Perspectives

Antimicrobial resistance in the WHO African region: current status and roadmap for action

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ABSTRACT

The high burden of communicable diseases in African countries engenders extensive antimicrobial use and subsequent resistance with substantial health, financial and societal implications. A desktop analysis to ascertain whether countries in the WHO African region have implemented the WHO Policy Package to combat antimicrobial resistance (AMR) revealed that just two countries (4.3%) have national AMR plans in place, 14.9% (7) have overarching national infection prevention and control (IPC) policies, 93.6% (44) have essential medicines lists and 91.5% (43) have national medicines policies and treatment guidelines intimating rational use. None currently have representative national surveillance systems nor do any incentivize research and development into new medicines and diagnostics. A regional situational analysis to identify scalable good practices within African, resource-constrained country contexts under the auspices of WHO-AFRO is a necessary initial step towards the development of national and regional action plans in concert with incremental progress towards achieving the objectives of the policy package and global action plan. While it is clearly the responsibility of governments to develop, resource and implement plans, regular reporting to and/or monitoring and evaluation by an overarching body such as WHO-AFRO will ensure persistent incremental progress within continuous quality and accountability improvement paradigms.

Keywords antibiotic resistance, essential medicines, infection control, rational medicines use, surveillance, WHO global action plan, WHO policy package

Antimicrobial resistance—a global perspective

The escalating antimicrobial resistance (AMR) pandemic is a global public health threat with extensive health, economic and societal implications. Resistance emerges because of selection pressure from rational and indiscriminate antimicrobial use in human health as well as in the veterinary, agriculture and environmental sectors. Infections caused by resistant bacteria result in longer duration of illness, higher mortality rates and increased costs associated with alternative treatment. AMR further constrains procedures that rely on antimicrobial prophylaxis,[1,2] and AMR is recognized as a threat to the world economy.[3]

The 'Antimicrobial Resistance Global Report on Surveillance' by the World Health Organization (WHO) showed high resistance rates in bacterial pathogens frequently implicated in common hospital, community and food-chain-related infections in all WHO regions. Five out of six (5/6) WHO regions reported >50% resistance to third-generation cephalosporins and fluoroquinolones in *Escherichia coli*, 6/6 and 2/6 regions reported >50% resistance to third-generation cephalosporins and carbapenems, respectively, in *Klebsiella pneumoniae*, while 5/6 regions reported >50% resistance to methicillin in *Staphylococcus aureus* as examples of common causative bacteria in hospitals and the community. All six WHO regions further reported >25% resistance to penicillin in *Streptococcus pneumoniae*, 3/6 regions reported >25% resistance to fluoroquinolones and third-generation cephalosporins in non-typhoidal Salmonella and *Neisseria gonorrhea*, respectively, and 2/6 regions reported >25% resistance to fluoroquinolones in *Shigella spp.* as examples of common causative bacteria in largely community settings.[2] Antibiotic resistance (ABR) is thus a global phenomenon.

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Infectious diseases and AMR in the WHO African region

Communicable diseases remain the leading cause of death in African countries, responsible for the majority of years of life lost as well as the vast majority of deaths of children under 5 years old. The level of poverty as well as the risk factors for communicable diseases in the WHO African region are significantly higher than in other WHO regions, correlating well with the number of reported cases of selected infectious diseases.[4]

The high burden of communicable diseases and especially the HIV and AIDS burden points to a scenario of extensive antimicrobial use and subsequent resistance as shown in the WHO's global report on the surveillance of AMR[2] as well as a systematic review of AMR among clinically relevant bacterial isolates in sub-Saharan Africa.[5] Combining published data and data submitted by countries, resistance rates ranged from 0–87% to 0–98% to third-generation cephalosporins and fluoroquinolones in *E. coli,* respectively, 8–77% to 0–4% to third-generation cephalosporins and carbapenems in *K. pneumoniae,* respectively, 0–100% to methicillin in *S. aureus,* 1–100% to penicillin in *S. pneumoniae*, 0–35% to fluoroquinolones in non-typhoidal Salmonella, 0–9% to fluoroquinolones in *Shigella spp.*, and 0–12% to third-generation cephalosporins in *N. gonorrhea.*[2] The systematic review by Leopold *et al.*[5] over the period 1990–2013 similarly evidenced high prevalence of ABR in clinical bacterial isolates to commonly used antibiotics. Resistance to chloramphenicol and third-generation cephalosporins in Enterobacteriaceae from patients with febrile illness showed a median prevalence range of 31–94.2% and 0–46.5%, respectively. *Salmonella enterica* Typhi showed a median resistance prevalence range of 15.4–43.2% against naladixic acid while ABR in Gram-positive isolates or isolates implicated in respiratory tract infection, meningitis, urinary tract infections or nosocomial infections intimated a high prevalence of resistance to chloramphenicol, trimethoprim/sulphamethoxazole and tetracyclines.[5]

Despite limitations such as data availability from a limited number of countries and settings, the scarcity of information from central or southern Africa, the exclusion of South Africa in the case of the systematic review, the predominance of information from east sub-Saharan Africa, minimal surveillance-based information, limited laboratory capacity to monitor ABR, the scarcity of quality-assured data and biases related to hospital-based, urban settings and isolates from febrile patients, the Africa region clearly carries a substantial ABR burden,[2,5] albeit an underestimated one as the nature, extent and sequelae of ABR are not quantified.

Implementation of the WHO policy package to combat AMR in the WHO African region

Despite a series of World Health Assembly (WHA) Resolutions on AMR since 1998, the 2001 WHO Global Strategy for the Containment of AMR and the 2005 WHA resolution calling for rational use of antimicrobial agents by providers and consumers,[6] political will began to visibly emerge, predominantly in the developed world, only after the 2011 World Health Day campaign 'Combat drug resistance—no action today, no cure tomorrow',[7] when the WHO launched the 6-point AMR policy package to combat AMR which essentially reframed the crucial actions to be taken by governments to engender change among all stakeholders.[6]

A desktop analysis was conducted to ascertain whether countries in the WHO African region had implemented one or more of the aspects contained in the WHO Policy Package to Combat AMR. Information in Table 1 was sourced from one or more of the WHO Essential Medicines and Health Products Information Portal, the WHO Essential Medicines Selection website, the WHO Drug Resistance website, the WHO Medicines Pharmaceutical Sector Country Profiles Data and Reports website, the Network for Medicines and Development (ReMeD) website, the World Bank website, country government, specifically Ministry of Health websites as well as Google using the following search terms per country: AMR, essential medicines, standard treatment guidelines, national drug formulary, national drug policy, national drug regulatory authority, surveillance, infection control policy, veterinary use of antibiotics and drug development. Any document that made mention of any of these was reviewed and relevant information extracted as appropriate. The existence of an essential medicines list together with a national medicine policy served as a proxy for 'access to quality essential medicines' while the existence of standard treatment guidelines together with a national medicine policy served as a proxy for 'rational medicine use'.

Table 1 shows the extent to which 47 African countries have implemented the WHO Policy Package to Combat AMR (Individual country analyses may be found in the Supplementary data).

Two countries (4.3%) have national AMR plans in place and 14.9% (7) have overarching national infection prevention control (IPC) policies. Some 93.6% (44) of countries have essential medicines lists and 91.5% (43) have national medicines policies and treatment guidelines intimating rational use. None currently have national surveillance systems that routinely generate representative, robust data on antimicrobial use and resistance although several countries have implemented pilot surveillance projects and South Africa has a national

Table 1 Implementation status of WHO policy package to combat AMR in the WHO African region

Country	National AMR plan	Surveillance on antimicrobial use and resistance	Access to quality essential medicines	Rational medicine use	IPC	Innovation, research and development
Total (47)	2	0	44	43	7	0
%	4.3	0.0	93.6	91.5	14.9	0.0

laboratory-based surveillance programme on selected bacterial and fungal pathogens (see Supplementary data). None of the countries incentivize research and development into new medicines and tools. These results resonate with the WHO worldwide country situation analysis of response to AMR in that of the 8 (17%) countries that responded from the WHO African region, one had a national plan in place while two evidenced national coordination, national focal points and national policies. Six of the eight respondents conducted surveillance in bacteria in general while six, five, four and one countries further conducted surveillance in tuberculosis, HIV, malaria and influenza, respectively. Seven countries had essential medicines lists and 4 countries evidenced IPC programmes.[8]

The role of members states

That governments of member states are wholly responsible for designing, resourcing and implementing comprehensive national AMR polices and strategic plans using the One Health approach is not negotiable. It is imperative that governments coordinate and engage all stakeholders in the development, implementation, monitoring and evaluation of the national AMR strategy/plan, including but not limited to relevant Ministries and institutions responsible for human, animal and the environmental health in both the public and private health sectors, health professional organizations and associations, research councils and funders, universities, civil society, patient advocacy groups, and national and international non-governmental organizations.

The WHO Consultative Experts' Meeting on Combating Antimicrobial Resistance in the African Region in May 2015 showcased good practice in several diverse AMR-related aspects in different countries. South Africa, for example, has published its AMR National Strategy Framework 2014–24 which provides 'a structure for managing AMR to limit further increases in resistant microbial infections and improve patient outcomes' via four strategic objectives viz., (i) establish national and health establishment governance structures to strengthen, coordinate and institutionalize interdisciplinary AMR efforts, (ii) optimize surveillance and early detection of AMR and enable reporting of resistance trends at local,

regional and national levels to optimize empiric and targeted antibiotic choice, (iii) enhance infection prevention and control to contain the spread of resistant microbes to patients in healthcare settings, focusing on hand hygiene and patient isolation (community measures include preventing infection through vaccination programmes and improvements in water and sanitation), and (iv) implement antimicrobial stewardship to promote appropriate use of antimicrobials in human and animal health. Health system strengthening is acknowledged as central to the success of the strategy, and the interventions are underpinned by education (of health professionals within undergraduate and postgraduate curricula as well as via continuous professional education courses), public awareness and a sustained multi-pronged communication and information campaign. Oversight and governance are mooted to ensure that the strategy is implemented in all relevant sectors.[9]

Ghana's AMR Policy is awaiting Cabinet approval and is based on a situational analysis which included the current situation on antibiotic use and resistance in Ghana, rational antibiotic use, hospital infection prevention and control, laboratory diagnostics and protocol requirements, national surveillance systems for antibiotics, antibiotic manufacturing, distribution and use, regulation and enforcement, use in veterinary practice and agriculture, information management and regional issues (http://ghndp.org/antimicrobialresistance/images/pdfs/report_gh_react_amr_ttt_launch.pdf). There are thus African examples that can be shared and adapted by other African countries.

Acknowledging the urgent need for action, member states are required to develop comprehensive national action plans while simultaneously implementing existing evidence-based AMR prevention and containment interventions, the latter as incremental activities in response to the Global Action Plan (GAP) as suggested in Table 2, informed, in part, by the proceedings of the Expert Consultation of May 2015.

The role of WHO-AFRO

It is incumbent upon WHO-AFRO to assume the leadership role of monitoring, evaluating and reporting on the progress of member states towards implementation of the WHO Policy Package and the GAP to combat AMR. In recognition

Table 2 Incremental progress towards the WHO policy package and global action plan

Global action plan (GAP)[a]	Policy package[b]	Incremental progress			Potential regional partners
All member states are urged to have in place national action plans on AMR aligned with the GAP within 2 years of the endorsement of the GAP by the WHA	1. Commit to a comprehensive, financed national plan with accountability and civil society engagement	Establish national steering committee	Undertake situational analysis and priority setting on AMR	Develop plan with objectives, targets, indicators responsible persons/institutions and timeframes	WHO Regional Office for Africa Food and Agriculture Organization of the United Nations (FAO) Regional Office for Africa World Organization for Animal Health (OIE) Regional Representation in Africa Foreign Policy and Global Health Initiative Group of Nations[c]
Objective 1: Improve awareness and understanding of AMR through effective communication, education and training	Integrated into policy recommendations 1, 4 and 5 detailed above and below.	Include AMR in school, health professional and veterinarian curricula	Institute mandatory continuous professional development (CPD) on AMR and/or licensure for the prescription and dispensing of antimicrobials	Institute multimedia campaigns with consistent, sustained messages on AMR	African Federation of Public Health Associations
Objective 2: Strengthen the knowledge and evidence base through surveillance and research	2. Strengthen surveillance and laboratory capacity.	Set up/optimize one or more national reference laboratories with standard operating procedures (SoPs) in place. Develop or adapt standard methodology for the collection of antimicrobial consumption in health facilities	Reference laboratories undertake active sentinel surveillance and participate in external quality assurance. Ascertain antimicrobial sales and consumption in human health in daily-defined doses/1000 patient days/population	Reference laboratories undertake active integrated surveillance, generating electronic data that can be shared nationally and globally. Ascertain antimicrobial consumption in agriculture using the population correction unit in addition to use in humans	African Society for Laboratory Medicine East African Public Health Laboratory Network Ecumenical Pharmaceutical Network (EPN) WHO Collaborating Centre for HIV/AIDS, Tropical Diseases Research, Polio Immunization, Viral Hemorrhagic Fevers and Anti-Microbial Resistance (WHO-NET). Kenya Medical Research Institute (KEMRI) Proposed African Centers for Disease Control and Prevention

Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures	5. Enhance infection prevention and control (IPC)	Develop/enhance, implement and monitor SoPs related to infection prevention and control in health facilities	Additionally develop/enhance, implement and monitor SoPs related to infection prevention and control within communities	Additionally develop/enhance, implement and monitor SoPs related to infection prevention and control in animal health and agricultural practices	Infection Control Africa Network
Objective 4: Optimize the use of antimicrobial medicines in human and animal health	3. Ensure uninterrupted access to essential medicines of assured quality. 4. Regulate and promote rational use of medicines including in animal husbandry and ensure proper patient care	Implement surveillance-informed and/or evidence-based treatment guidelines/algorithms and associated essential medicines for infections in human and (food) animal health	Institute surveillance-informed AMR stewardship programmes in human and animal health	Set up and/or empower Drug Regulatory Authorities to regulate the registration, prescription, dispensing, use and quality assurance of antimicrobials	African Medicines Regulatory Harmonization Programme EPN Proposed African Medicines Agency
Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries and increase investment in new medicines diagnostic tools, vaccines and other interventions	6. Foster innovations and research and development for new tools	Fund/leverage funding for basic research on the nature and extent of AMR	Participate in south–south and north–south consortia conducting research on AMR, including new antimicrobial medicines and diagnostic agents	Investigate the antimicrobial potential of traditional medicines	Africa Regional Headquarters for Drugs for Neglected Diseases Initiative (DNDi) Africa Network for Drugs and Diagnostics Innovation (ANDI) Federation of African Manufacturers Association African Development Bank Academia

[a]http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_20-en.pdf?ua=1

[b]http://www.who.int/world-health-day/2011/policybriefs/en/

[c]Brazil, France, Indonesia, Norway, Senegal, South Africa and Thailand.

of the fact that African countries are in different stages of readiness to address AMR, WHO-AFRO should in the first instance commission a regional situational analysis to identify scalable good practices within African, resource-constrained country contexts as an initial step towards the development of national and regional action plans within African health systems fraught with competing imperatives.

WHO-AFRO may adapt and build on the lines of enquiry contained in the situational analysis conducted by the European Centre for Disease Prevention and Control in its country missions on AMR[10] such that the situational analysis in the WHO-AFRO region speaks comprehensively to the GAP. This must however occur in concert with incremental progress towards meeting the objectives of the GAP by individual member states as stated above.

WHO-AFRO can further assist by (i) harnessing the capacities and networks of cognate regional associations and organizations such as the NEPAD Agency's African Medicines Regulatory Harmonization Programme, African Medicines Agency, African Federation of Public Health Associations, the Ecumenical Pharmaceutical Network, Infection Control Africa Network and the African Society of Laboratory Medicine, (ii) strengthening the implementation of the Regional Integrated Disease Surveillance and Response Strategy, (iii) facilitating country adaption of the Guide for Establishing Laboratory-Based Surveillance for Antimicrobial Resistance, (iv) promoting responsible use of antimicrobials and (v) facilitating the adaptation of existing good practices on AMR interventions from member states and other WHO regions to the different African country and health system contexts.

While the WHO has no jurisdiction over member states and can merely facilitate and support the implementation of WHA resolutions, it is able to steer progress by creating an environment of healthy competition between member states by the publication of league tables. If the incremental progress is based on a point system, member states with the highest points or greatest change in points should be commended and showcased as exemplars.

The way forward

Addressing AMR necessitates strong political will and sustained human, infrastructural and operational resources to comprehensively understand the nature and extent of AMR and its real-time evolution to inform and update action plans for prevention and containment within national health systems fraught with competing imperatives.

AMR regional and national action plans require co-ordinated, multi-pronged, multi-stakeholder, multidisciplinary partnerships between public and private sectors, governments and multinational pharmaceutical industry, non-profit organizations and civil society, and healthcare professionals, communities and patients, underpinned by unequivocal national, regional and international policy frameworks that suspend sectoral interests for public good.

WHO-AFRO is well placed to establish multidisciplinary and multi-sectorial regional platforms for policy discourse and sharing good practice on the management of AMR within and across African countries while monitoring and evaluating incremental progress towards the objectives of the GAP within continuous quality and accountability improvement paradigms.

Supplementary data

Supplementary data are available at the *Journal of Public Health* online.

Conflict of interest statement

S.Y.E. is a member of the Global Respiratory Infection Partnership sponsored by Reckitt and Benckiser.

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