



ANTIMICROBIAL RESISTANCE

Global Report
on Surveillance

2014
Summary



World Health
Organization

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Summary

Antimicrobial resistance (AMR) is an increasingly serious threat to global public health. AMR develops when a microorganism (bacteria, fungus, virus or parasite) no longer responds to a drug to which it was originally sensitive. This means that standard treatments no longer work; infections are harder or impossible to control; the risk of the spread of infection to others is increased; illness and hospital stays are prolonged, with added economic and social costs; and the risk of death is greater—in some cases, twice that of patients who have infections caused by non-resistant bacteria.

The problem is so serious that it threatens the achievements of modern medicine. A post-antibiotic era—in which common infections and minor injuries can kill—is a very real possibility for the 21st century.

Determining the scope of the problem is the first step in formulating an effective response to AMR. "Antimicrobial resistance: Global report on surveillance 2014", produced in collaboration with Member States and external partners, is WHO's first attempt to obtain an accurate picture of the magnitude of AMR and the current state of surveillance globally. The report focuses on antibacterial resistance (ABR), as the state of surveillance in ABR is not generally as advanced as it is for diseases such as tuberculosis (TB), malaria and HIV.

The most important findings of this report are:

- Very high rates of resistance have been observed in all WHO regions in common bacteria (for example, *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus*) that cause common health-care associated and community-acquired infections (urinary tract infections, wound infections, bloodstream infections and pneumonia).
- Many gaps exist in information on pathogens of major public health importance. There are significant gaps in surveillance, and a lack of standards for methodology, data sharing and coordination. Overall, surveillance of ABR is neither coordinated nor harmonized.

Despite the limitations of current surveillance, it is clear that ABR has reached alarming levels in many parts of the world. There is an urgent need to strengthen and coordinate collaboration to address those gaps. Lessons learned from long-standing experience in TB, malaria and HIV programmes may be usefully applied to ABR and are discussed in the report.

WHO is developing a global action plan for AMR that will include:

- development of tools and standards for harmonized surveillance of ABR in humans, and for integrated surveillance in food-producing animals and the food chain;
- elaboration of strategies for population-based surveillance of AMR and its health and economic impact; and
- collaboration between AMR surveillance networks and centres to create or strengthen coordinated regional and global surveillance.

AMR is a global health security threat that requires action across government sectors and society as a whole. Surveillance that generates reliable data is the essential foundation of global strategies and public health actions to contain AMR.

Key findings and public health implications of ABR are:

- Very high rates of resistance have been observed in bacteria that cause common health-care associated and community-acquired infections (e.g. urinary tract infection, pneumonia) in all WHO regions.
- There are significant gaps in surveillance, and a lack of standards for methodology, data sharing and coordination.

Key findings from AMR surveillance in disease-specific programmes are as follows:

- Although multidrug-resistant TB is a growing concern, it is largely under-reported, compromising control efforts.
- Foci of artemisinin resistance in malaria have been identified in a few countries. Further spread, or emergence in other regions, of artemisinin-resistant strains could jeopardize important recent gains in malaria control.
- Increasing levels of transmitted anti-HIV drug resistance have been detected among patients starting antiretroviral treatment.

Surveillance of ABR and sources of data

There is at present no global consensus on methodology and data collection for ABR surveillance. Routine surveillance in most countries is often based on samples taken from patients with severe infections – particularly infections associated with health care, and those in which first-line treatment has failed. Community-acquired infections are almost certainly underrepresented among samples, leading to gaps in coverage of important patient groups.

Nevertheless, it is critical to obtain a broad picture of the international scope of the problem of ABR.

To accomplish this, WHO obtained, from 129 Member States, the most recent information on resistance surveillance and data for a selected set of nine bacteria–antibacterial drug combinations of public health importance. Of these, 114 provided data for at least one of the nine combinations (22 countries provided data on all nine combinations).

Some data sets came from individual surveillance sites, or data from several sources rather than national reports. Many data sets were based on a small number of tested isolates of each bacterium (<30), adding to uncertainty about the precision of the data; this reflects a lack of national structures to provide an overview of the situation and limited capacity for timely information sharing. Most data sets, individual sites or aggregated data, were based on hospital data. Non-representativeness of surveillance data is a limitation for the interpretation and comparison of results.

The data compiled from countries indicate where there may be gaps in knowledge and lack of capacity to collect national data. Among WHO regions, the greatest country-level data were obtained from the European Region and the Region of the Americas, where long-standing regional surveillance and collaboration exist.

Current status of resistance in selected bacteria

In the survey forming the basis for this part of the report, information was requested on resistance to antibacterial drugs commonly used to treat infections caused by seven bacteria of international concern. The chosen bacteria are causing some of the most common infections in different settings; in the community, in hospitals or transmitted through the food chain. The main findings are summarized in the following tables:

Bacteria commonly causing infections in hospitals and in the community

Name of bacterium/ resistance	Examples of typical diseases	No. out of 194 Member States providing data	No. of WHO regions with national reports of 50% resistance or more
<i>Escherichia coli</i> / - vs 3 rd gen. cephalosporins - vs fluoroquinolones	Urinary tract infections, blood stream infections	86 92	5/6 5/6
<i>Klebsiella pneumoniae</i> / - vs 3 rd gen. cephalosporins - vs 3 rd carbapenems	Pneumonia, blood stream infections, urinary tract infections	87 71	6/6 2/6
<i>Staphylococcus aureus</i> / - vs methicillin "MRSA"	Wound infections, blood stream infections	85	5/6

Bacteria mainly causing infections in the community

Name of bacterium/ resistance	Examples of typical diseases	No. out of 194 Member States providing data	No of WHO regions with national reports of 25% resistance or more
<i>Streptococcus pneumoniae</i> / - non-susceptible or resistant to penicillin	Pneumonia, meningitis, otitis	67	6/6
Nontyphoidal <i>Salmonella</i> / - vs fluoroquinolones	Foodborne diarrhoea, blood stream infections	68	3/6
<i>Shigella species</i> / - vs fluoroquinolones	Diarrhoea ("bacillary dysentery")	35	2/6
<i>Neisseria gonorrhoea</i> / - vs 3 rd gen. cephalosporins	Gonorrhoea	42	3/6

The high proportions of resistance to 3rd generation cephalosporins reported for *E. coli* and *K. pneumoniae* means that treatment of severe infections likely to be caused by these bacteria in many settings must rely on carbapenems, the last-resort to treat severe community and hospital acquired infections. These antibacterials are more expensive, may not be available in resource-constrained settings, and are also likely to further accelerate development of resistance. Of great concern is the fact that *K. pneumoniae* resistant also to carbapenems has been identified in most of the countries that provided data, with proportions of resistance up to 54% reported. The large gaps in knowledge of the situation in many parts of the world further add to this concern. For *E. coli*, the high reported resistance to fluoroquinolones means limitations to available oral treatment for conditions which are common in the community, such as urinary tract infections.

High rates of methicillin-resistant *Staphylococcus aureus* (MRSA) imply that treatment for suspected or verified severe *S. aureus* infections, such as common skin and wound infections, must rely on second-line drugs in many countries, and that standard prophylaxis with first-line drugs for orthopaedic and other surgical procedures will have limited effect in many settings. Second-line drugs for *S. aureus* are more expensive; also, they have severe side-effects for which monitoring during treatment is advisable, increasing costs even further.

Reduced susceptibility to penicillin was detected in *S. pneumoniae* in all WHO regions, and exceeded 50% in some reports. The extent of the problem and its impact on patients is not completely clear because of variation in how the reduced susceptibility or resistance to penicillin is reported, and limited comparability of laboratory standards. Because invasive pneumococcal disease (e.g. pneumonia and meningitis) is a common and serious disease in children and elderly people, better monitoring of this resistance is urgently needed.

The resistance to fluoroquinolones among two of the major causes for bacterial diarrhoea, nontyphoidal *Salmonella* (NTS) and *Shigella species*

were comparatively lower than in *E. coli*. However, there were considerable gaps in information on these two bacteria, particularly from areas where they are of major public health importance. Some reports of high resistance in NTS are of great concern because resistant strains have been associated with worse patient outcomes.

In *N. gonorrhoeae*, finally, decreased susceptibility to third-generation cephalosporins, the treatment of last resort for gonorrhoea, has been verified in 36 countries and is a growing problem. Surveillance is of poor quality in countries with high disease rates, where there is also a lack of reliable resistance data for gonorrhoea, and where the extent of spread of resistant gonococci may be high.

Health and economic burden due to ABR

Evidence related to the health and economic burden due to ABR in infections caused by *E. coli*, *K. pneumoniae* and MRSA was examined through systematic reviews of the scientific literature. Patients with infections caused by bacteria resistant to a specific antibacterial drug generally have an increased risk of worse clinical outcomes and death, and consume more health-care resources, than patients infected with the same bacteria not demonstrating the resistance pattern in question. Available data are insufficient to estimate the wider societal impact and economic implications when effective treatment for an infection is completely lost as a result of resistance to all available drugs.

AMR in disease-specific programmes

Tuberculosis

Globally, 3.6% of new TB cases and 20.2% of previously treated cases are estimated to have multidrug-resistant TB (MDR-TB), with much higher rates in Eastern Europe and central Asia. Despite recent progress in the detection and treatment of MDR-TB, the 84 000 cases of

MDR-TB notified to WHO in 2012 represented only about 21% of the MDR-TB cases estimated to have emerged in the world that year. Among MDR-TB patients who started treatment in 2010, only 48% (range 46%–56% across WHO regions) were cured after completion of treatment (with 25% lost to follow-up). The treatment success rate was lower among extensively drug-resistant (XDR-TB) cases.

Malaria

Surveillance of antimalarial drug efficacy is critical for the early detection of antimalarial drug resistance, because resistance cannot be detected with routine laboratory procedures. Foci of either suspected or confirmed artemisinin resistance have been identified in Cambodia, Myanmar, Thailand and Viet Nam. Further spread of artemisinin-resistant strains, or the independent emergence of artemisinin resistance in other regions, could jeopardize important recent gains in malaria control.

HIV

HIV drug resistance is strongly associated with failure to achieve suppression of viral replication and thus with increased risk for disease progression. Data collected between 2004 and 2010 in low- and middle-income countries showed increasing levels of transmitted anti-HIV drug resistance among those starting antiretroviral treatment (ART). Available data suggest that 10%–17% of patients without prior ART in Australia, Europe, Japan and the United States of America (USA) are infected with virus resistant to at least one antiretroviral drug.

Influenza

Over the past 10 years, antiviral drugs have become important tools for treatment of epidemic and pandemic influenza, and several countries have developed national guidance on their use and have stockpiled the drugs for pandemic preparedness.

However, widespread resistance to adamantanes in currently circulating A(H1N1) and A(H3N2) viruses have left neuraminidase inhibitors as the antiviral agents recommended for influenza prevention and treatment. Although the frequency of oseltamivir resistance in currently circulating A(H1N1)pdm09 viruses is low (1%–2%), the emergence and rapid global spread in 2007/2008 of oseltamivir resistance in the former seasonal A(H1N1) viruses has increased the need for global antiviral resistance surveillance.

AMR in other related areas

Antibacterial resistance in food-producing animals and the food chain

Major gaps exist in surveillance and data sharing related to the emergence of ABR in foodborne bacteria and its potential impact on both animal and human health. Surveillance is hampered by insufficient implementation of harmonized global standards. The multisectoral approach needed to contain ABR includes improved integrated surveillance of ABR in bacteria carried by food-producing animals and in the food chain, and prompt sharing of data. Integrated surveillance systems would enable comparison of data from food-producing animals, food products and humans.

Resistance in systemic candidiasis

Systemic candidiasis is a common fungal infection worldwide and associated with high rates of morbidity and mortality in certain groups of patients. Although it is known that antifungal resistance imposes a substantial burden on health-care systems in industrialized countries, the global burden of antifungal-resistant *Candida* is unknown. Resistance to fluconazole, a common antifungal drug, varies widely by country and species. Resistance to the newest class of antifungal agents, the echinocandins, is already emerging in some countries.

Next steps

This report shows major gaps in ABR surveillance, and the urgent need to strengthen collaboration on global AMR surveillance. WHO will therefore facilitate:

- development of tools and standards for harmonized surveillance of ABR in humans, and for integrating that surveillance with surveillance of ABR in food-producing animals and the food chain;
- elaboration of strategies for population-based surveillance of AMR and its health and economic impact; and
- collaboration between AMR surveillance networks and centres to create or strengthen coordinated regional and global surveillance.

AMR is a global health security threat that requires concerted cross-sectional action by governments and society as a whole. Surveillance that generates reliable data is the essential basis of sound global strategies and public health actions to contain AMR, and is urgently needed around the world.



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