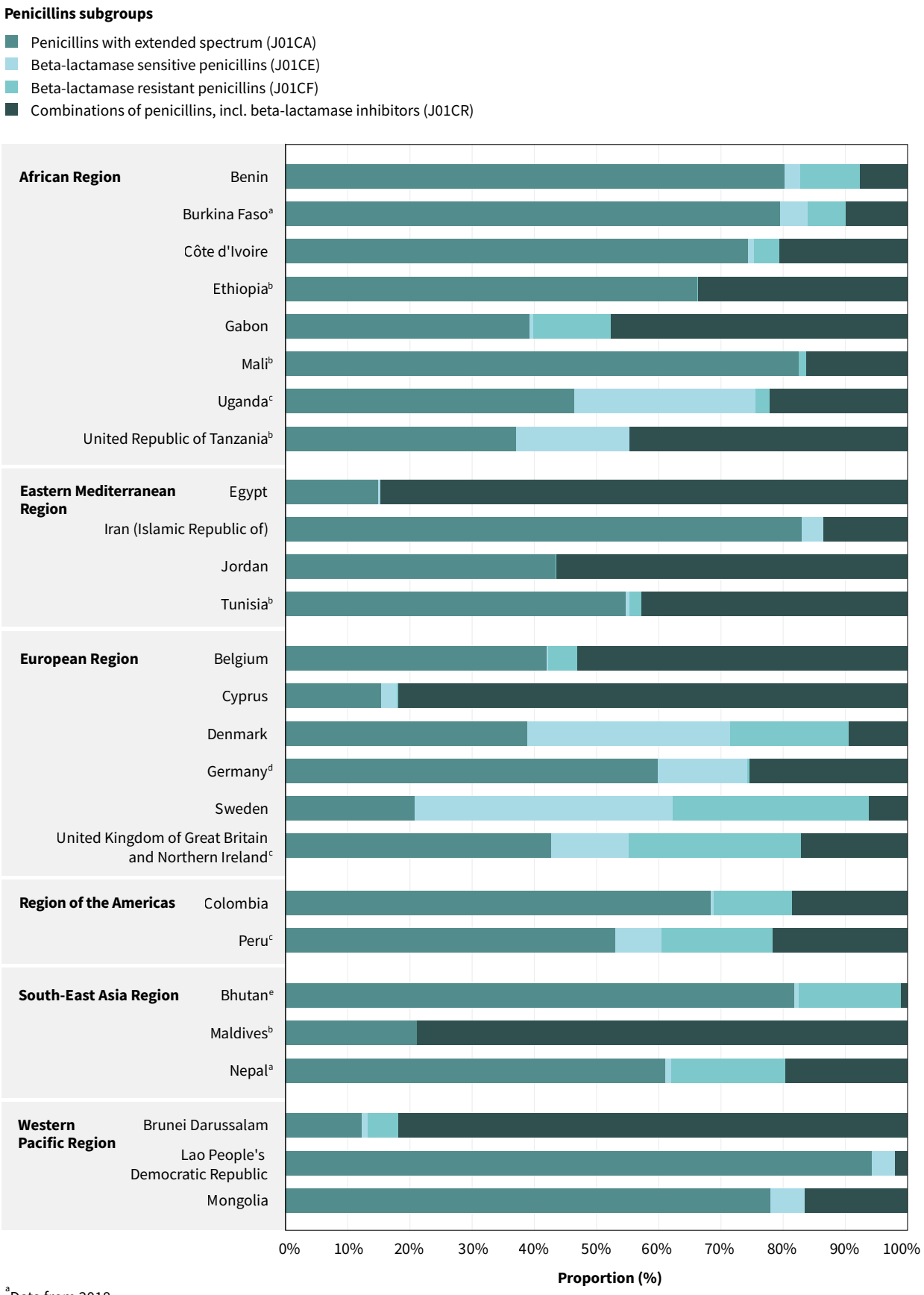
	Benin	Burkina Faso	Côte d'Ivoire	Ethiopia	Gabon	Mali	Uganda	United Republic of Tanzania	Colombia	Peru	Egypt	Iran (Islamic Republic of)	Jordan	Tunisia	Belgium	Cyprus	Denmark	Germany	Sweden	United Kingdom of Great Britain and Northern Ireland	Bhutan	Maldives	Nepal	Brunei Darussalam	Lao People's Democratic Republic	Mongolia	Median relative consumption (% (range))	Percentage of CTAs (%)
Ceftriaxone	2	1	1	2		2	1	1	4	1	1	1	2		5	3		1		7	1	1		1	1		23 (2-69)	77
Procaine benzylpenicillin							2			2		3															14 (0-20)	12
Combinations of beta-lactamase-sensitive penicillins								2																			12 (12-12)	4
Metronidazole				1	1				3	5			1	5		2	4			6	3			3			5 (1-68)	42
Gentamicin										3	5	4		2		9		3		3	5				2	2	5 (0-25)	38
Vancomycin										8					7	6		4									3 (0-10)	15
Amoxicillin			3																	8							2 (0-10)	8
Cefazolin									5			2		6	2			6			2					1	2 (0-71)	27
Ciprofloxacin	1					1										7							1				1 (0-77)	15
Ampicillin	3	2																			4				4		1 (0-16)	15
Benzathine benzylpenicillin		3	2															5									1 (0-17)	12
Clindamycin									1	6		6															1 (0-21)	12
Cefalotin									7																		1 (0-4)	4

Table 4.3 (Continued). Antibacterial substances that made up 75% (DU75) of parenteral consumption in 26 CTAs in 2020

Piperacillin and beta-lactamase inhibitor									8						3	4	1		2	4		3		6			1 (0-28)	31
Meropenem										7					6	5	5	7	5	9		5		4			1 (0-10)	35
Cefotaxime											2			3					3								1 (0-19)	12
Amoxicillin and beta-lactamase inhibitor														1	1					2	6	4		5			1 (0-23)	23
Cefuroxime															8	1	2			10		2					1 (0-19)	19
Benzylpenicillin																	3		4								1 (0-11)	8
Cloxacillin																	6		1					2			1 (0-28)	12
Ofloxacin					2																						0 (0-24)	4
Chloramphenicol							3																				0 (0-11)	4
Ampicillin and beta-lactamase inhibitor									2		3																0 (0-13)	8
Oxacillin									6																		0 (0-7)	4
Amikacin										4																	0 (0-5)	4
Cefepime											4																0 (0-3)	4
Levofloxacin												5				8											0 (0-6)	8
Teicoplanin														4						5							0 (0-13)	8
Flucloxacillin															4					1							0 (0-12)	8
Ceftazidime															9												0 (0-3)	4
Tobramycin																		2									0 (0-18)	4
Streptomycin																									3		0 (0-11)	4

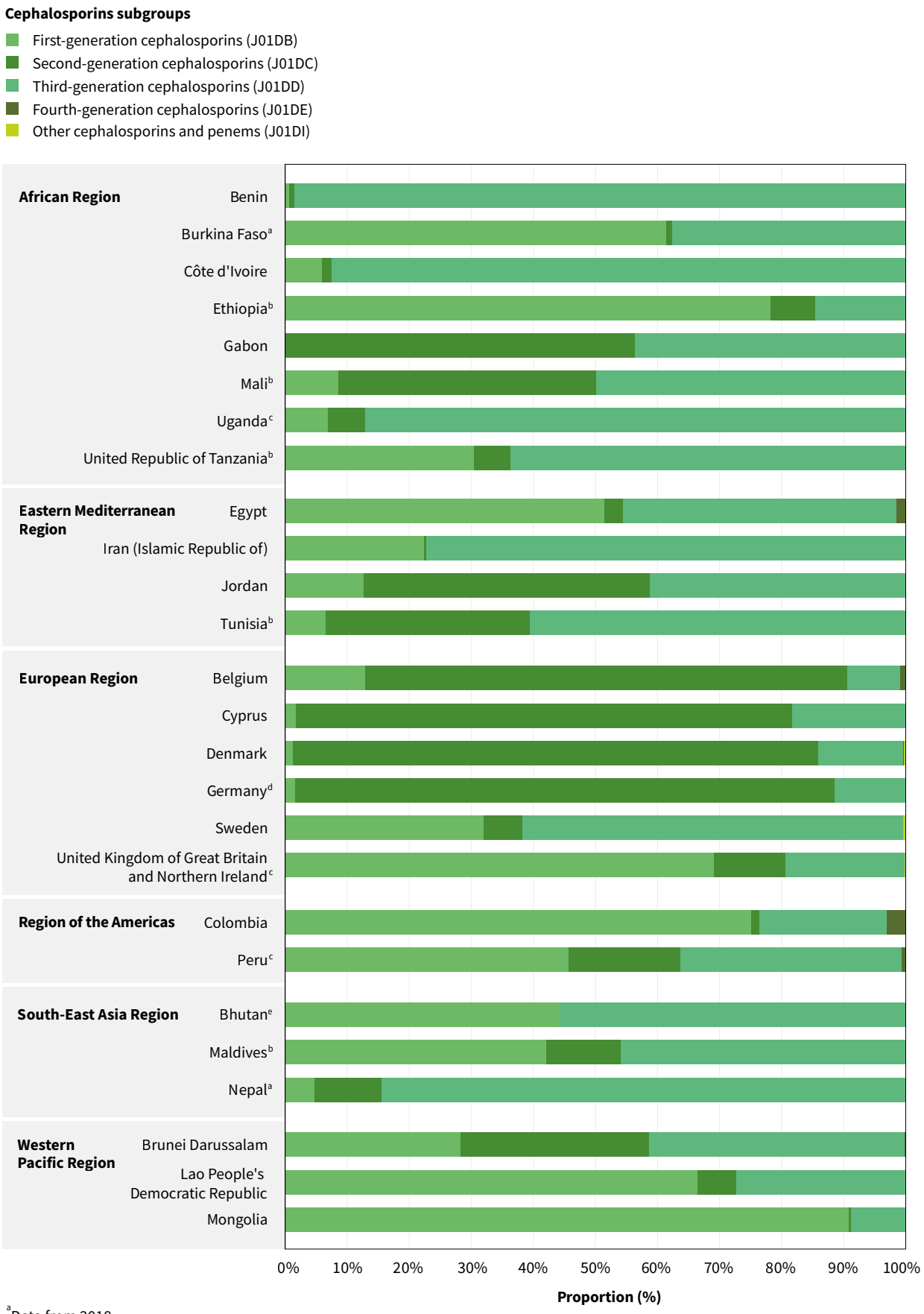
Note: Substances are sorted according to the median relative consumption calculated in all CTAs with substance consumption greater than 0. Panels are coloured according to the AWaRe classification: Access (green), Watch (yellow), Reserved (red), and Not classified/not recommended (grey) *(15)*. The numbers shown in the table next to the antibiotics refer to the rank of use, for example, 1 equals the most often consumed antimicrobial. Please note that for Burkina Faso and Nepal, the table displays 2018 data; for Ethiopia, Mali, United Republic of Tanzania, Tunisia, and the Maldives, data are from 2019; Uganda and the United Kingdom of Great Britain and Northern Ireland data are only from the public sector; Germany data are only from the community level; and Bhutan data are only from the hospital level.

Fig. 4.6. Relative consumption of penicillins (ATC J01CA, J01CE, J01CF, and J01CR) by chemical subgroups (ATC4 level) of the total consumption of penicillins in 26 CTAs in 2020



[a] Data from 2018
[b] Data from 2019
[c] Only public sector reported
[d] Only community consumption reported
[e] Only hospital consumption reported

Fig. 4.7. Relative consumption of cephalosporins ((ATC J01DB, J01DC, J01DD, J01DE, and J01DI) by chemical subgroups (ATC4 level) of the total consumption of cephalosporins in 26 CTAs in 2020



[a] Data from 2018
[b] Data from 2019
[c] Only public sector reported
[d] Only community consumption reported
[e] Only hospital consumption reported

Table 4.4. Total consumption of antibacterials (ATC J01, A07AA, P01A), in 26 CTAs in 2020, expressed in tonnes

CTAs	Tonnes
Benin	92.2
Burkina Faso[a]	242.0
Côte d'Ivoire	74.9
Ethiopia[b]	122.6
Gabon	16.5
Mali[b]	102.2
Uganda[c]	1528.6
United Republic of Tanzania[b]	1101.9
Colombia	698.6
Peru	173.8
Egypt	1355.4
Iran (Islamic Republic of)	1635.6
Jordan	115.6
Tunisia[b]	166.2
Belgium	80.1
Cyprus	8.9
Denmark	43.2
Germany[d]	228.2
Sweden	53.9
United Kingdom of Great Britain and Northern Ireland[c]	372.0
Bhutan[e]	3.4
Maldives[b]	3.4
Nepal[a]	357.8
Brunei Darussalam	1.2
Lao People's Democratic Republic	76.0
Mongolia	95.2

[a] Data from 2018.
[b] Data from 2019.
[c] Only public sector reported.
[d] Only community consumption reported.
[e] Only hospital consumption reported.

5 The way forward

The early GLASS implementation phase has successfully engaged more than one-half of the world's CTAs and fostered and reported a vast wealth of AMR data. It is also starting to monitor AMC, a major driver for AMR. Nevertheless, this report demonstrates low surveillance coverage in most CTAs providing AMR data to the new global system, which raises concerns about data representativeness. In addition, less than one-half of CTAs (48.6%) have all their reporting laboratories enrolled in external quality assessment, which might affect data quality. While most high-income CTAs have mature surveillance systems and can provide representative data, less-resourced CTAs often cannot provide high-coverage quality data at this stage of the development of their health and surveillance systems. But no CTA must be left behind and WHO commits to meeting this knowledge gap to ensure a full global picture of AMR that includes LMICs. Therefore, GLASS will prioritize leveraging the capacities of low- and mid-income CTAs to generate, analyse, report and use accurate and representative data for policy-making.

In the next phase, GLASS will support the implementation of periodic, national AMR prevalence surveys. These will involve intermittent, strategic sampling of a population subset to help overcome the paucity of high-quality representative AMR data in LMICs where surveillance infrastructures remain sparse, diagnostic stewardship is weak, and/or access to quality laboratory services is limited. The advantages of prevalence surveys include, but are not limited to quality, coverage, representativeness of data, assessment of trends, and comparability between geographical locations. This approach will be piloted in selected countries and scaled up globally with a focus on LMICs. In addition to the valuable information for policy development, the surveys will also contribute to global reporting on AMR SDG indicators. WHO is looking forward to collaborating with CTAs, WHO Collaborating Centres, and other international partners to scale-up this surveillance strategy.

It should be emphasized that GLASS will continue to support routine AMR surveillance. The application of national AMR prevalence surveys will not compete, but rather complement and help strengthen continuous surveillance using data originating from routine clinical practice. Moreover, national AMR prevalence surveys are expected to provide a quality assured platform upon which specialized studies can be delivered according to CTA needs and/or to address knowledge gaps, such as those related to attributable mortality and drivers of AMR, among others. Efforts to improve the quality and representativeness of AMR data will be supported by diagnostic stewardship, microbiology laboratory strengthening, coverage of diagnosis by insurance schemes, and relevant digital health tools. At the same time, WHO will build capacity at national level to optimally benefit from the interpretation of AMR and AMC surveillance data for (sub)national policy development. Expanding monitoring of AMC is another priority for GLASS's next phase. The monitoring of national AMC will be scaled up to inform policies and guidance at both national and global levels, including efforts to improve access and prevent mis/overuse of antimicrobials.

The current COVID-19 crisis has further revealed to the world the acute need for better systems to detect and respond to emerging threats early. AMR is among the global threats of deepest concern, with severe consequences to human health and economies *(3)*. Humanity will need to tackle this threat for many years and decades to come. It is our collective duty to support the continuous development of sustainable, good-quality AMR and use surveillance systems globally. GLASS, the global WHO system, is developing rapidly and the system's robustness is a major legacy to future generations.

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Annex 1 Bacterial pathogen and antibiotic combinations under GLASS-AMR surveillance

Table A1. Bacterial pathogen and antibiotic combinations under GLASS-AMR surveillance

	Acinetobacter spp.	*E. coli*	*K. pneumoniae*	*N. gonorrhoeae*	*Salmonella* spp.	*Shigella* spp.	*S. aureus*	*S. pneumoniae*
Aminoglycosides								
Amikacin	•							
Gentamicin	•			•				
Spectinomycin				•				
Carbapenems[§]								
Doripenem	•	•	•		•			
Ertapenem		•	•		•			
Imipenem	•	•	•		•			
Meropenem	•	•	•		•			
Second generation cephalosporins								
Cefoxitin[¥]							•	
Third generation cephalosporins								
Ceftriaxone		•	•	•	•	•		•
Ceftazidime		•	•		•	•		
Cefotaxime		•	•		•	•		•
Cefixime				•				
Fourth generation cephalosporins								
Cefepime		•	•					
Fluoroquinolones								
Ciprofloxacin		•	•	•	•	•		
Levofloxacin		•	•		•	•		
Macrolides								
Azithromycin				•		•		
Penicillins								
Ampicillin		•						
Oxacillin[¥]							•	•
Penicillin G								•

Table A1 (Continued). Bacterial pathogen and antibiotic combinations under GLASS-AMR surveillance

	Acinetobacter spp.	*E. coli*	*K. pneumoniae*	*N. gonorrhoeae*	*Salmonella* spp.	*Shigella* spp.	*S. aureus*	*S. pneumoniae*
Polymyxins								
Colistin	•	•	•					
Sulfonamides and trimethoprim								
Co-trimoxazole		•	•					•
Tetracyclines								
Minocycline	•							
Tigecycline	•							

The above table shows the antibiotics that have been prioritized for surveillance of resistance in each pathogen during the early implementation years (2016-2020) for each antibacterial class. Under each class, one or more of the antibiotics listed may have been tested and reported from each CTA.

§ Imipenem or meropenem is preferred to represent the group when available.

¥ Both cefoxitin and oxacillin are penicillinase-stable beta-lactams. The CLSI and EUCAST recommend the use of cefoxitin instead of oxacillin when using the disk diffusion method to determine resistance against methicillin for *S. aureus* (58, 59). However, cefoxitin is a surrogate for testing susceptibility to oxacillin (methicillin, nafcillin). Recognizing that CTAs have reported either or both drugs, methicillin resistance in *S. aureus* (that is, MRSA) has been calculated in this report by considering AST results for both oxacillin and/or cefoxitin.

Annex 2 Methodology for the measurement and surveillance of AMC

Consumption in weight was obtained by converting the numbers of DDDs consumed at the substance level (5th ATC group level) and the route of administration to weight. Since the DDD allocation for colistin (ATC code J01XB01) is defined in million units (MU) and not in weight units, a conversion factor of one million units (MU) = 78.74 mg was applied to calculate the weight of consumption expressed as DDD. For combined products for which DDDs are expressed in unit doses, the weight was calculated based on the number of grams of each substance per DDD. The indicators used in the report for AMC are summarized in **Table A2**.

The consumption in DDD is presented as the number of DDDs per 1000 inhabitants per day. The denominator (population size) was obtained from the World Population Prospects 2019 *(40)* for all CTAs, except for Member States of the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) where the Eurostat population at January 2022 was used *(41)*. For CTAs with incomplete data coverage, the population size was adjusted by the level of coverage of the system indicated by the CTA.

To obtain the relative consumption of antibacterials by AWaRe categories (%), antibacterial substances (J01, A07AA, P01AB) were classified according to the 2021 version of the AWaRe classification *(15)*.

To obtain the DU75 by CTA, antibiotic substances accounting for 75% of the consumption measured in DDD were listed by route of administration. The DU75% was calculated for oral and parenteral formulations separately. Results are shown for each CTA as the ranking of consumption at substance level (fifth ATC group level), as percentages of total consumption (as median and range calculated including all the CTAs with consumption >0% for the substance), and as the proportion of CTAs that included the substance in their DU75. In addition to reporting the numbers of antibacterial agents in the DU75% segment, substances are classified in colour codes according to the AWaRe classification to facilitate the identification of Watch and Reserve antibacterials that may be consumed widely and be targets for stewardship activities.

Table A2. List of indicators used in the report to describe AMC

Category (unit(s))	
Estimates of total volume of consumption by antimicrobial classes (DDD per 1000 inhabitants per day)	
• Antibacterials (J01, A07AA, P01AB) • Antimycotics and antifungals for systemic use (J02, D01B) • Antivirals for systemic use (J05) • Drugs for the treatment of tuberculosis (J04A) • Antimalarials (P01B)	Key indicator reported in the first WHO global report on AMC *(49)*. It can be roughly interpreted as the number of individuals per 1000 inhabitants on antibiotic treatment per day. It allows to monitor AMC over time and across CTAs.
Estimates of volume of consumption by antimicrobial subgroups (DDD per 1000 inhabitants)	
• Intestinal antiinfectives (A07A) • Tetracyclines (J01A) • Amphenicols (J01B) • Beta-lactam antibacterials, penicillins (J01C) • Other beta-lactam antibacterials (J01D) • Sulfonamides and trimethoprim (J01E) • Macrolides, lincosamides and streptogramins (J01F) • Aminoglycoside antibacterials (J01G) • Quinolone antibacterials (J01M) • Combinations of antibacterials (J01R) • Other antibacterials (J01X) • Antimycotics for systemic use (J02A) • Agents against amoebiasis and other protozoal diseases (P01A)	Key indicator reported in the first WHO global report on AMC *(49)*. It allows to monitor AMC over time and across CTAs.
Relative consumption of antibacterials by route of administration (%)	
• Oral • Parenteral • Inhalatory • Rectal	Oral administration is generally regarded as the most acceptable and economical method of administration of antimicrobials and is a proxy for use in the community. Hospitalized patients initially on intravenous antibiotics can often safely be switched to an oral equivalent once they are clinically stable. Oral medication is associated with fewer complications, lower health care costs, and earlier hospital discharge.

Category (unit(s))	
Relative consumption of antibacterials by AWaRe categories (%)	
• **Access:** Antibiotics intended to be used as first- and second-choice therapy. These antibiotics should be consistently available in appropriate quality and for an affordable price in every CTA. • **Watch:** Mainly broad-spectrum antibiotics, which should only be used for specific indications because of their higher potential to induce the development of resistance or their unfavourable benefit–risk balance (or both). • **Reserve:** Last-resort antibiotics that should only be used if other antibiotics do not work anymore. • **Unclassified/Not recommended:** group of medicines not specifically identified in previous groups. Some unclassified agents are included in WHO's list of "not recommended antibiotics", often the fixed-dose combinations of multiple broad-spectrum antibiotics whose use is neither evidence-based nor recommended in high-quality international guidelines. It is impossible to assess the use of "not recommended" antibiotics. These combination medicines do not always have an assigned ATC code and therefore are not included in data collection.	WHO introduced the AWaRe categorization as part of the 2017 Model List of Essential Medicines. The methodological approach considers the treatment guidelines of the most frequent infectious disease syndromes. The AWaRe categorization is an antimicrobial stewardship tool to assist CTAs in their efforts towards optimizing antimicrobial use. The overall goal is to reduce the use of Watch and Reserve group antibiotics and to increase the relative benefit and availability of Access group antibiotics, where needed. The AWaRe classification is a tool for monitoring antibiotic consumption, defining targets, and monitoring the effects of stewardship policies that optimize antibiotic use and curb AMR. The WHO 13th General Programme of Work 2019–2023 includes a CTA-level target of at least 60% of total antibiotic consumption being Access group antibiotics.
Drug utilization 75% (DUT75) (Rank, %)	
• DUT75 – parenteral formulation antibacterial substances (ATC5) • DUT75 – oral formulation antibacterial substances (ATC5)	This indicator is based on the observation that consumption tends to be concentrated in a relatively small number of agents. DU75 can allow to identify the frequent use of restricted and special use antibacterials that may be consumed widely and be targets for stewardship activities. Identification of DU75 substances according to the AWaRe classification is facilitated by colour codes.
Relative consumption of penicillins by chemical subgroups (%)	
• Extended-spectrum penicillins (J01CA) • Beta-lactamase-sensitive penicillins (J01CE) • Beta-lactamase-resistant penicillins (J01CF) • Combinations of penicillins, including beta-lactamase inhibitors (J01CR)	J01C is often the most consumed antibacterial subgroups in the community. Substances from this group mainly belong to the Access group, with the exception of extended-spectrum penicillins (J01CA) that are 47% from the Access group.
Relative consumption of cephalosporins by chemical subgroups (%)	
• First-generation cephalosporins (J01DB) • Second-generation cephalosporins (J01DC) • Third-generation cephalosporins (J01DD) • Fourth-generation cephalosporins (J01DE) • Other cephalosporins and penems (J01DI)	Cephalosporins are often the most consumed antibacterial subgroups in hospitals. All first-generation cephalosporins substances (J01DB) belong to the Access groups. All other cephalosporins are classified as a Watch group, except for ceftazidime/avibactam (third-generation cephalosporins). All fourth-generation cephalosporins are reserved.

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